Ibero-American Chapter DOHaD

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6th International Symposium on Metabolic Programming and Microbiome

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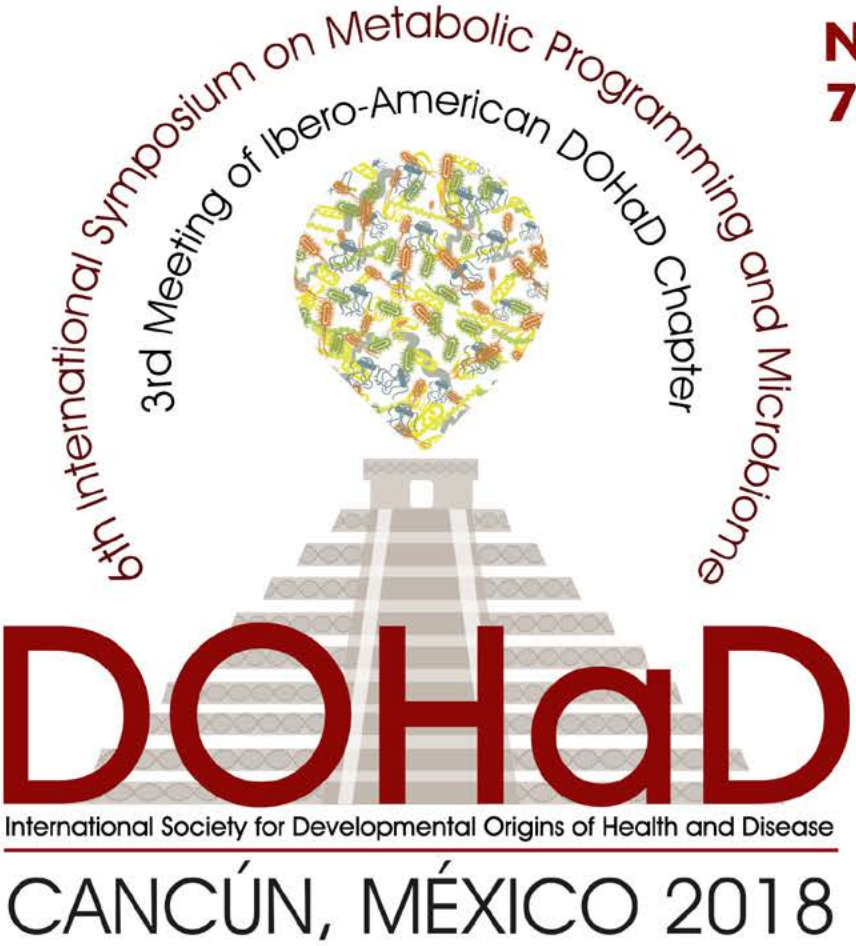

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Book of Abstracts

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B100044
Basic Science
Microbiome

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Fecal microbiota transplantation during lactation promotes protection of pancreatic islet function in obese female rats

Intestinal microbiota is involved in many physiological processes. Recently, it has been implied that the microbiota is involved in obesity onset. The first contact happens during early life but the effects of microbiota in metabolic programming at adulthood are still not understood. The aim of this work was to evaluate the transplantation of fecal microbiota during lactation to female offspring rats from lean and obese mothers.

NL and SL males and females (parents), from different litters, were mated, NL male vs NL female; SL male vs SL female. At birth, the litter was standardized in the 3rd day of life to NL or SL. From the 10th until the 25th day of life the offspring received gavage of a solution containing the diluted feces of the opposite dam. Four experimental groups were created: normal litter offspring saline (NLS), normal litter offspring fecal microbiota (NLM), small litter offspring saline (SLS), small litter offspring microbiota (SLM).

Fecal microbiota transplantation caused decreased body weight gain during life and increased fat deposition in SLM animals. Early life obesity caused glucose intolerance in SLS and SLM groups, fecal microbiota transplantation protected against insulin resistance. All groups had increased secretory response of insulin to glucose 5.6 and 8.3 mmol/L; however, fecal microbiota transplantation lowered secretory response to glucose 16.7 mmol/L from NLM and SLM groups. Fecal microbiota transplantation also lead to decreased cholinergic insulinotropic response. NLM animals showed increased adrenergic insulinostatic response, SLM animal

Fecal microbiota transplantation caused protection against pancreatic islet dysfunction caused by obesity in early life.

small litter • programming • fecal microbiota

ORAL | Friday 9th, 12:30-13:30 hrs.

B100044

B100294
Basic Science
Microbiome

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Endogenous Cannabinoids as a Link to Fetal Programming Through Microbiome

Obesity-driven changes in the microbial landscape of pregnancy may represent a basis for epigenetic programming of obesity in offspring. Increase in Lactobacilli spp. has been demonstrated in maternal obesity and dietary modulation of Lactobacilli strains has been reported to restore metabolic balance and attenuate inflammatory responses, hence might be a target for microbiome-related intervention in pregnancy. We extensively described changes in Endogenous cannabinoid system (ECs) in maternal undernutrition and maternal obesity. ECs plays critical role in the gut-host interaction in metabolic disorders. Probiotics, containing Lactobacilli, stimulated ECs in vivo and in vitro. The aim of the study was to evaluate effect of endogenous cannabinoid (Anadamide) on the growth of L. Plantarum –

Materials and methods. L. plantarum (Louis Pasteur institute, Paris, France) was plated on 40 ml of MRS (De Mann, Rogosa, and Sharpe) agar containing a 30 ?M AEA for 24 hours at 37oC, subsequently lawn was transferred to MRS media and exposed to spatula, which was subsequently placed in the continuous-flow culture system. A Nikon D3200 digital camera and timer set to 2.5 minutes was utilized to capture a time-lapsed video for capturing the dynamic phases of growth of L. plantarum biofilm. Biofilm was collected, weighed, flash frozen, and stored at -80oC until further analyses, e.g. RNA seq. Additionally the real time cell analyzer (RTCA) xCELLigence (ACEA Bioscience Inc., San Diego, CA) equipment, based on impedance measurement, was used to monitor the formation of L. biofilm. We further Results. The weight of the AEA modified biofilm was 4.29 ± 0.7 g (n=4) vs control (CTR) 3.42 ±.0.3 g (n=6), p=0.077), with weight of the attached phase 0.56 ± 0.05 g (n=4) (vs. 0.46 ± 0.09g, n=5, p=0.56) and the weight of the detached phase 3.73±0.6 g (n=4) (vs. 3.13 ± 0.24 g (n=4), p=0.19).

AEA stimulates biofilm growth of L. Plantarum in vitro. Considering presence of the fetal ECs deficiency in maternal obesity, these study might provides link between nero-endocrine and microbial milieu as a mechanism of fetal programming.

endocannabinoids • biofilm • lactobacillli

ORAL | Friday 9th, 12:30-13:30 hrs.

B100294

B100307
Basic Science
Microbiome

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Guarana (Paullinia cupana Mart) seed powder induce dysbiosis in obese and lean rats, utilizing ViaComplex software to present dysbiosis in microbiota analy

Gut microbes are affected by diet, and plant polyphenols may have positive effect on gut microbiota. Guarana (Paullinia cupana Mart.) is a non-traditional medicinal plant widely applied worldwide. Guarana yields an alkaloid and polyphenol-rich seed with antimicrobial, antioxidant, and anti-inflammatory properties, where caffeine is the major compound. Microbiota studies often require an holistic approach due to massive data resulting from sequencing analysis. Gene expression also present great amount of data, requiring bioinformatic tools to visualize variations in genetic expression according to pathologies or conditions. Landscape analysis are utilized to better visualize gene expression profiles. ViaComplex offers an useful tool to show gene network and expression.

We utilized a standard diet, who simulate a western diet with high-fat, high-sugar, high-salt content, and a low-fibre content), but does not exhibit food heterogeneity and its efficient in induce obesity. Wistar rats received diet for 30 days before treatments and throughout treatment, in order to induce western diet-associated gut dysbiosis. Guarana, caffeine or saline were administered via gavage daily for 90 days. We evaluated gut microbiota alterations via 16S sequencing in animals treated with Guarana seed powder(GSP), caffeine or saline, in obesity and lean phenotypes. These GSP dose was selected based in the usual dose consumed by the humans, caffeine dose were selected based on GSP caffeine content. GSP was previously characterized, containing Caffeine (34.19 mg/g), Theobromine (0.14 mg/g), Catechin (3.76 mg/g), and Epicatechin (4.05 mg/g). GSP or caffeine were unable to attenuate adiposity obese rats, despite having effects in gut microbiota. GSP and caffeine groups decreased microbial diversity compared to control group in obese and lean rats. Obesogenic diet decreased Bacteroidetes/Firmicutes ratio and Lactobacillus abundance compared to.
The software ViaComplex was adapted to utilize in microbiota or microbiome analysis, utilizing taxon abundance as gene expression and grouped taxons utilizing the network generating software Medusa 3.0. The images resulting from this analysis are visible representations of general dysbiosis, able to be utilized not only for gut microbiota, but also for environmental microbial data. Obesogenic diet induced gut dysbiosis, as observed in landscape graphics. GSP and Caffeine also had an effect in intestinal microbiota, we can observe general gut microbiota alterations in Landscape images. In the present work we utilized classic relative abundance and diversity analysis to represent gut dysbiosis, and also propose Landscape graphical analysis as a efficient tool to visualize microbial enterotypes.

Microbiota • Viacomplex • Obesity

ORAL | Friday 9th 12:30-13:30 hrs.

B100307

B100316
Basic Science
Microbiome

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Exploring Gut Microbiota composition in two Mexican isolated indigenous communities

For many years, the role of the human-gut microbiome remained unknown and ignored. Now it represents one of the most notable lines of study for evolutionary, biological and biomedical sciences. It is known that multiple factors influence gut bacterial composition. Nonetheless, such studies have mainly focused on industrialized urban populations, notably leaving rural or isolated communities less attended. Studying these kind of populations is particularly important because they could inform us about the real influence of modern artificial factors over gut bacterial populations. Therefore, we explore gut bacterial composition in children and adults of two natural isolated indigenous-communities located in a Mexican region called “Montaña Alta de Guerrero”.

Communities Plan de Gatica and Naranjo located in the Montaña Alta de Guerrero, Guerrero were contacted beforehand, providing consent and willingness to participate in the present research. We collected all fecal samples (N=73) from two different indigenous communities, both encompassing 33 children 5 to 11 years old; 19 female adults 23 to 50 years old and 21 male adults 23 to 50 years old. All mothers reported natural mode of delivery, lactancy for at least 2 years and no subject within the sample had consumed meds. DNA was extracted from fecal samples with the DNeasy Blood and Tissue Kit. For sample amplification we used the V4 hypervariable region of the 16S rRNA gene; Bacteria and Archaea 515F/806R universal primers were used. Samples were sent to The Yale Center for Genome Analysis, where they were sequenced using the Illumina MiSeq300 platform. OTU’s were obtained with QIIME version 2.0 using RDP and Greengenes databases. We found evident differences between adult male and female gut-microbiome compositions, as well as more similarity between mothers and their offspring’s microbiota. We also found a visible prevalence of the classes Clostridia.

There is a strong predominance of Clostridia in female adults and children in these isolated communities. It is possible though that this similarity between both groups is due to the existence of a close resemblance between maternal and offspring microbiota. On the other hand male adults present a great abundance of Clostridia but also Bacteroidia; these noticeable sex differences in gut bacterial composition could be influenced by sex hormones, differences in diet between sexes, or even different habits due to social roles. Further analysis of factors involved in such composition differences and their possible consequences to health are essential. Lastly, it seems very important to explore

gut microbiota in a population where bacterial communities aren't exposed to artificial factors and strong modern day where environmental pressures such as antibiotics are not present. It is the first time that a mexican isolated indigenous community gut-microbiota is explored and through these studies we will be able to answer what are the most important modern day factors influencing the human gut microbiota and which bacterial communities are the ones that ar

Gut microbiome • Isolated • Indigenous

ORAL | Friday 9th 12:30-13:30 hrs.

B100433
Basic Science
Microbiome

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Uncaria tomentosa reduces inflammation in gut from obese mice

High fat diet (HFD) can induce gut microbiota diversity changes leading to impair intestinal permeability. As consequence, there is elevation of particle transit such as lipopolysaccharides (LPS) in the circulation. This condition is associated with low grade systemic inflammation and metabolic disorders. The gut barrier constitutes mainly by mucus layer produced by goblet cells and tight junctions of the enterocytes. Both mucus and junctions prevent the passage of bacterial products such as LPS from lumen to internal milieu. The aim of this study was to analyze the effect of the anti-inflammatory herbal extract Uncaria tomentosa (UT) on features of gut inflammation and intestinal barrier of HFD fed mice.

C57BL6 male mice fed with HFD for 10 weeks were treated with Uncaria tomentosa for 5 consecutive days (50 mg/kg). The animals were euthanized and the cecal region of the intestine was removed for histological and immunohistochemical analyzes. The HFD promoted intestinal inflammation, reduction of the goblet cells by 42% and reduction of the claudin tight junction by 37% when compared to control (100%). UT treatment reduced the inflammatory process and increased the tight junction expression by 28%, with no change in the number of the goblet cells.

These data indicate that UT had an anti-inflammatory effect in the HFD induced inflammatory infiltrate in cecal region and reversed the claudin tight junction expression. We considered this herbal extract may contribute to enhance the barrier function of the gut and to reduce the development of metabolic disorders related to obesity.

High-fat-diet • Intestine • Inflammation

Poster | Thursday 8th 10:40-11:40 hrs.

B100433

B10072
Basic Science
Breast milk and early feeding

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Decreased Thermogenesis in Brown Adipose Tissue Contributes to Obesity in Male and Female Rats Programmed by Early Weaning

Epidemiological data have shown that exclusive breastfeeding up to 6 months has been considered protective concerning several metabolic diseases in adult life. In fact, studies have demonstrated that early weaning is a risk factor for obesity. In rats, our group reported the long-term adverse effects of breast milk deprivation at the end of lactation, where adult male rats were programmed for the development of metabolic syndrome. It is known that changes in the brown adipose tissue (BAT) function, impairing its thermogenic capacity, is related to obesity onset. Here we aimed to evaluate the long-term effects of two early weaning models on BAT autonomic nerve activity and thermogenesis biomarkers in obese adult animals.

Experiment was approved by Animal Care and Use Committee. At birth, litters were adjusted to 3 male and 3 female pups. Wistar lactating rats with their pups were separated into: control - dams whose pups ate milk throughout lactation; non-pharmacological early weaning (NPEW) - dams were involved with a bandage interrupting suckling in the last 3 days of lactation; pharmacological early weaning (PEW) - dams were bromocriptine-treated (0.5 mg/twice day/ip) 3 days before standard weaning. Offspring were killed at PN180. For BAT autonomic sympathetic nerve evaluation, the Bio-Amplificator (InsightÃ‚Â®) was used and the mean number of peaks were recorded for 10 min in 10 sec intervals. Thermogenesis biomarkers were measured by Western blot (UCP1, ÃŽÂ²3-AR, TRa1, TRb1, PGC1a, and CPT1a). Male rats of both early weaning models had lower BAT autonomic nervous activity in basal condition, with no change in BAT mass. Concerning the females, only PEW group had lower BAT autonomic nerve activity, while NPEW group had an increase of BAT mass. The NPEW males showed only lower UCP1 content, whereas females of both early weaning groups presented lower ÃŽÂ²3-AR and PGC1a contents.

Thus, early weaning induces lower BAT thermogenic capacity in adult life with sex-related differences, which can contribute to gender diferences in obesity development.

early weaning • obesity • thermogenesis

ORAL | Wednesday 7th 16:40-17:40 hrs.

B10072

B10074
Basic Science
Breast milk and early feeding

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Effects of Early Weaning on Glycemic Homeostasis and Function of Pancreatic Beta Cell in Young and Adult Male Rats

Early weaning has negative impacts on the health and metabolism of the offspring leading to the development of obesity and changes in the glycemic homeostasis. However, few studies have shown on the offspring whether dietary restriction at the end of lactation can lead to dysfunction of pancreatic islets, promoting changes in the mechanisms of insulin secretion and action in the short and long-term.

Wistar lactating rats and their pups were divided in: Control (C n=10), standard weaning at PN21; Non-pharmacological early weaning (NPEW n=9), mothers were wrapped with an adhesive bandage on the last 3 days of lactation; Pharmacological early weaning (PEW n=9), mothers received bromocriptine to inhibit prolactin (1mg/Kg BW/day) on the last 3 days of lactation. One male pup of each litter/group was killed in PN45. Offspring were studied at PN180. Body weight, biochemical parameters and insulin secretion in isolated islets were evaluated. At the end of lactation, NPEW and PEW pups showed lower body weight (vs C). At PN45, NPEW and PEW groups showed an increase of insulin secretion stimulated by 5.6, 11.1 and 16.7 mM of glucose (vs C), with 22.0 and 27.0 mM of glucose, only PEW pups showed higher insulin secretion (vs C). At PN170, PEW animals presented higher area under the curve of oral glucose tolerance test (vs C and NPEW). In PN180, NPEW and PEW animals were normoglycemic and hypoinsulinemic (vs C). Insulin secretion was lower in NPEW group (vs C) in 22.0 and 27.0 mM, while PEW group presented a reduction only in 27.0 mM of glucose (vs C).

For the first time, we demonstrated distinct alterations, on both short and long term, in the insulin secretion of male rats at different ages submitted to early weaning. Thus, we suggest that the increase of insulin secretion in isolated islets stimulated with different glucose concentrations at early life can compensate malnutrition at the end of lactation, and that such changes could lead to the hyposecretion of insulin in these animals in adult life.

early weaning • obesity • type 2 diabetes

Poster | Thursday 8th 10:40-11:40 hrs.

B10074

B10093
Basic Science
Breast milk and early feeding

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Maternal treatment with methylglyoxal during lactation leads to disruption of glycemic homeostasis in offspring early in life

Advanced Glycation End products (AGEs) and it precursors consumption is related to metabolic alterations associated to diabetes, such as Î²-cell dysfunction and insulin resistance. Environmental disturbances in the perinatal life lead offspring to metabolic dysfunction. Thereby, we hypothesized that maternal treatment with methylglyoxal (MG), an AGE precursor, during the suckling phase, may impair offspring glucose homeostasis.

Pregnant Wistar rats were kept in standard conditions until natural delivering. All animals had free access to standard chow and water through all the experimental period. Delivery was considered day 0, in day 1 rats litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups: Control (CO), whose mothers received saline 0,9% by gavage (1mL/kg), and Methylglyoxal (MG), treated daily by gavage with methylglyoxal (60mg/kg). Treatment starts at day 1 after birth and halt at the end of lactation. Offsprings were euthanized by quick decapitation at day 7, 14 and 21. Blood and tissue samples were collected for further analysis. No differences were observed in body weight gain among groups; however, MG offspring showed increased adiposity as evidenced by elevated mass in perigonadal and mesenteric fat pad ($p<0,05$) at day 21. Interestingly, MG pups showed decreased insulin levels at day 14 ($p<0,05$) and 21 ($p<0,0001$). Despite a high tendency to increased glucose levels at day 21 ($p=0,0528$), no statistical difference were observed in this parameter.

The present research shows for the first time that maternal intake of MG during lactation leads to offspring impaired insulin levels and increased adiposity, which may predispose these animals to the development of type 2 diabetes later in life.

Methylglyoxal • Insulin • Lactation

Poster | Wednesday 7th 17:40-18:40 hrs.

B10093

B10100
Basic Science
Breast milk and early feeding

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Parental obesity programs pancreatic islet disfunction in obese female rat offspring

A new prospect to study obesity is that early life insults program metabolic diseases later in life. Obesity is transmitted to the following generation, and females whose were especially important in this transmission, whereas the offspring can be programmed to obesity by parental metabolic health, from both mother and father. The current study tested the influence of parental obesity to program female offspring to metabolic diseases in adulthood.

Wistar rats were mated and the offspring had their litter size adjusted to 9 pups per dam (NL) and 3 pups per dam (SL). Those were mated at 90th days old and the offspring had their litter size adjusted, only female offspring were used, creating four experimental groups: Normal Litter parents with normal litter offspring (NLNL); Normal Litter parents with Small Litter offspring (NLSL); Small Litter parents with Normal Litter offspring (SLNL) and Small Litter Parents with Small Litter offspring (SLSL). Early overfeeding caused increased body weight at 21th and 90th days old. Parental obesity caused increased fat deposition at adulthood in SLNL and SLSL. It also caused decreased total cholesterol and HDL-C levels in SLNL and SLSL groups, leading to increased atherosclerosis risk. SLSL animals had fasting hyperinsulinemia compared with all groups and insulin resistance. Analyzing insulin secretion of isolated pancreatic islets, NLSL and SLNL animals had decreased secretion at 5.6, 8.3 and 16.7 mmol/L of glucose. NLSL animals had increased cholinergic response and decreased M3 antagonist 4-DAMP. All groups had lower adrenergic response compared to isle.

Parental obesity programmed metabolic dysfunction in female rats, associated to lower insulin secretory response to cholinergic and adrenergic agents. We can also suggest that parenteral programming an unbalanced autonomic nervous system activity.

Parental obesity • Insulin • Early nutrition

Poster | Wednesday 7th 17:40-18:40 hrs.

B10100

B10261
Basic Science
Breast milk and early feeding

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Effect of breast milk on dental caries development

Dental caries is a biofilm-sugar dependent disease. The biofilm accumulated on tooth surface, when frequently exposed to fermentable carbohydrates, produces acids that cause tooth demineralization. In the biofilm, Streptococcus mutans, the most cariogenic bacteria, is able to metabolize several carbohydrates including the lactose present in the breast milk. Therefore, it has been questioned if breastfeeding could provoke dental caries. Once breast milk presents high lactose concentration, it could be metabolized in the biofilm, inducing tooth demineralization. However, the relationship between breast milk consumption and dental caries development is controvesial. Therefore, the aim of this study was to evaluate the effect of breast milk on dental caries development.

S. mutans UA159 biofilms were formed on saliva-coated enamel slabs (n:8/group). Biofilms were grown in UYETB medium and exposed 8x/day for 3 min to the treatments: 1) 0.9% NaCl (negative control); 2) Breast milk (BM); 3) 7% Lactose solution (BM active control), and 4) 10% sucrose (positive control). During biofilm formation, the pH of the culture medium was measured 2x/day and stored for calcium concentration analysis. Biofilms were harvested after 120 h, and the percentage of surface hardness loss (%SHL), colony forming units (CFU) and amount of soluble and insoluble extracellular polysaccharides (EPS) were evaluated. Data were analyzed by one-way ANOVA and Tukey test (alpha: 5%). No difference was found between the acidogenicity of the biofilm exposed to breast milk and negative control group. Hence, breast milk metabolization was not able to cause significant mineral loss, being sucrose the carbohydrate that caused the highest demineralization and calcium releasing (1.5 mM). Regarding EPS and CFU counts, sucrose group presented the highest values, and no difference was found when breast milk was compared to the 0.9% NaCl exposure.

Therefore, it is suggested that breast milk metabolization is not able to induce dental caries development.

Human milk • Breastfeeding • Dental caries

Poster | Wednesday 7th 17:40-18:40 hrs.

B10261

B10310
Basic Science
Breast milk and early feeding

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Chronic swimming training is effective to restore hypothalamic expression of leptin and GLP1 receptor in small litter rats

Lactation is an important window of development characterized by changes in the rate of proliferation and differentiation in various organs, including hypothalamic neurons. Important peripheral hormonal signals, such as leptin and glucagon-like peptide 1 (GLP1), modulate the synapse within the hypothalamic nucleus, resulting in effects on food intake and body weight. Rats raised in small litter (SL) during lactation present early postnatal overfeeding, developing lifelong obesity; an event that appears involves changes in the signaling of leptin and GLP1 in the hypothalamus. Physical exercise is an effective tool to avoid obesity. We evaluated the effects of chronic swimming training on the expression of leptin and GLP1 receptor in the hypothalamus of male rats raised in SL.
Female Wistar rats were mated and after birth the number of pups of the litters was adjusted to 9 pups/mother for the normal litters (NL) and 3 pups/mother for small litters (SL); only male was used. At 21 days of lactation the rats were weaned and subdivided into Exercised (E) or Sedentary (S), forming 4 experimental groups: SL-S; SL-E; NL-S and NL-E (n=6 rats). Exercised rats practiced swimming 3 times/week during 30 min; for 8 weeks. At 92 days of life were euthanized, body weight and white adipose depots were weighed. Hypothalamus was isolated and the expression of Lep and GLP1 receptors (Lepr and GLP1r) evaluated by PCR. Data were mean ± SEM. Anova with pos-Tukey test ($p<0.05$). SL-S presented high adipose tissue content (34,8%) compared to NL-S group ($p<0.05$). Swimming training reduced the body weight (9,64% and 18%) and adipose tissue content (46,5% and 40,6%), respectively in the SL-E and NL-E groups in relation to S groups ($p<0.05$). Expression of Lepr and GLP1r in hypothalamus was increased 44-fold and 2-fold respectively in SL-S compared than NL-rats ($p<0.05$). SL-E rats presented a reduction of 72% and 18% respectively in Lepr and GLP1r compared to
Chronic swimming training is able to prevent obesity in SL rats an event that may be related to changes in neural hypothalamic pathways, being effective in normalizing the expression of GLP1r and Lepr in the hypothalamus. These data suggest that chronic and early exercise modifies hypothalamic signaling as an event that may be central to correcting the neuronal changes induced by lactational overnutrition.

lactation • hypothalamus • swimming

Poster | Thursday 8th 10:40-11:40 hrs.

B10310

B110070
Basic Science
Intervention studies

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Different statistical approaches to characterization of adipocyte size in offspring of obese rats: effects of maternal or offspring exercise intervention

Adipocyte size (AS) distribution is central to energy regulation. We evaluated approaches to characterization of AS distribution in Wistar rat offspring (F1) of control (C) and obese (MO) mothers (F0) with and without F0 or F1 exercise. We hypothesize that different AS distribution will be observed depending on the nature of exercise intervention.

Retroperitoneal fat cross-sectional AS was measured in C and MO F1, showing different distribution. F0 (F0ex) or F1 (F1ex) exercise effects on AS were compared in each maternal diet group by mean, median, cumulative distributions, data dispersion and extreme values based on gamma distribution modelling. F1 metabolic parameters: body weight, retroperitoneal fat, adiposity index (AI), serum leptin, triglycerides and insulin resistance index (IRI) were measured. MO AI was higher than C and male MOF1ex AI lower than MO. Median AS was higher in male and female MO vs. C. Male and female MOF0ex and MOF1ex reduced median AS. Lower AS dispersion was observed in CF1ex and MOF1ex males vs. CF0ex and MOF0ex respectively. MO reduced small and increased large adipocyte proportions vs. C; MOF0ex increased small and MOF1ex the proportion of large adipocytes vs. MO. MOF0ex reduced IRI in males and triglycerides in females vs. MO. F1ex reduced male and female leptin. MOF0ex reduced F1 median AS while MOF1ex reduced median AS and data dispersion.

F0 and F1ex have gender specific benefits effects on AS. AS distribution characterization helps explain adipose tissue metabolism changes in different physiological conditions and design efficacious interventions to prevent and/or recuperate adverse developmental programming outcomes. Optimization of exercise regimens is needed in obese women and their obesity prone offspring. This work was supported by Consejo Nacional de Ciencia y Tecnología of Mexico and Newton Fund Research Councils UK and (I000/726/2016 FONCICYT/49/2016).

Adipocyte • Adipose Tissue • Maternal Obesity

ORAL | Thursday 8th 15:00-16:00 hrs.

B110070

B110143
Basic Science
Intervention studies

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Metabolic Programming • State University of Maring, Brasil

Metformin early chronic treatment improves autonomic nervous system and metabolic dysfunctions in offspring programed to obesity

Metformin is an antidiabetic drug used for the treatment of diabetes and metabolic diseases. Autonomic nervous system (ANS) imbalance is associated with metabolic diseases. The aim this study was to test whether metformin could improve ANS activity in obese rats.

Methods and Results: Obesity was induced by neonatal treatment with monosodium L-glutamate (MSG). From twenty-one-day-old to 100-day-old, MSG-rats were treated with metformin 250 mg/kg body weight/day, or saline. Rats were euthanized to biometric and biochemical parameters evaluation. ANS electrical activity was recorded. Metformin normalized the hyper vagal response in MSG-rats. Insulin secretion stimulated by glucose in isolated islets was increased in MSG rats, while, cholinergic response was reduced. Metformin treatment normalized the cholinergic response, which involved mostly the pancreatic beta cell muscarinic receptor type M3mAChR. Protein expression of muscarinic receptors M3mAChR was increased in MSG-obesity rats; while metformin treatment decreased the expression by 25%.

Chronic metformin treatment was effective to normalized ANS activity and alleviating obesity in MSG-rats.

MSG-obese rats • Metformin • Insulin

Poster | Friday 9th 11:10-12:10 hrs.

B110143

B110155
Basic Science
Intervention Studies

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Intervention Studies • Laboratory Of Experimental Physiology, Department Of Physiological Sciences, Health And Biological Sciences Centre, Federal University Of Maranhão, São Luís (Ma), Brazil.

High-protein diet reverts metabolic syndrome caused by post-weaning high-sucrose intake in male rats.

Consumption of added sugars has been considered a worldwide public health concern by its implied association with the epidemic of obesity, type 2 diabetes mellitus and metabolic syndrome (MetS). Dietary manipulation is a primary factor in controlling and preventing obesity and its comorbidities, although much of the approaches have prioritized low-fat and/or low-carbohydrate interventions. On the other hand, current studies have suggested high-protein diets to promote greater weight loss and metabolic outcomes in both human beings and rodents. Thus, this work sought to evaluate the metabolic and body composition changes induced by high-protein diet (HPD, 35% protein) in adult Wistar rats with MetS induced by sucrose-rich diet.

Weaned male Wistar rats were randomized into 2 groups: rats fed a standard chow (CT/CT, 10% sucrose) and rats fed a high-sucrose diet (HSD, 25% sucrose) for a 20-week observational period. Subsequently, HSD-fed animals were randomized into 3 new groups: rats maintained on HSD diet (HS/HS); rats submitted to HSD replacement by standard chow (HS/CT); and those with HSD replaced by HPD (HS/HP), which were followed up for additional 12 weeks period. Post-weaning exposure to HSD led to MetS phenotype at adulthood, herein characterized by central obesity, glucose intolerance, dyslipidaemia and insulin resistance. Only HPD feeding was able to revert weight gain and adipose tissue accumulation, as well as restore adipose tissue lipolytic response to sympathetic stimulus. HPD or withdrawal from HSD promoted very similar metabolic outcomes upon the 12-week nutritional intervention. HS/HP and HS/CT rats showed reduced fasting serum levels of glucose, triacylglycerol and total cholesterol, which were correlated with the improvement of peripheral insulin sensitivity. Both nutritional interventions restored liver morphofunctional patterns, but only HPD restored lipid peroxidation.

Our data showed that 12-week intake of an isocaloric moderately high-protein diet consistently restored high-sucrose-induced obesity in addition to the attenuation of other important metabolic

outcomes, such as improvement of glucolipid homeostasis associated to increased insulin sensitivity and reversal of hepatic steatosis. On the other hand, simple withdrawal from high-sucrose consumption also promoted the abovementioned metabolic outcomes with no impact on body weight. Thus, both nutritional interventions show themselves to be mutually efficient, potentially helping health professionals to make better decisions on how to treat patients with MetS associated or not to overweight/obesity.

Highprotein diet • Highsucrose diet • MetS

ORAL | Thursday 8th 15:00-16:00 hrs.

B110175
Basic Science
Intervention studies

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Intake of Omega-3 Polyunsaturated Fatty Acids during development and the preference for palatable diet in adult life of intrauterine growth restricted rats.

Intrauterine growth restriction (IUGR) is defined when the fetus does not reach the expected size determined by its genetic potential for a certain gestational age. Studies demonstrated that IUGR increases the risk of chronic disorders such as obesity, cardiovascular disease and hypertension. Studies show that the preference for palatable food is programmed in these individuals. Omega-3 Polyunsaturated Fatty Acids favor the metabolism, decrease cardiovascular risk and can modulate the functioning of the mesocorticolimbic dopaminergic system, involved in food preferences towards palatable foods.

IUGR was induced by maternal food restriction (FR group: 50% food restricted diet, starting on day 10 of gestation; Adlib group: Ad libitum diet during pregnancy). At birth, pups were cross-fostered to Adlib dams, generating AdLib/AdLib and FR/AdLib groups (pregnancy/lactation). At postnatal day 21, pups were randomly allocated to receive diets throughout life: high levels of fish oil (a source of EPA and DHA) or low levels of fish oil or standard rat chow (without fish oil). In adulthood, rats were exposed for 7 days to a monitoring computerized system of food consumption (BioDaqÂ®) receiving only their diets (days 1 to 4 - habituation period) and their diets + a palatable diet (days 5 to 7 - food choice test). Over the first 4 days all the groups demonstrated an increase in food consumption, showing that they adapted to the BIODaqÂ® without differences between groups (AdLib p=0.150; FR p=0.155).When analyzing the total consumption of palatable food, there was no interaction between group and diet (p=0.159). Also, there was no group effect (p=0.979), however we found an isolated effect of the diet (p=0.001).

Higher consumption of palatable food was found in rats that received standard chow diet compared to low fish oil and high fish oil diets. The consumption of palatable food was lower in the groups that received fish oil diets compared to standard chow diet, independently of the neonatal group and of the amount of fish oil available in the manufactured diets. It remains to be established which component of the manufactured diets was responsible for the lower consumption of palatable food in comparison to the groups receiving standard rat chow diet.

Omega-3 • Palatable food • Rats

Poster | Wednesday 7th 17:40-18:40 hrs.

B110175

B110192
Basic Science
Intervention studies

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Administration of different nanoparticles with progesterone on reproductive parameters

Progesterone is a steroid hormone widely used in veterinary medicine with the aim of synchronizing the estrous cycle for artificial insemination in females of economic interest. A biocompatible but non-biodegradable intravaginal silicone device is currently used for this purpose and must be removed manually after synchronization. Micropolymers and nanoparticles are an alternative for the encapsulation of progesterone, since they would optimize the process, reducing the handling. This work aimed to identify the effect of the administration of progesterone by two different encapsulating biopolymers. Synchronization of the estrous cycle, sexual receptivity, maternal weight gain during the gestational period, number of pups and weight gain until weaning were analyzed.

Six groups (n = 5-11 animals/group) was administered subcutaneously with a solution containing vegetable oil or progesterone; empty lipidic solid nanoparticles (NLS) or containing 10 ng of progesterone (NLS 10); empty polymethyl methacrylate particles (PMMA) or containing 2.5 ng of progesterone (PMMA 2.5). Control group did not received administration. One- or two-way ANOVA and $p<0.05$ were used to statistical analysis. In estrous cycle analysis, significant main effects were evidenced for treatment ($F_{5, 70} = 122.8$; $p<0.0001$), but no effect of day of estrous cycle control ($F_{3, 42} = 1,383$; $p=0.2610$) or interaction of day of estrous cycle control and treatment ($F_{15, 210} = 1.112$; $p=0.3470$) were detected. Sexual receptivity of females treated with progesterone, NLS 10 and PMMA 2.5 ($F_{5, 25} = 5.532$; $p = 0.015$) was increased as well as the plasma prolactin levels in females receiving PMMA 2.5 ($F_{6, 35} = 3,114$, $p=0,0150$). No difference in body weight gain during pregnancy ($F_{6, 26} = 0,6625$; $p=0,6803$) and in the number of offsprings ($F_{6, 26} = 0,6625$; $p = 0,6803$) and offsprings of mothers treated with PMMA 2.5 or progesterone showed more weight gain ($F_{6, 1}$

These results suggest that subcutaneous administration of PMMA 2.5 and NLS 10 were efficient to induce a synchronism on estrous cycle and could be used as an alternative method to program the artificial insemination. Moreover, the use of nanoparticles as a carrier of progesterone are also interesting since it increased female sexual receptivity. Although the number of offspring was not altered by the progesterone with or without nanoparticles, the increase in weight gain in offspring of these groups could be signalizing a programming and the stimulus of prolactin secretion observed in PMMA 2.5 group can also be associated with an increase in milk intake by breastfeeding.

Nanoparticles • Progesterone • Reproduction

Poster | Thursday 8th 10:40-11:40 hrs.

B110192

B110207
Basic Science
Intervention studies

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Effects of Omega-3 polyunsaturated fatty acids consumption throughout development on metabolic outcomes of intrauterine growth restricted rats

Intrauterine growth restriction (IUGR), a condition observed when fetal growth is less than expected, is related to increased risk of fat deposition and chronic diseases such as cardiovascular disease, hypertension and diabetes in adult life. Populations that consume a diet with Omega?6/Omega?3 polyunsaturated fatty acids (PUFAs) ratio closer to 2/1 have health benefits compared to those that consume a Western diet (n?6/n?3 >15/1), highlighting the role of Omega-3 PUFAs in maintaining body homeostasis and providing protection against chronic diseases. However, it is not known if vulnerable populations such as IUGR individuals could have particular benefits of a higher intake of Omega-3 during development, and this study was design to explore this hypothesis in an animal model.

IUGR was induced by maternal food restriction of 50% (FR), starting on day 10 of gestation; and control dams (Adlib) received an ad libitum diet. At birth, pups were cross-fostered to control dams generating the following groups (pregnancy/lactation): Adlib/Adlib (Control) and FR/Adlib (IUGR). At postnatal day (PND) 21, pups were randomly allocated to receive one of the three diets throughout life: high levels of fish oil (a source of Omega-3) (HFO), low levels of fish oil (LFO) or standard rat chow (SC) (without fish oil). Body weight and food intake were monitored weekly from PND 21 to 60. Abdominal fat was measured in adulthood. GEE and two-way ANOVA were used to analyze the data. There was an interaction between time and neonatal group (Wald=26.9; df=6; p<0.001), and an interaction between time and diet (Wald=212.4; df=12; p<0.001) when analyzing body weight measures over time. When analyzing the calories consumed, an interaction between time, neona-

tal group and diet was observed (Wald=21.4; df=12; p=0.04). There was only an effect of the diet on the % of abdominal fat, rats that consumed SC had higher abdominal fat (SC:1.9±0,06; LFO: 1.3±0.06; HFO: 1.3±0,06).

The results of body weight showed that IUGRs were lighter than Controls throughout life, and rats that received SC were heavier than the other groups after 34 days of life. According to the triple interaction time*neonatal group*diet observed on calories consumed: Control and IUGR rats that received SC ate fewer calories at weaning but exceeded the other groups in adulthood; IUGR rats that received HFO kept eating fewer calories over time; and Control rats exposed to LFO ate more than the other groups at weaning but decelerate the consumption throughout time. Therefore, the results showed that there was no difference between Control and IUGR groups that received diets with low or high levels of fish oil on metabolic outcomes. However, standard chow consumption was associated with increased abdominal fat and body weight independently of the neonatal group. A possible benefit for the IUGR group that consumed high fish oil diet was observed in the caloric consumption, since this group did not accelerate calories' intake throughout life.

Omega-3 PUFAs, IUGR, Metabolism

Poster | Thursday 8th 10:40-11:40 hrs.

B110209
Basic Science
Intervention studies

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(-)-Epicatechin Administration Reduces Adiposity in Male Offspring from Obese Mothers

Obesity is a multifactorial disease characterized by an increase in the number of adipocytes, where genetics factors and poor regulation of energy play an important role in its development. On the other hand, the generation of obesity models and its pharmacological interventions, have allowed us to understand the physiopathological mechanisms of this disease. In this sense, the flavonoid Epicatechin treatment in high-fat diet induced obesity models, decreases the amount of visceral fat and improve metabolic alterations, showing beneficial effects to prevent obesity. However, it is not known if Epicatechin administration induces the same effects in a model of maternal obesity, where epigenetic programming and the predisposition to the development of obesity differ from o.

From weaning (day 21) and throughout pregnancy and lactation female rats ate Control (C â€“ 5% fat) or obesogenic diet (MO â€“ 25% fat). Female rats were mated on day 120. After weaning, offspring ate C diet. At postnatal day 230, sixteen males per group (C and MO) from different litters were randomly selected to be treated with 1 mg/kg of Epicatechin (C+Epi and MO+Epi); twice per day for two weeks. Male offspring from MO group had higher insulin, triglycerides and leptin serum levels and adiposity index in comparison with C. Adipocyte size was increased in MO compared to C. No changes were observed in body weight and cholesterol serum levels. Epicatechin intervention in the MO group (MO+Epi), induced a significant decrease in the amount of visceral fat and in the size of adipose cells, as well as a lower insulin, leptin and triglyceride serum levels and HOMA-IR, when compared with the untreated offspring from MO group. Body weight, glucose and cholesterol remained unchanged. Epicatechin intervention in C group (C+Epi) reduced adipocyte size as compared to C.

Maternal obesity leads to metabolic dysfunction (glucose and lipid metabolism) in the male offspring. Our results show that treatment with Epicatechin in offspring of obese mothers induces a significant decrease in fat mass and the size of the adipose cell, as well as insulin, triglycerides and leptin, in addition to equaling all these parameters in the group MO+Epi to those observed in the C group. It is important to mention that these results are similar to those reported in diet-induced obesity models, which shows that treatment with Epicatechin is equally effective in our obesity model, where genetic programming and predisposition to the development of obesity is different from other models. Further studies will be needed to explore the effect of Epicatechin in this model of obesity to develop predictive and therapeutic tools as well as to find the mechanisms by which Epicatechin manages to revert the obesogenic effects in the offspring of obese mothers.

Epicatechin • Adiposity • Male offspring

Oral |Thursday 8th 15:00-16:00 hrs.

B110209

B110260
Basic Science
Intervention studies

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Resveratrol intervention in obese pregnant rats improves maternal and offspring metabolism

Obesity involving women of reproductive age is increasing dramatically worldwide. Maternal obesity accompanied by a high fat/high sugar diet consumption prior to and throughout pregnancy and lactation programs offspring to develop deficits in reproductive, cognitive, cardiovascular, and metabolic function. Effective health strategies are essential to prevent adverse outcomes in the mother and the offspring. We hypothesized that maternal resveratrol (Res) dietary intervention prior to and throughout pregnancy and lactation in obese mothers would improve maternal and offspring metabolism.

From weaning (day 21) F0 female Wistar rats were randomly assigned to either chow (C – 5% fat) or high-fat diet (MO – 25% fat). One month before mating (day 90) and during pregnancy and lactation, half of the rats per group were treated with 20 mg/kg/day of Res orally (CRes and MORes) and maintained on their respective diets. Offspring (F1) were waned onto C diet. Body weight, total fat, adiposity index, as well as glucose, triglycerides (TG) and serum leptin levels were determined in both F0 (end of lactation) and F1 (postnatal day – PND 130). At the end of lactation body weight, total fat, adiposity index, TG and serum leptin levels were higher in F0 from MO vs C. Res intervention in MO (MORes) reduced body weight, total fat, and adiposity index and improved leptin serum levels vs MO, while TG concentration were not affected. At PND 130, F1 from MO group had higher body weight, fat, adiposity index, TG and serum leptin levels. In F1 females from the MORes dams, total fat was reduced, and body weight and serum TG levels were improved vs MO; while in F1 males TG and serum leptin levels were similar to C. Similar glucose among groups (F0 and F1). CRes

Maternal resveratrol intervention prior to and throughout pregnancy and lactation reduced the unwanted effects of maternal obesity in offspring lipid metabolism in a gender specific manner; lower leptin secretion was observed in males and lower fat accumulation in females. Further studies are needed to determine the mechanisms involved in the sexually dimorphic effects of maternal resveratrol intervention.
This work was supported by the Newton Fund RCUK-CONACyT (Research Councils UK–Consejo Nacional de Ciencia y Tecnología) I000/726/2016 FONCICYT/49/2016.

Maternal obesity • Intervention •Resveratrol

Oral | Thursday 8th 15:00-16:00 hrs.

B110260

B110300
Basic Science
Intervention studies

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Effect of Resveratrol Administration on Maternal and Offspring Health in a Rodent Model of Diet-Induced Obesity in Pregnancy

Accumulating evidence supports the intrauterine environment as a therapeutic target for interventions to reduce the adverse effects of maternal obesity, in particular the risk for childhood obesity and cardio-metabolic disease in later life. The aim of the current study was to determine the effects of resveratrol supplementation during rat pregnancy and lactation on offspring cardiometabolic health in adulthood.

Rats were fed standard or obesogenic diet ad libitum (Ob) from 6 weeks before mating through to the end of lactation at 21d postpartum. At mating, they were further assigned to vehicle or resveratrol (Res) treatment (50 mg/kg/day, gestational day [GD] 0 to GD18). Dams were euthanised at GD16 and at 4, 9 and 18d of lactation and the liver and placenta were collected for analysis. Glucose tolerance was analysed in the offspring at 90d of age. Supplementation with Res did not influence energy intake, glucose homeostasis or weight gain during pregnancy. However, weight loss during lactation in obese dams was diminished with Res (weight change [g] -26.3±6 vs. -10.1±3 g; Ob vs. Ob+Res; $p<0.05$, One-way ANOVA). In addition, Res treatment in obese dams prevented altered expression of PPAR? and SIRT-1 in liver, and CAT1 in the placenta (43.6±7.1 vs. 4.7±1.5, 882.7±179 vs. 234.7±47.2, and 1.6±0.1 vs. 1.1±0.08, relative expression levels, $p<0.05$). Furthermore, Res treatment in control dams was associated with impaired glucose tolerance in female offspring (1199.9±67 vs. 976.3±60 Area Under the Curve for the time-course response to glucose, $p<0.05$).

Supplementation with resveratrol during pregnancy restored indices of lipid metabolism and endogenous antioxidant defence in obese dams. However, resveratrol at 50mg/kg/d may have deleterious effects in pregnant lean subjects, with implications for glucose homeostasis in adult offspring. Further studies are warranted for optimising the dose and timing of resveratrol intervention in obese pregnancy. This work was funded by Nestec Ltd. and Tommy's Charity at King's College London Department of Women and Children's Health.

Obesity • Resveratrol • Metabolic

Oral | Thursday 8th 15:00-16:00 hrs.

B110300

B110355
Basic Science
Intervention studies

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Manipulating the Maternal Gut Microbiome in Obese Pregnancy to Improve Offspring Outcomes

It is now widely recognised that diet and nutrition in pregnancy are modifiable risk factors for the future metabolic health of the offspring. Epidemiological studies are extensively supported by animal models which have been invaluable in providing mechanistic insight into the phenomenon of developmental programming and its role in long- term health and disease. Linked to this phenomenon is the emerging role of the gut microbiome in linking immunity, metabolism and the transgenerational transmission of a healthy or dysmetabolic phenotype. We have investigated the therapeutic potential of polydextrose (PDX) a soluble starch with prebiotic properties, in preventing the dysbiosis observed in obese mice, and the influence on offspring appetite and energy expenditure.

Female mice were fed a control (Con), or obesogenic diet (Ob) or Ob supplemented with 5% PDX (Ob-PDX) 6 weeks before mating and throughout pregnancy and lactation. Offspring were weaned onto control diet. At 6 months, energy intake (EI) and energy expenditure (EE) were measured by indirect calorimetry, and glucose-tolerance-tests were performed. Offspring of control (OffCon) obese (OffOb) and supplemented (OffObPDX) dams were also challenged for 3-weeks with Ob. ObPDX demonstrated significantly improved glucose tolerance (AUC, i.p. GTT) at gestational day 16 (GD16). TNF-? and CSF-1 showed a 4 and 3 –fold decrease respectively in ObPDX dams ($P<0.05$). OffOb showed increased body weight and fat mass at 6 months ($P<0.001$), had decreased brown adipose tissue mass ($P<0.01$) lower EE ($P<0.001$) and impaired glucose metabolism ($P<0.05$) compared with controls. The Ob dietary challenge resulted in greater EI, reduced EE and accelerated weight gain in OffOb versus controls ($P<0.05$) which was prevented in the OffObPDX group. Maternal PDX supplementation increased the percentage of Bacteroides in OffObPDX compared to OffCon (Bac+[%EUB+] OffCon: 6.11 ± 031 versus OffObPDX; 49.38±7.79,

Maternal obesity adversely influences energy balance and risk of obesity in offspring, which is prevented by maternal dietary intervention with Polydextrose. Associated changes in inflammatory markers and gut microbiota composition are implicated. Polydextrose is a low calorie, neutral tasting, conden-

sation polymer of D-glucose, sorbitol, and citric acid, which is water soluble and resistant to digestion in the human small intestinal tract. PDX is partially fermented by endogenous microbiota in the large intestine, leading to physiological and prebiotic effects consistent with its classification as a soluble dietary fibre. Polydextrose supplementation, therefore, in obese and diabetic pregnancy offers the potential to improve the metabolic profile during pregnancy, modify energy balance and reduce the risk of obesity and metabolic syndrome in the offspring. This work was supported by a BBSRC Industrial CASE Studentship (Tate and Lyle) and the Newton Fund RCUK-CONACYT Research Partnerships MR/N029259/1.

Obese • Pregnancy • Prebiotic

Oral | Friday 9th 12:30-13:30 hrs.

B110408
Basic Science
Intervention studies

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Cognitive Deficit, but not Anxiety Behavior, is Present in Middle-Aged Mice With Monosodium L-Glutamate Neonatally Induced Obesity

Neonatal treatment with monosodium L-glutamate (MSG) induces hypothalamic lesions on median eminence, arcuate and ventromedial nuclei. Thus, MSG-treated rodents develop growth hormone (GH) and insulin-like growth factor 1 (IGF-1) deficiency and hyperinsulinemia at young ages, exhibiting early hypoglycemia and absent catch up growth. Therefore, they develop obesity, hyperleptinemia, type II diabetes mellitus and hypertriglyceridemia. Besides, six-month old MSG mice develop cognitive deficit and hyperphosphorylation of tau protein in hippocampus. As hyperinsulinemia and GH deficiency themselves are predisposing conditions to impaired cognition, we hypothesized that MSG mice could present deficit at earlier adult age.

Swiss mice pulps were treated with a 20% solution of MSG (4g/Kg day) or a 9% saline solution (0,1g/10g day) by subcutaneous injection for five intercalated days at the first ten days of life (n=8, for each group). Animals were weighted twice a week. Serum triglycerides, glycemia, TyG Index and Lee Index were assessed each 30 days of life, until 90 days old. Thereafter, Open Field Maze (OFM), Elevated Plus Maze (EPM), Forced Swim (FS) and Morris Maze (MM) were performed with 135-day old mice. Serum triglycerides, glycemia, TyG Index and Lee Index were assessed too. Statistical analysis was performed by Student test t or one-way ANOVA (Newman-Keuls post-test). MSG mice had lower nasoanal length and weight at all ages. 30-day old MSG mice exhibited hypoglycemia and lower serum triglycerides, but greater Lee Index. However, 90-day old MSG mice got hypertriglyceridemia, and 135-day old MSG mice acquired hyperglycemia and insulin resistance, assessed by TyG Index.MSG mice have no anxiety/depressive behavior on EPM, OFM or FS, respectively. On MM, MSG mice had a greater latency to target zone and fewer time in target zone, which is related to cognitive impairment.

MSG mice present early cognitive deficit, which can be associated to GH deficiency and early hyperinsulinemia. As these animals did not demonstrated any anxious behavior, anxiety symptoms could not be appointed as a contributing feature for cognitive impairment, despite the hypercorticosteronemia described for this model. Neither depressive behavior. Further studies are necessary to appoint what factors are more relevant for the disruption and decline of cognition in these mice.

Cognitive deficit • MSG • Obesity

Oral | Thursday 8th 15:00-16:00 hrs.

B110408

B120039
Basic Science
Others

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Ritalin treatment at adolescence programs to overweight and metabolic alterations at adulthood in male rats

Ritalin (methylphenidate) is a psychostimulant used in the treatment of Attention Deficit Hyperactivity Disorder, one of the most common behavioral disorders at adolescence. Methylphenidate inhibits the reuptake of dopamine mainly in the striatal nucleus and prefrontal cortex. Adolescence, as well as pregnancy and lactation, is considered a sensitive period of development, since neural connections, including dopaminergic system, are still being formed in the brain. Therefore, stressful insults in this phase can permanently modulate the development of systems, programming metabolic diseases and behavioral changes in adult life. We evaluated the effect of Ritalin treatment during adolescence on biometrical parameters, glucose metabolism and anxiety of offspring adult ma

From weaning, Wistar male rats received Ritalin by gavage (Rit; 1 mg/kg/day) for 30 days, whereas control rats received saline (Sal; NaCl 0.9%) in the same volume. From 51 to 110 days-old both groups were untreated. At 51 and 110 days-old the experimental procedures were performed. During treatment, Rit animals presented 12% of reduction in food intake ($P<0.01$), however there was no difference in body weight. At 51 days-old fat tissue stores were equal between groups and fasting insulinemia was decreased in 50% ($P<0.05$). Glucose tolerance and insulin sensitivity assessed by ivGTT and Kitt showed no differences between groups. Animals presented ansiogenic-like effect ($P<0.05$) as demonstrated by inhibitory avoidance in the elevated T-maze. After treatment, Rit group showed an increase of 23% in body weight ($P<0.01$) and the final weight was 6% higher. Fat tissue stores were increased by approximately 20% ($P<0.05$) in treated animals. ivGTT showed higher glucose levels in Rit group at 15 ($P<0.05$), 30 ($P<0.05$) and 45 minutes ($P<0.01$) and Rit animals are insulin resistant, as demonstrated in Kitt ($P<0.05$). At 110 days-old there were no difference between gr

Ritalin treatment at adolescence programs male rats to overweight and metabolic alterations; however, no behavioral changes at adulthood.

Ritalin • Anxiety • Overweight

Poster | Thursday 8th 10:40-11:40 hrs.

B120039

B120071
Basic Science
Others

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Male Rat Offspring of Obese Mothers (MO) Exhibit Altered Adipogenic Gene Expression Related to Insulin Resistance in Fat Tissue

Maternal (F0) obesity (MO) is associated with offspring (F1) visceral adipose tissue hypertrophy. However, regulation of adipose tissue expansion and related metabolic outcomes in response to MO is not well understood. We aimed to determine gene expression changes involved in differentiation and maintenance of mature adipocytes in F1 adult male MO.

At postnatal day (PND) 21, female Wistar rats (F0) were weaned to either a control diet (C= 4 kcal/g) or a high energy obesogenic diet (MO= 5 kcal/g). All F0 were mated with control male rats at PND 120. Offspring (F1) of both groups were weaned onto C diet (n=6 litters/group) and named according to their maternal group. At F1 PND 110, one male of each litter was euthanized. Adiposity Index (AI=Total visceral fat weight x 100/ body weight), Insulin Resistance Index (IRI) and serum leptin and triglycerides (TG levels determined. Adipocyte Size (AS) as cross-sectional area in histologic slides and mRNA expression of 84 genes related with regulation of adipogenesis in a qPCR array were determined in retroperitoneal depot samples. Data with $p<0.05$ and a fold change >2, for gene expression, were considered significant. MO led to increased F1 AI, IRI, serum leptin and TG and retroperitoneal adipose tissue hypertrophy. Agt, Fasn, Mapk, Ppara, Retn, Slc2a4, Tcf7l2, Wnt5b expression were significantly decreased.

Maternal obesity predisposes F1 to metabolic problems, increases IRI and hypertrophy of adipose tissue. Decreased expression of genes associated to glucose metabolism in fat tissue, e.g. Slc2a, suggests that insulin resistance in MOF1 is associated to alterations in the adipogenic profile programed by MO. This work was supported by: Consejo Nacional de Ciencia y TecnologÃa, MÃ©xico (CONACyT) and Newton Fund Research Councils, UK (I000/726/2016 FONCICYT/49/2016) and CONACyT- and Agence Nationale de la Recherche, France (ANR- CONACyT 2015-16-273510).

Maternal Obesity • Adipogenesis • Adipose Tissue

Poster | Friday 9th 11:10-12:10 hrs.

B120071

B120088
Basic Science
Others

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Ritalin treatment at adolescence does not exacerbate the effect of fructose consumption in adulthood

Metabolic syndrome is characterized by obesity, dyslipidemia, hyperglycemia and cardiovascular diseases. In addition to sedentary lifestyle, the consumption of hypercaloric diet has been considered as one of the causes for the metabolic syndrome. Fructose consumption increased in the past decade, mainly due to the use of high fructose corn syrup (HFCS). At adolescence, Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common behavioral disorders and Ritalin (methylphenidate) is a psychostimulant used in the treatment. We evaluated whether Ritalin treatment at adolescence can exacerbate the effects of fructose consumption on biometrical parameters and glucose metabolism of adult male rats.

From weaning, male Wistar rats received Ritalin by gavage (Rit; 1 mg/kg/day) for 30 days, whereas control rats received saline (Sal; NaCl 0.9%) in the same volume. From 51 to 80 days-old both groups were untreated. At 81 days-old animals, a batch of control animals received water, another batch received Fructose (10%) and Rit animals received Fructose in the water until 110 days-old. At this age, intravenous glucose tolerance test (ivGTT) was performed and fat tissue stores were removed. Fructose supplementation induced metabolic dysfunction, such as increased fat tissue accumulation and glucose intolerance, compared with Sal-Water group. We observed no difference in final body weight among Sal-Fru and Rit-Fru groups. In the same way, periepididymal, retroperitoneal and mesenteric fat pads presented no difference between Sal-Fru and Rit-Fru animals. Both groups were presented equal glucose tolerance, as showed by ivGTT.

Ritalin treatment at adolescence does not exacerbate the effect of fructose consumption in adulthood.

Ritalin • Fructose • Adolescence

Poster | Thursday 8th 10:40-11:40 hrs.

B120088

B120089
Basic Science
Others

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Moderate physical training develop benefic effect on cardiovascular alterations induced by HFD intake after detraining: metabolic programming on adu

The increase of hypercaloric diets such as high fat and sugar diets, and physical inactivity has a high correlation with increase of metabolic and cardiovascular diseases, even when consumed for a short-term period. Physical training is indicating for prevent or treat the metabolic disease; however, the benefic effect is related to continuity of the training. When physical training is performed on window metabolic programming the preventive effect against changes installations may be prolonged. Thus, the objective this study was test whether moderate physical training, performed three times to week during four weeks on adult life develop long lasting protection on cardiovascular risks induced by high fat diet intake after

90-days-old rats were submitted to moderate physical training, three times a week, during 30 days. Following this period, at 120 days-old, rats received a hypercaloric diet (high fat diet -HFD) or a commercial diet (NFD) for 30 days. Sedentary animals also received the same diets. Body weight and food intake was evaluated weekly. At age 150 days-old, a catheter was implanted in the femoral for blood pressure recordings. After four days, blood pressure recording was performed for posterior analysis of systolic, diastolic, media blood pressure and pulse interval. Beat-to-beat data were analyzed to calculate power spectra of systolic blood pressure and pulse interval. After euthanasia, mesenteric fat store were removed and weight and total blood was stoked for posterior analysis of lipid profile. HFD increased blood pressure, pulse pressure, low frequency blood pressure variability, body weight gain, fat pad stores and induced dyslipidemia. Interestingly, physical training was able to decreased blood pressure, LDL cholesterol and body fat stores in animals feed with HFD.

Physical training effect did not last totally after a training cessation on protection against alterations induced by HFD intake. However we show that, while, even after a period of detraining and HFD

intake, previous trained animals had resistance to develop cardiometabolic alterations, which point for the first time that the benefice of physical training on late adult life may be partially maintained after a four weeks of detraining period

Detraining • Programming • HFD intake

Poster | Thursday 8th 10:40-11:40 hrs.

B120092
Basic Science
Others

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Neonatal Treatment with Methylglioxal Program Offspring of Wistar Rats to Develop Inflammation, Oxidative Stress and Metabolic Dysfunctions at Adulthood

Increased levels of Advanced Glycation End-products (AGEs) in the organism is associated with hyperglycemia, which is due to AGE-induced cell dysfunction. AGEs are formed from by-products of glucose metabolism, of which Methylglyoxal (MG) is the most reactive. During evolution, the organisms developed important system of detoxification of MG, the System of the Glioxalases. Inflammation and oxidative stress reduce the levels of GSH impair this system, increasing even more the endogenous levels of MG. Therefore, our aim was to study the effects of chronic administration of an AGE precursor, MG, on the metabolism and pancreatic islet function of the offspring treated with MG during the two first weeks of lactation.

After birth, the offspring were divided into 3 groups: Control Group (CON, n=20) treated with saline injection (0.9% Kg of BW/day),Methylglyoxal 6mg Group (MG â€“ 6mg, n=20), treated with Methylglyoxal (6mg/Kg of BW/day) and Methylglyoxal 20mg Group (MG â€“ 20mg, n=20), treated with Methylglyoxal (20mg/Kg of BW/day) during the first 15 days of the lactation period. Part of the animals in each group was used for analyses at 21 or 90 days. Was performed ivGTT following euthanasia for tissue collection. The sample of blood and tissues was used for analyses of biometric and biochemistry parameters, lipid profile, oxidative stress and inflammation. Both MG groups show decrease in BW at 21 days-old, and in main fat pads at 90 days old. The liver of MG groups was lighter that CON group at 90 days-old and shows low HDL and high LDL. VLDLc increase only in MGs 21 days-old groups. The MG groups show insulin resistance in both concentration and both ages. At 90 days-old, the MG groups show increase in inflammation by Myeloperoxidase analysis and oxidative stress. All data were analyzed for ANOVA one-way with significance for p<0,05.

The neonatal treatment with Methylglyoxal program Wistar offspring rats to develop metabolic dysfunctions at adulthood with insulin resistance and disbalance in metabolism of liver, kidney and pancreas and adipose tissue. These treatment leads too for significant inflammation and oxidative stress.

Methylglyoxal • Inflammation • Oxidative Stress

Poster| Friday 9th 11:10-12:10 hrs.

B120092

B120106
Basic Science
Others

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Male intersex and feminization in fish induced by exposure to metformin

The occurrence of intersex fish, where male reproductive tissues show evidence of feminization, has been found in freshwater systems around the world, indicating the potential for significant endocrine disruption across species in the ecosystem. Metformin is one of the most widely prescribed antidiabetic drugs in the world. Interactions between insulin signaling and steroidogenesis suggest potential endocrine-disrupting effects of metformin. The aim of this study was to determine whether a chronic exposure to different concentrations of metformin, including to levels found environmentally, would cause detectable endocrine disruption to juveniles Astyanax altiparanae, a small characid fish widely distributed in South America.

Fourty days post-hatch, fishes were divided into 4 tanks of 50 individuals. Three tanks were dosed with metformin at 50 ug/L, 100 ug/L and 10 mg/L and one control tank. After 90 days of exposure, male were euthanized, and the weight and length of each fish were measured. Gonads were fixed and submitted to hystological analisis by light (LM) and scanning electron microscopy (SEM). After exposition period, at which point clear males and females were distinguishable, the sex ratio was assessed. In the control group the sex ratio was significantly similar to the expected according to the chi-square test. However, at concentration of 50 ug and 100 ug a significative prevalence of females was detected. Surprisingly at the concentration of 10 mg/L, based on the observation of secondary sexual characteristics, no male was detected. Metformin-exposed male had occurrence of intersexuality in the two largest concentrations. Analyzes by SEM showed alterations in the external morphology of the gonads and in the production of spermatozoa between the treated fishes and control. Significant differences in weight and lenght for metformin-treated fishes could also be obse

Metformin causes the development of intersex gonads in males and suppression of the late spermatogenesis (stage where mature sperm predominate). The quantity of fish intersex observed was dependent dose. Metformin also reduced the size of treated fish and altered sex ratio (female/male). The present study suggest that metformin acts as an endocrine disruptor. Studies of the effects of metformin in other species, should offer a better understanding of the endocrine of metformin exposure and its effects on survival and reproductive success in the aquatic environment.

Intersex • Fish • Gonads

Poster | Thursday 8th 10:40-11:40 hrs.

B120106

B120111
Basic Science
Others

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Association of SNPs in AD CY5 and CDKAL1 genes with birth weight, neonatal glucose, insulin, and insulin resistance: evidence for the fetal insulin hypothesis

The fetal insulin hypothesis is a proposed mechanism for the developmental origins of adult disease. It suggests that genetic factors regulating fetal insulin secretion and sensitivity could be participating in the association of low birth weight with increased risk of metabolic diseases in later life, as insulin is a growth factor in utero. SNPs in ADCY5 and CDKAL1 genes have been consistently associated with low birth weight, type 2 diabetes, and lower insulin secretion in adults. However, their association with fetal insulin secretion or insulin resistance has not been proven. In the present study, we aimed to evaluate the association of rs11708067 polymorphism in ADCY5 and rs7754840 polymorphism in CDKAL1 with birth weight, neonatal glucose, insulin, C-peptide, and insulin resistance.

A cohort of 218 healthy neonates born at term from normal pregnancies were recruited in Guanajuato. Genotyping for rs11708067 in ADCY5 was performed by RFLPS and for rs7754840 in CDKAL1 by qPCR with TaqMan probe in genomic DNA. Cord blood C-peptide and insulin concentrations were measured by ELISA. Both SNPs were in Hardy-Weinberg equilibrium. Allele frequencies were A(0.7)/G(0.3) for rs11708067 and C(0.33)/G(0.67) for rs7754840. Lower birth weight (p=0.04), cord blood insulin (p=0.02), and C-peptide (p=0.004) concentrations were found in AA and AG compared to GG genotypes for rs11708067 ADCY, suggesting a dominant model. We also found an inverse association of the A allele of rs11718067 with neonatal insulin (p=0.016) and C-peptide (p<0.001), adjusted by maternal and fetal glucose, and pregestational weight. Cord blood insulin and C peptide concentrations positively correlated with birth weight. No differences were found for glucose or HOMA-IR between genotypes. For rs7754840 in CDKAL1, no differences between genotypes were found in birth weight, glucose or HOMA-IR, nor association with insulin or C-peptide concentrations. Our results show for the first time an association of allele A in rs11708067 ADCY5 with neonatal in-

sulin and C peptide, with lower concentrations of both in the AA/AG neonates. We also confirm previous associations with birth weight. This indicates that the genetic influence on lower fetal insulin secretion may be present not only in low birth weight, but also in normal weight neonates. Therefore, an increased genetic risk of later glucose metabolism alterations and T2DM may be already evident at birth. The fact that rs11708067 genotype could be altering both fetal insulin secretion and birth weight supports the fetal insulin hypothesis. It also underlines the interaction between genetic and environmental factors in the developmental origins of adult diseases, especially important in a population with genetic susceptibility to them, such as Mexicans. More studies are needed to identify other SNPs in candidate genes that could be mediating both fetal growth and insulin resistance or secretion. Knowledge of the genetic mechanisms of DOHaD will surely improve our reach in the prevention and diagnosis of metabolic diseases. Supported by CONACYT (CB-2013-222563) and UG-DAIP (1089/2016)

Fetal insulin • ADCY5 SNP • CDKAL1 SNP

Poster | Wednesday 7th 17:40-18:40 hrs.

B120180
Basic Science
Others

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Pubertal protein malnutrition does not reduce skeletal muscle mitochondrial function and mitigates the effects of high-fat diet on weight gain and fat accum

The thrifty phenotype hypothesis states that nutritional restriction in early stages of life is associated with the onset of obesity and insulin resistance later in life. The consumption of high-fat diet (HFD) after protein restriction (PR) is still controversial. PR during gestation and lactation can exacerbate insulin resistance induced by HFD in adult mice. On the other hand, PR during gestation can also prevent weight gain in old mice fed with HFD. The metabolic alterations of protein restrict mice fed with HFD is not fully elucidated yet. Since skeletal muscle accounts for the majority of metabolic rate, we hypothesize that this tissue may have an important role on the phenotype of protein restricted mice fed with HFD. Therefore, we assessed the glucose homeo

Male C57BL/6 mice were fed a control (14% protein-CD) or a protein-restricted (6% protein-RD) diet for 6 weeks. Afterward, mice received an HFD for 8 weeks (CH and RH).CH mice developed glucose intolerance and insulin resistance when compared to CD mice. RH displayed reduced weight gain, fat accumulation and showed no differences in fasting plasma glucose and insulin levels when compared to CH mice. Besides, RH displayed glucose intolerance as well as insulin resistance at the same magnitude as CH mice. Both RD and RH mice displayed increased in EE during dark-cycles (DC) when compared to CH mice. CH mice displayed reduced gastrocnemius citrate synthase (CS), PGC1alpha protein content and reduced levels of tricarboxylic acid cycle intermediates (TCACI) malate and oxaloacetate when compared to CD. RH mice displayed increased protein content of CS and PGC1alpha when compared to CH. In addition, RH mice displayed increased malate and alpha-ketoglutarate levels when compared to CH. RD and CH mice displayed higher levels of gastrocnemius malonyl-CoA when compared to CD. RH mice showed lower levels of malonyl-CoA than RD mice. Finally, CH mice sh

In conclusion, our data show that protein undernourishment after weaning does not potentiate fat accumulation and insulin resistance in adult young mice fed with HFD. This outcome is associated with increased skeletal muscle mitochondrial oxidative capacity and reduced lipids accumulation.

Protein restrict • High-fat diet • Skeletal muscle

Poster | Thursday 8th 10:40-11:40 hrs.

B120180

B120218
Basic Science
Others

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Maternal dietary intake of alpha-Lipoic Acid during pregnancy and lactation in Wistar rats prevents development of metabolic syndrome in the adult offspring

Lipoic acid (LA) is an antioxidant that reaches fetal circulation after maternal oral intake. The anti-obesogenic properties of LA are given by a modification of genes related with metabolism and energy expenditure. On the other hand, the fetal period is characterized by strong changes in gene expression that if altered, can influence the phenotype of the organism in the postnatal life. In a pilot study, we found that maternal intake of LA improved energy expenditure and reduced fat deposition in the Wistar rat offspring. Thus, we hypothesized that maternal intake of LA during the period that the appetite regulatory network is established in the fetal rat, modifies offspring metabolism and prevents metabolic changes induced by administration of a fructose-rich diet duri

Pregnant Wistar rats were fed ad-libitum with standard diet (food) + LA (0.4% wt/wt) from day 14 of gestation to day 20 of lactation (n=4) or food (n=4). At 3 months of age, male offspring born from LA fed rats (L) or controls (Ct) were randomly assigned to be fed ad-libitum, with food + 10% fructose in drinking water (F) or food + tap water (C); resulting in 4 groups: LF, LC, CtF and CtC (n=6/group). Food intake and body weight (BW) were measured twice at week. Animals were euthanized after 30 days for samples collection. The expressions of key genes involved in metabolism were measured through qRT-PCR and levels of hepatic reactive oxygen species (ROS) and blood metabolites through spectrophotometry. Results were analyzed by t-test and significance was set at $p<0.05$. Average daily BW gain, total BW gain, and total fat tissue at necropsy were higher in CtF group followed by CtC, LF and LC groups. There were no differences between groups in Kcal intake per day. mRNA expressions of NPY and AGRP in hypothalamus and PPARd, PPARg, SREBF-1 and FASN in liver, ROS levels in liver and plasmatic levels of glucose and triglycerides were higher in CtF group follo

Several reports have shown that treatment with LA to adult rats is able to prevent development of metabolic syndrome. However, results presented here suggest that maternal LA intake also causes a beneficial effect in the offspring metabolism and even prevents detrimental metabolic effects induced by the continuous intake of fructose. These effects are achieved in the offspring by increasing their energy expenditure, reducing fat tissue deposition, inhibiting the expression of hypothalamic orexigenic neuropeptides and the expression of genes related with fatty acid uptake and synthesis in liver, and preventing the increase of ROS production in liver and glucose and triglycerides levels in blood. In summary, maternal LA intake permanently modifies fetal metabolism in a way that after

born, the adult offspring can be less likely to develop the symptomatology associated with metabolic syndrome, which can be induced by a fructose rich-diet, such as higher BW, increased adipose tissue, hyperglycemia and hypertriglyceridemia. Further investigations will be conducted to determine the mechanism of action of LA in the fetuses.

Antioxidants • Metabolism • Gestation

Poster | Friday 9th 11:10-12:10 hrs.

B120271
Basic Science
Others

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Metabolic Syndrome
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Sucrose-rich Diet Induces Cannabinoid Receptor 1 Down-regulation and Hyperinsulinemia

The endocannabinoid system is present in tissues that regulate the glycemia, like adipose tissue, and muscle, where diets that induce metabolic syndrome (MS) change the Cannabinoid Receptor 1 (CB1) expression. In the pancreatic beta-cell, endocannabinoids are synthesized and released in situ as a result of calcium entry after depolarization and have an autocrine effect on CB1 which is coupled to Gi/0 protein. Upon activation it decreases intracellular cAMP concentration and inhibits voltage-gated calcium channels. This decreases the calcium entry that releases insulin, resulting in glucose intolerance. Pancreatic beta-cell contains a full endocannabinoid system that responds to acute glycemic challenges, however its participation in MS hyperinsulinemia has not been explored.

We used male Wistar rats of 8 weeks age and 250-280 grs divided in a control group and a sucrose-rich diet group (SRD), for 8 weeks. We assessed metabolic syndrome components: hyperinsulinemia by ELISA, hypertrygliceridemia by colorimetric assay, and visceral adiposity by bioimpedance and direct weighting. For determining the presence of CB1 in the pancreatic beta-cell, cell culture was performed followed by immunofluorescence. In control and SRD rats western-blot was used for quantification of CB1 content and immunofluorescence of paraffin-imbedded sections for determination of the cellular type in which it changed. All image analysis was made with ImageJ and statistical analysis with Graphpad Prism6, unpaired t test results are expressed as mean±SEM. CB1 was present in cultured alpha and beta-cells, mean integrated density of 37.91±3.03 a.u. for alpha-cells and 16.57±8.69 for beta-cells $p<0.001$. Whole-islet CB1 content was decreased in SRD rats 3.57±0.52 a.u. vs 0.97±0.28, $p <0.05$. This decrease occurred in pancreatic beta-cells 38349±6415, for control, 17548 ±1704, for SRD, $p<0.05$. This decrease correlated with hyperinsulinemia, 1.42±0.24 for control.

Sucrose-rich diets induce several features of MS, including hyperinsulinemia. Despite the insulin differences between groups no significant plasma glucose difference was found. There are several regulating systems of insulin release, among which endocannabinoid system appears to participate by impeding hyperinsulinemia. Our results show that the SRD resulted in CB1 down-regulation

in pancreatic beta-cells, and this decrease correlates with hyperinsulinemia in the absence of an increased plasma glucose. This suggests that the endocannabinoid system dysregulation that has been reported in other tissues also participates at the pancreatic islet level, allowing for hyperinsulinemia to take place. Clarifying the endocannabinoid system dysregulation in chronic diseases like metabolic syndrome opens the possibility of more accurate therapeutic strategies, like peripherally restricted agonists or tissue-selective activation, that take into account how this system is modified by disease. This work was supported with UNAM-DGAPA-PAPIIT grant IV100116.

Cannabinoid • Beta-cell • Metabolic Sx.

CARTEL | Wednesday 7th 17:40-18:40 hrs.

B120298
Basic Science
Others

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Diets with imbalanced levels of folic acid and vitamin B12 are related to fatty acid profile in mothers and offspring

Folic acid (FA) and vitamin B12 are essential during gestation. It is likely that food fortification and supplementation with FA are raising FA/B12 ratio in pregnant women, disrupting normal metabolism with unsuspected consequences in some cellular processes. Some studies have evaluated the effect of low vitamin B12 diets in pregnant mice on lipid metabolism, founding a lower mRNA expression of CPT-1 (a beta-oxidation marker) and lower DHA levels in male offspring. However, this effect has not been evaluated in mothers and their offspring treated with high FA and low vitamin B12 diets. The aim of this study was to determine the expression of lipid metabolism markers and fatty acid profile in the liver of mothers and offspring mice treated with high FA and low vitamin B12 diets.
Female mice (C57BL/6) were fed with normal FA and B12 diets (CG) or high FA/B12 ratio (TG; FA: 8 mg/kg diet + Vitamin B12: 5 µg/kg diet, Research Diets) before and during pregnancy. Livers were obtained by cesarean (day 19; n=13). Fatty acid profile levels in liver of mothers and offspring was determined by gas chromatography. Total RNA was isolated from livers of mothers and offspring (at day 60) using Trizol (Invitrogen, USA). mRNA expression of PPAR-alpha, CPT-1, ACOX1 and FAS by RT-qPCR. In liver of TG mothers, saturated, monounsaturated and polyunsaturated fatty acid (SFA, MFA, PUFA, p=0.028) were lower, DHA+EPA/linolenic acid ratio was higher (p=0.045) and n6/n3 ratio was lower (p=0.028). In liver of TG female offspring SFA, MFA and PUFA and the n6/n3 ratio were higher (p=0.0026), but the DHA+EPA/linolenic acid was lower (p=0.0009) than GC. No changes were found in liver of GT male offspring. mRNA expression of PPAR- alpha and CPT-1 were significantly higher in TG mothers compared to CG (p=0.031 and 0.0159 respectively). No changes were found in mRNA expression of ACOX1 and FAS. The mRNA expression of these lipid metabolism markers did not change in the female offspring
Liver of mothers fed with high FA and low B12 diets had lower total fatty acid content (SFA, MFA, PUFA) and n6/n3 ratio and higher DHA+EPA/linolenic acid than CG. Also, mRNA expression of PPARa and CPT-1, two enzymes involved in lipid metabolism, was higher suggesting a higher B-oxidation capacity. In offspring liver, despite TG female show higher total fatty acids concentration and lower DHA+EPA/linolenic acid ratio, the mRNA expression of the enzymes did not change, indicating a lower capacity to synthesize long-chain fatty acids by the female offspring liver. We did not determine mRNA expression in liver of male offspring.

High folic acid • Low Vitamin B12 • Lipid metabolism

CARTEL | Friday 9th 11:10-12:10 hrs.

B120298

B120350
Basic Science
Others

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Immunology

Proportion of Intestinal Intraepithelial Lymphocyte (Iiel) Depend on the Genetic and Intestinal Microbiota

Genetic background and gut dysbiosis change the proportion of intestinal intraepithelial lymphocytes in mice

Intestinal intraepithelial lymphocytes (iIELs) represent a cellular defense against enteropathogenic microorganisms. These lymphocytes have regulatory functions and cytolytic activity. In C57BL7/6j mice there is a similar proportion of iIELs expressing TCR?? and TCR??. Interestingly, some iIELs subsets depend on thymic maturation, like TCR??+CD8??, while other subsets are thymus-independent as TCR??+CD8??+ and TCR??+CD8??. On other hand, development and maturation of iIELs is determined by factors like gut microbiota, binding of TCR with its antigen, vitamin D, high-fat diet, and it has been suggested that genetics and dysbiosis could also determine the proportions of iIELs. Our aim was to find out the influence of genetics and dysbiosis on proportion of TCR?? and TCR?? on iIELs.

iIELs were isolated from the small intestine of mice strains C57BL/6, A/J, C57BL/10, CBA, SJL, 129, C3H, DBA, NFS, Balb/cAnN and stained with fluorescent antibodies anti TCR?? and TCR?? and analyzed by flow cytometry. Non infected mice were used as control and dysbiosis was induced by oral S. Typhimurium infection. Similar proportions of TCR and TCR in C57BL/6, A/J CBA and SJL mice strains were found; while a greater proportion of TCR was found in C57BL/10, 129, C3H, DBA and NFS mice strains. Interestingly, the proportion of TCR?? was greater than TCR?? in Balb/cAnN strain. To determine the influence of the microbiota on proportion of TCR?? or TCR??, dysbiosis was induced by oral S. Typhimurium infection in all mice strains. The proportions of iIELs were analyzed 10 days after infection. After infection induced dysbiosis, it is shown an important increase on the proportion of TCR in C57BL/6, C3H and Balb/cAnN strains. Unlike in C57BL/10 and CBA mice strains there was an increase on TCR. Finally A/J, 129, DBA and NFS mice strains did not have significant changes on the proportion of iIELs. SJL mice strain was highly susceptible to infection by S. Typhimurium.

In this work, we have shown that genetics and intestinal microbiota changes play an important role on the proportion of iIEL subsets expressing TCR?? or TCR??. These findings are important, because suggest that an effective local immune response could be depend of these factors. Likewise, it is highly probable that susceptibility or resistance to infection by enteropathogenic microorganisms could be regulated by both genetic factors and gut microbiota.

iIELs • Dysbiosis • Genetics

Poster | Wednesday 7th 17:40-18:40 hrs.

B120350

B120380
Basic Science
Others

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Is ART safe? Effect of In Vitro Fertilisation (IVF) and Embryo Culture Duration on Mouse Development and Postnatal Health

Over the last 30 years, assisted reproductive technologies (ART) have continued to expand as a clinical procedure to overcome infertility and currently account for approximately 3-4% of births in Europe. However, the long-term consequences of ART have yet to be fully defined. Research shows that ART is linked with some adverse perinatal and postnatal outcomes, including an increase in low birth weight and an increased risk of genomic imprinting disorders and altered DNA methylation.Indeed, our own study in mice revealed sustained hypertension throughout adulthood coupled with cardiovascular and metabolic dysfunction induced by preimplantation embryo culture. The impact of prolonged embryo culture is in particular a concern in clinical ART as women move towards childbearing in later life

Experimental groups (8-13 litters each): NM (natural mating, non-superovulated); IV-ET-2Cell (2-cell embryos derived in vivo from superovulated mothers (SOM) and immediately transferred (ET) to recipients; IV-ET-BL (blastocysts derived in vivo from SOM and immediate ET); IVF-ET-2cell (2-cell embryos generated by IVF from SOM, short culture and ET); IVF-ET-BL (blastocysts generated by IVF from SOM, long culture and ET). IVF blastocysts after prolonged culture developed slower and comprised reduced TE and ICM cell numbers compared with in vivo generated blastocysts (n= 50-87 per treatment). IV-ET-2Cell(n=57), IV-ET-BL(n=47), IVF-ET-2Cell(n=75) and IVF-ET-BL(n=42) groups compared with NM controls(n=80), showed increased body weight, increased SBP, impaired GTT and abnormal organ:body weight ratios in both genders, independent of litter size. SBP and ACE for IVF-ET-BL males was increased compared to IV-ET-BL males. SBP for IVF-ET-BL males was increased compared to IVF-ET-2Cell males. However, glucose concentration, AUC and serum insulin in male IVF-ET-BL was reduced compared with IVF-ET-2Cell males, but serum glucose and G:I ratio did not show significant differences.

In conclusion, reproductive treatments affect the development and potential of preimplantation embryos, influencing postnatal development and physiology compared with undisturbed reproduction. In particular, prolonged embryo culture, with normalised SO, IVF and ET, may adversely affect male offspring cardiovascular but improve the metabolic profile compared with short culture.

However, female health is less sensitive. We believe that the current study design is necessary to discriminate between ART factors (such as SO, ET and IVF procedure) and looks into the effect of the duration of culture per se on postnatal health. The study might contribute to new interest in discovering the mechanism that cause these significant postnatal differences. However, further work is being carried out to investigate the effect of IVF and length of culture on liver tissues of offspring and offspring across the five treatment groups. In addition, we will examine the correlation between cardiovascular profile with other postnatal factors such as growth weight and metabolic profile.

Systolic BP • Area Under Curve • Angiotensin CE

Poster | Thursday 8th 10:40-11:40 hrs.

B120380
Basic Science
Others

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Is ART safe? Effect of In Vitro Fertilisation (IVF) and Embryo Culture Duration on Mouse Development and Postnatal Health

Over the last 30 years, assisted reproductive technologies (ART) have continued to expand as a clinical procedure to overcome infertility and currently account for approximately 3-4% of births in Europe. However, the long-term consequences of ART have yet to be fully defined. Research shows that ART is linked with some adverse perinatal and postnatal outcomes, including an increase in low birth weight and an increased risk of genomic imprinting disorders and altered DNA methylation.Indeed, our own study in mice revealed sustained hypertension throughout adulthood coupled with cardiovascular and metabolic dysfunction induced by preimplantation embryo culture. The impact of prolonged embryo culture is in particular a concern in clinical ART as women move towards childbearing in later life

Experimental groups (8-13 litters each): NM (natural mating, non-superovulated); IV-ET-2Cell (2-cell embryos derived in vivo from superovulated mothers (SOM) and immediately transferred (ET) to recipients; IV-ET-BL (blastocysts derived in vivo from SOM and immediate ET); IVF-ET-2cell (2-cell embryos generated by IVF from SOM, short culture and ET); IVF-ET-BL (blastocysts generated by IVF from SOM, long culture and ET). IVF blastocysts after prolonged culture developed slower and comprised reduced TE and ICM cell numbers compared with in vivo generated blastocysts (n= 50-87 per treatment). IV-ET-2Cell(n=57), IV-ET-BL(n=47), IVF-ET-2Cell(n=75) and IVF-ET-BL(n=42) groups compared with NM controls(n=80), showed increased body weight, increased SBP, impaired GTT and abnormal organ:body weight ratios in both genders, independent of litter size. SBP and ACE for IVF-ET-BL males was increased compared to IV-ET-BL males. SBP for IVF-ET-BL males was increased compared to IVF-ET-2Cell males. However, glucose concentration, AUC and serum insulin in male IVF-ET-BL was reduced compared with IVF-ET-2Cell males, but serum glucose and G:I ratio did not show significant differences.

In conclusion, reproductive treatments affect the development and potential of preimplantation embryos, influencing postnatal development and physiology compared with undisturbed reproduction. In particular, prolonged embryo culture, with normalised SO, IVF and ET, may adversely affect male offspring cardiovascular but improve the metabolic profile compared with short culture.

However, female health is less sensitive. We believe that the current study design is necessary to discriminate between ART factors (such as SO, ET and IVF procedure) and looks into the effect of the duration of culture per se on postnatal health. The study might contribute to new interest in discovering the mechanism that cause these significant postnatal differences. However, further work is being carried out to investigate the effect of IVF and length of culture on liver tissues of offspring and offspring across the five treatment groups. In addition, we will examine the correlation between cardiovascular profile with other postnatal factors such as growth weight and metabolic profile.

Systolic BP • Area Under Curve • Angiotensin CE

Poster | Thursday 8th 10:40-11:40 hrs.

B120413
Basic Science
Others

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Neurosciences. Maternal High-Fat Diet Effects on Neurogenesis and Cell Densities in the Cortex and Hippocampus of the Adult Offspring Mouse Brain
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Maternal high-fat diet effects on neurogenesis and cell densities in the cortex and hippocampus of the adult offspring mouse brain

Obesity is a global health problem, and the number of reproductive-age women with obesity continues to increase. Cases of maternal obesity induced by a high-fat diet (HFD) have increased in recent years. Different studies have described that maternal HFD can affect the normal development of several organs, making offspring more susceptible to certain diseases. Animal obese models suggest that a maternal HFD during gestation is a risk factor for developing physiological and behavioural dysfunctions in offspring. We test the hypothesis in mice that maternal HFD during pregnancy changes the structure and cellular organisation of the cortex and modifies neurogenesis in the adult hippocampus.

Female mice were fed different diets from conception: normal fat diet (NFD), HFD throughout gestation and lactation (HFD) or embryonic HFD (Emb-HFD: HFD for 3 days, NFD thereafter). After weaning, the offspring were maintained on NFD. At week 26, 6 male and 6 female brains were collected per group and analysed for new-born neurons (doublecortin DCX), and mature neurons (NeuN) in the dentate gyrus, and astrocytes (S100?) and microglia (Iba1) in the cortex. In the cortex, S100b+ cell density increased in the Emb-HFD group (layer5; $p<0.05$). In the HFD group, the cortex displayed an increase in S100b+ (layer1; $p<0.05$; layer2/3; $p<0.001$; layer4; $p<0.01$; layer5; $p<0.001$ and layer6; $p<0.01$) cell density. We also observed an increase in Iba1+ cell density (layer1; $p<0.001$; layer2/3; p?0.0001; layer4; p?0.0001; layer5; p?0.0001; layer6; $p<0.001$. In the dentate gyrus of the hippocampus, the HFD group presented an increase in newborn neurons (DCX+/NeuN-$p<0.001$) and a decrease in mature neurons (DCX-/NeuN+ $p<0.05$). The HFD group, showed an increase in Iba1+-cells at PND1 ($p<0.01$) and at 26weeks in the Subgranular Zone, and Granule Cell layer ($p<0.05$, and $p<0.01$ respec

Our data showed that the HFD and Emb-HFD groups had a greater density of astrocytes and microglia cells, in different layers of the cortex. Similarly, we observed that the offspring of mothers fed a HFD had a higher density of newborn neurons and a reduced density of mature neurons in the dentate gyrus, indicating that exposure to a maternal HFD can generate changes in adult neurogenesis. Different studies based on maternal obesity have shown that the nutritional environ-

ment influences the maturation of astrocytes and microglia cells. Here, we observe how maternal HFD, in the absence of obesity in both mother and offspring, is capable of inducing changes in cell densities, suggesting that an unhealthy diet is inducing these changes in the offspring brain. In many cases we observed a graded response (NFD<Emb-HFD<HFD) suggesting a very early induction of diet-induced responses, well before any neural differentiation, with exacerbated effects upon continued HFD challenge. This suggests that not only diet during pregnancy is crucial for proper glial cell density and neurogenesis, but also the time of exposure also is critical to determine the size of the effects in

Maternal diet • High-Fat Diet • Neurogenesis

Poster | Wednesday 7th 17:40-18:40 hrs.

B120465
Basic Science
Others

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Post-weaned and long-term exposure to high-sucrose diet induces obesogenic biochemical profile without increased body weight gain in rats

Nutritional insults in early stages of life have been demonstrated to increase the predisposition for late in life development of chronic non-communicable diseases, such as the metabolic syndrome (MS), a worldwide public health concern. Evidence shows that exposure of adult rodents to high concentrations of added sugars leads to several metabolic dysfunctions, mainly obesity, insulin resistance, dyslipidemia and hepatic steatosis, however the effects of such exposure since early stages of life are less described. In this context, this study aims to assess the metabolic outcomes of continuous exposure to high-sucrose diet since weaning until adulthood in rats.

Weaned male Wistar rats were fed a high-sucrose diet (HSD; n = 8; 25% of sucrose) until 120 days of life (adulthood) and compared to age-matched rats fed a standard chow (CTR; n = 8). Body weight, energy intake, fasting serum glucose levels and lipid profile (triglycerides and total cholesterol), visceral and non-visceral fat accumulation, glucose and insulin tolerance as well as insulin resistance (TyG index) were assessed in both groups. Post-weaning exposure to HSD induced a MS phenotype characterized by marked increase of 28% in visceral fat accumulation (periepididymal fat; $p<0.01$) even without relevant body weight gain. HSD animals also presented increased triglycerides levels (~ 200% of elevation; $p<0.001$) and fasting glycemia after 30 and 60 days of follow-up. Total cholesterol levels did not present changes. Finally, HSD animals presented glucose intolerance and insulin resistance.

Our set of data reinforce the metabolic programming concept, which establish that nutritional insults at early stages of life increase the predisposition to late development of MS and others metabolic outcomes. Data herein presented shows that post-weaning and prolonged intake of sucrose leads to MS development, marked by visceral fat pad accumulation, hyperglycemia, hypertriglyceridemia and insulin resistance, however without body weight changes, reinforcing that obesogenic biochemical profile anticipates weight gain and obesity.

Highsucrose diet • Metabolic syndrome • Obesity

Poster | Thursday 8th 10:40-11:40 hrs.

B120465

B120466
Basic Science
Others

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Effects of Metformin Exposure on Adult Fish

The occurrence of intersex fish, where male reproductive tissues show evidence of feminization, has been found in freshwater systems around the world, indicating the potential for significant endocrine disruption across species in the ecosystem. Metformin is one of the most widely prescribed antidiabetic drugs in the world. Interactions between insulin signaling and steroidogenesis suggest potential endocrine-disrupting effects of metformin. The aim of this study was to determine whether a chronic exposure to metformin, in a level found environmentally, would cause detectable endocrine disruption to adults males of Astyanax altiparanae, a small characid fish widely distributed in South America.

Fishes were divided into 2 tanks of 10 individuals. One tank were dosed with metformin at 100 ug/L and one tank control containing only dechlorinated water. After 30 days of exposure, all fishes were euthanized, and their gonads were fixed and submitted to hystological analysis by light microscopy (LM). 40% metformin-exposed male fishes had occurrence of intersexuality against none of the control fishes. Observation of histology slides showed the presence of perinucleolar oocytes (PO) and early vitellogenic occytes (EV) scattered throughout testis. The development of fishes intersex suggests that within adult testicular tissue, relatively undifferentiated gonial stages are permanently present that can be induced to differentiate along a female pathway given a suficient dose of metformin.

Sex differentiation in fish is subject to modification by external factors environmental. The present study suggest that metformin acts as an endocrine disruptor on male adults fishes whose had already reached gonadal differentiation.

Endocrine disrup • Fishes • Gonads

Poster | Thursday 8th 10:40-11:40 hrs.

B120466

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
International Society for Developmental Origins of Health and Disease
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B20018
Basic Science
Maternal nutrition and gestational disorders

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Insulin-like growth factor-I is increased in the adult testis after sub-nutrition during the pre and post-natal periods in rats

In rats, undernutrition during pre and post-natal life decreases in seminiferous tubule diameter and Sertoli cell number in rat testis. Moreover, in adult sheep Sertoli cells, sub-nutrition disrupts claudin, a tight junction protein, and restores immaturity features (Guan et al. 2016). Sertoli cells thus seem to be a major site for the programming consequences of undernutrition on testis function. They produce insulin-like growth factor-I (IGF-I) to regulate many aspects of spermatogenesis, including proliferation, apoptosis, meiosis and differentiation. Given the role of IGF-I in testis function, and its reputation as a biomarker of undernutrition, we tested whether its presence in seminiferous tubules is affected by pre and post natal undernutrition.

Wistar rats (n = 40; 120 days old) were allocated to: Control (standard diet); UNP, (50% of standard diet during pregnancy); UNL, (50% of standard diet during lactation); and UNPL (50% of standard diet during both pregnancy and lactation). After weaning (Day 22), male pups were fed a standard diet until age 160 days, when their testes were collected and fixed in formaldehyde. Paraffin-embedded, hematoxylin-eosin stained, 5µm sections were processed by immunohistochemistry against insulin-like growth factor I (IGF-I;Abcam ab9572; USA). The distribution of IGF-I immunostaining and the area stained were quantified by ImageJ (Version 1.52b 6 May 2018). Treatment effects were assessed by analysis of variance (ANOVA). IGF-I was observed in the cytoplasm of Sertoli cells in seminiferous tubules; it was also observed in spermatogonia and, with lower intensity, in elongated spermatids. Peritubular cells showed weaker immunostaining than Sertoli cells. IGF-I was also localized in interstitial cells, with strong staining in Leydig cell cytoplasm. Compared to the Control, IGF-I immunostaining area was greater in UNPL($P=0.003$) but smaller in UNP ($P<0.0001$).

In Sertoli cells, sub-nutrition affected the immunoexpression of IGF-I, a major growth factor which is thought to act as an autocrine and paracrine regulator of spermatogenesis. As an autocrine regulator, it would operate through Sertoli IGF receptors (Froment et al. 2007). Moreover, depending on the duration of sub-nutrition, IGf-I immunoexpression can be upregulated (throughout pre and post-natal life) or downregulated (during pregnancy) by sub-nutrition. Thus, IGF-I seems to be involved in the programming of the adult testis by pre and early post-natal nutritional history. IGF-I

is involved in the autocrine promotion of Sertoli cell proliferation, differentiation and activity, and is seen as a major factor regulating Sertoli cell number at puberty (Pitetti et al. 2013), a crucial determinant of adult fertility (Monteiro et al. 2014). In addition, IGF-I is thought to regulate germ cell self-renewal (Kuo et al. 2018), proliferation and survival (Borland et al. 1984), and the production of testosterone by Leydig cells (Moore and Morris 1993; Baker et al. 1996), concepts also supported by our observations of IGF-I.

Programming • Testis • Subnutrition

Oral | Wednesday 7th 15:20-16:20 hrs.

B20020
Basic Science
Maternal nutrition and gestational disorders

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Time-Restricted Feeding During Pregnancy Leads to Metabolic Dysfunction in Adult Rat Offspring

Time-restricted feeding (TRF) is one of various forms of intermittent fasting (IF) regimens. It has gained much attention in the media as an alternative form of IF because approximately 20% of individuals cannot adhere to IF form of dietary restriction. However, little is known about the effect of TRF during pregnancy and the impact of this regimen on energy metabolism in adult rat offspring. Therefore, the aim of the present study was to investigate the effects of TRF during pregnancy and to assess the long-term metabolic status of both males and females offspring from birth to adulthood.

Pregnant Wistar rats were fed a chow diet and subjected to ad libitum (AD) or fed during the light phase (LP) or fed during the dark phase (DP). Glucose, lipid metabolism and insulin secretion were studied in adult males and females offspring. TRF regimen did not alter food intake and body composition of both dams and offspring. However, both males and females offspring from LP and DP fed dams had an increase in fasting glucose levels, altered lipid profile with the females offspring exhibiting impaired glucose tolerance. Glucose-stimulated insulin secretion and autonomic function of pancreatic islets were altered in both males and females offspring from LP and DP fed dams.

Our data suggest that TRF regimen during pregnancy could program adult rat offspring to metabolic dysfunction.

Pregnancy • Insulin • Metabolism

Poster | Wednesday 7th 17:40-18:40 hrs.

B20020

B20055
Basic Science
Maternal nutrition and gestational disorders

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Maternal obesity reduces mammary gland cell proliferation during gestation: Benefits of resveratrol intervention in a rat model

Gestational mammary gland (MG) differentiates to produce milk during lactation. Maternal obesity (MO) delays MG maturation, and negatively affects milk quality and quantity (1). Early interventions prevents negative alterations by MO. Maternal resveratrol treatment has never been used to determine the effects of MG cell differentiation. We hypothesis that maternal resveratrol intervention prevents MG proliferation in MO rat model induced by high fat diet. (1) Bautista CJ, Montano S, Ramirez V, Morales A, Nathanielsz PW, et al. (2016) Changes in milk composition in obese rats consuming a high-fat diet. Br J Nutr 115: 538-546.

Methods: We used rats that were fed on control (C = 5% fat,) or obesogenic diets (MO = 25% fat) during growth (21-120 days), pregnancy and lactation. At 90 postnatal days half of the rats of both groups were intervened with 20 mg.kg-1.d-1 of RES, (CRES and MORES). At 19 days of gestation (dG) maternal body and MG weight were recorded. The MG was obtained for histology analysis by H&E, immunofluorescence PCNA (proliferating cell nuclear antigen) protein detection and apoptosis by tunnel. Analysis by ANOVA, n= 7-9 mothers/group. *p<0.01 C vs MO, Groups with different letters showed differences in the same diet but different RES intervention. Results: Maternal body weight (C: 440 Â± 6. CRES: 420 Â± 5, MO: 523 Â± 11a*, MORES 480 Â± 7b*) and MG weight (C: 12.5 Â± 1, CRES: 11.8 Â± 2, MO: 35.6 Â± 5a*, MORES: 18.3 Â± 4b*) and MG fat percentage (C: 29 Â± 2, CRES: 36 Â± 0.5, MO: 59 Â± 5*, MORES: 57 Â± 6*) increased in MO compared to C and CRES. MORES reduced these parameters compared to MO. MG (lobule-alveolar area) PCNA and apoptosis cells in adipose tissue area, were increased in MO compared to C; MORES reduced the percentage of cells
Conclusion: maternal high fat diet negatively affects maternal MG maturation and proliferation at the end of gestation. Resveratrol intervention in obese mothers improves MG maturation, differentiation and cellular proliferation during gestation. It is important to design efficacious maternal intervention to prevent and/or recuperate adverse maternal and offspring outcomes. (this work was supported by Newton proyect)

Maternal obesity • Mammary gland • RES Intervention

Poster | Wednesday 7th 17:40-18:40 hrs.

B20055

B20066
Basic Science
Maternal nutrition and gestational disorders

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Evaluation of the Cholinergic Anti-inflammatory Pathway modulation in offspring of obese mothers

Maternal consumption of high fat diet (HFD) activates inflammatory pathways on early embryonic stages. This takes to a higher inflammatory cytokine levels. The offspring of obese dams have increased metabolic damages after inflammatory challenge and higher body weight gain than offspring of control dams. The innate immune system is capable of restore the homeostasis and it modulates the activating of the cholinergic antiinflammatory pathway through the cholinergic receptors a7nAChR and m1 mAChR. This system is dependent of acetylcholine which is released by the vagus nerve and it will inhibit the TNFa and others proinflammatory mediators. Here, we studied whether maternal HFD consumption is capable of modulate hypothalamic and hepatic cholinergic pathway of the offspring

Female Swiss mice were subjected to either standard chow or HFD during pregnancy and the lactation period. After weaning, only male offspring (SCO and HFDO) were used. The cholinergic receptors were measured by western blotting (WB), qPCR and immunofluorescence. The pathways proteins were evaluated in the liver and the hypothalamus by WB after challenge with PNU (IP) and McN-A-343 (ICV). Survival curve was performed using LPS (30 mg per kg bw IP). The hypothalamic level of a7 protein was downregulated in the HFD-O compared to the SCO mice. However, the hypothalamic M1 protein and the mRNA levels were elevated in the HFDO than the SCO mice. M1 positive cells in HFDO offspring seems to be more intense in the median eminence while in SC-O mice it was observed mainly in the arcuate nucleus. HFDO mice presented higher hypothalamic IL1B and IL10 and liver pSTAT3 level than SCO mice. The treatment with PNU (IP) did not change pSTAT3 level in the liver but, it reduced hypothalamic pSTAT3 in HFDO compared with the group without the stimulation. The hepatic pSTAT3 after treatment (ICV) with M1 agonist was higher in HFDO than SCO mice. Additionally, HFDO mice

Taken together these results show that the maternal consumption of high fat diet reduced a7nAChR receptor expression in the liver and the hypothalamus and increased the M1 mAChR in the hypo-

thalamus of HFDO mice. Increased expression of M1 mAChR in the hypothalamus seems resulted higher the hepatic activation of the STAT3 thought the central activation of the muscarinic receptor. This result can be related to higher survival to sepsis of HFDO compared to SCG mice.

Programming • Inflammation • Cholinergic

Poster | Wednesday 7th 17:40-18:40 hrs.

B20067
Basic Science
Maternal nutrition and gestational disorders

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Association of low-birth weight with intrauterine malnutrition and higher sepsis predisposition in Wistar rats

Metabolic disorders can also be caused by the imbalance of pro and anti-inflammatory responses in the body, similar to what is observed in the establishment of sepsis. In previous studies, our group demonstrated global intrauterine malnutrition resulted in low birth weight, hypocellularity in bone marrow and peripheral blood, reduction in leukocyte migration and decreased of the inflammatory mediators in Wistar rats. In this same model, we also observed reduction of acute and allergic pulmonary inflammation, decreased cytokines production and high levels of circulating corticosterone. The aim of this study was to correlate if the lower inflammatory response observed in malnourished rats could mean a higher propensity to develop infections in these animals.

Females Wistar rats in estrus were mated and, after confirmed the presence of spermatozoa in vaginal swab, were divided into two groups: G1 â€“ fed with normal diet; G2 â€“50% food restriction. Offspring G1 of normal birth weight (NBW) and offspring G2 of low birth weight (LBW). Six hours after sham operation or cecal ligation and puncture (CLP) in offspring male rats these rats were euthanasied.We observed hypothermia and hyperglycemia in animals with sepsis, and the glycemia of NWB with sepsis was higher than that of the LBW with sepsis group. Cytokines and the hormone Leptin were evaluated in serum and lung tissue by Multiplex. Both serum and lung tissue have shown that leptin increased during sepsis, as well as the cytokines IL-1Î², IL-10, IL-6, IL-8. These cytokines are higher in the NWB with sepsis than in the LBW with sepsis group.Bronchoalveolar lavage fluid showed a reduction in the cellular infiltrate (mononuclear cells) in both groups with sepsis. The peritoneal lavage presented an increase in the total cells number in NBW and LBW groups. Differential cell analysis showed that this increase was represented by polymorphonuclear cells (neutrophils).

Our preliminary results indicate that low birth weight rats with induced by intrauterine malnutrition are larger predisposed to systemic infection such as sepsis than animals of normal birth weight

Sepsis • Malnutrition • Inflammation

Poster | Friday 9th 11:10-12:10 hrs.

B20067

B20079
Basic Science
Maternal nutrition and gestational disorders

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Intestinal morphological changes in lactating obese rats fed with a high-fat diet

High-fat diet consumption induces disturbance in gut microbiota and the increase of gut permeability, thereby augmenting hyperglycemia and obesity. Similarly, maternal obesity during pregnancy is associated with alterations in the composition and diversity of the intestine microbiota. There are few studies related to the effects of maternal obesity in intestinal morphology. Studying the maternal intestine structure will allow us to understand a possible mechanism by which obese mothers programs their offspring to the development of metabolic diseases in adult life. The objective of this study was to investigate the effects of maternal high-fat diet intake on maternal intestinal morphology.

21-days-old female Wistar rats were fed with a control diet (C, 5% from vegetal fat) or a high-fat-diet (MO, 25% from animal fat) for 13 weeks to induce obesity and then mated. During pregnancy and lactation, rats were maintained in their respective diets. At the end of lactation, maternal glucose, triglycerides, cholesterol and leptin serum levels were determined, and maternal intestinal samples were collected for histological analysis; changes in the number of goblet cells, villus height and width, and crypts depth were measured. The results showed that high-fat diet consumption increased maternal body weight, fat accumulation as well as higher glucose, triglycerides and leptin serum levels in comparison with C. Villus height and crypts depth in the MO were significantly higher than in C. These morphological changes observed in the intestine of obese mothers indicate and increase in the intestinal permeability and fat absorption.

This study demonstrates that maternal high fat diet consumption modifies the morphology of the intestine, which probably affects intestinal fat absorption and may be related with the observed alterations in lipid metabolism and changes in milk composition1. These alterations in the mothers may predispose offspring to metabolic disease in later life. This work was supported by ANR-CONACyT 2015- 16-273510, SEP-CONACyT-2016 (287912) and RCUK-CONACyT I000/726/2016 FONCICYT/49/2016. Reference 1. (British Journal of Nutrition 115.3 (2016): 538-546)

Obesity • Pregnancy • Programming

Poster | Wednesday 7th 17:40-18:40 hrs.

B20079

B20097
Basic Science
Maternal nutrition and gestational disorders

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Fructose intake during adolescence of male rats changes redox status, autophagy process and endoplasmic reticulum stress according to perinatal maternal die

Consumption of maternal high-fat diet (HFD) is associated with changes in metabolic response pattern of offspring, increasing its susceptibility to obesity and metabolic diseases along life. Besides adolescent's own nutritional habits, maternal HFD also contributes to increase prevalence of obesity among adolescents. Fructose intake has increased specially in adolescence period and has been associated with early development of insulin resistance, dyslipidemia, obesity and hepatic steatosis. Here we tested the hypothesis that the high fat maternal diet may exacerbate the hepatic effects of excessive fructose intake in adolescent male rats and explore the contributing mechanisms, such as oxidative stress, autophagy and endoplasmic reticulum stress (ERS).

Female Wistar rats received standard (STD-9% fat) or high fat diet (HFD-29% fat) prior mating, throughout pregnancy and lactation. After weaning, offspring received standard chow and, from 25th to 45th day of age received water (STD) or fructose-drinking water (15%). Two-way ANOVA was used to statistical analysis, followed by Tukeyâ€™s post-test. HFD disrupted the hepatic redox status increasing the protein bound carbonyl (3x), thiol content (1.1x) and 4HNE hepatic protein expression (1.3x), a lipid peroxidation marker. Activities of antioxidant enzymes superoxide dismutase, glutathione peroxidase and catalase were decreased (20%) by fructose only in HFD offspring, highlighting its susceptibility to oxidative stress due fructose. The autophagy marker ATG3 exhibited increased hepatic protein expression (2.1x) only in fructose group from STD offspring and ATG12-ATG5 complex was reduced (38%) in HFD offspring. Some sensors involved in activation of the unfolded protein response were investigated and fructose increased hepatic protein expression of phosphorylated EIF2 (1.5x) and the ratio between phosphorylated PERK and total PERK only in STD offspring

The maternal diet changed metabolic responses of adolescence offspring to fructose intake, promoting differences in hepatic redox status, endoplasmic reticulum stress and autophagy process. Maternal HFD disrupted the hepatic redox status in adolescence offspring, highlighting its higher susceptibility to oxidative stress in response to fructose intake. The hepatic autophagy process was impairment in HFD offspring that received fructose while the ERS was initiated by fructose only in standard offspring. These results suggest that perinatal maternal HFD and fructose intake during adolescence period turn the offspring more susceptible to develop hepatic steatosis altering important mechanisms involved with the emergence of this disease, as oxidative stress, autophagy and endoplasmic reticulum stress.

Fructose • Maternal Obesity • Adolescents

Poster | Wednesday 7th 17:40-18:40 hrs.

B20097

B20119
Basic Science
Maternal nutrition and gestational disorders

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Maternal high-fat diet influences the metabolic response of male adolescent offspring to fructose intake

Fructose intake among adolescents has increased recently, and this has been associated with the early onset of obesity, insulin resistance and dyslipidemia. Maternal consumption of high-fat diet in perinatal period may also contribute to the development of obesity and its comorbidities throughout the life of the offspring, altering its response to metabolic insults. Then, maternal feeding behavior in the perinatal period associated to the elevated consumption of foods containing high levels of fructose by adolescents is worrisome, since both can generate negative effects on the health of offspring during adolescence. Here we investigated the effect of maternal high-fat diet consumption during perinatal period in the metabolic response of the adolescent offspring to fr

Female Wistar rats received standard (STD-9% fat) or high fat diet (HFD-29% fat) prior mating, throughout pregnancy and lactation. After weaning, male offspring received standard chow and, from 25th to 45th day of age, received water or fructose-drinking water (15%). Data analyzed by two-way ANOVA, followed by Tukeyâ€™s post-test. Fructose intake increased adiposity, serum leptin and triglycerides in STD and HFD offspring. HFD group showed higher liver weight and hepatic triglycerides, and fructose intake increased it in both groups. Fructose intake changed lipid metabolism, increasing hepatic protein expression of FAS, ACC, PPARÎ± and CPT1a in STD and HFD groups, indicating changes in fatty acids synthesis and Î²-oxidation. Fructose intake promoted higher serum glycemia in HFD group, with no change in serum insulin. Because excess fructose is known to interfere with insulin signaling, we analyzed the expression of some proteins involved in this pathway in liver. Maternal HFD increased total IRÎ², IRS1 and pAKT, and this was intensified for fructose intake in IRS1 and pAKT expression, showing that maternal HFD makes the offspring more susceptible.

Metabolic responses to fructose intake were altered by perinatal maternal diet in adolescent male offspring. Fructose administration was effective in increasing serum and hepatic triglycerides regardless of diet, suggesting a possible induction of hepatic steatosis caused by fructose intake during adolescence. In addition, the fructose consumption also promoted changes on hepatic lipids metabolism in standard and HFD groups, indicating increasing in Î²-oxidation and fatty acids synthesis. In high carbohydrate environment, the fatty acids synthesis is stimulated by insulin, and SREBP1c is a major mediator of this insulin action, and both are under investigation. Changes ob-

served on insulin pathway occurred according to maternal diet (preliminary results), indicating that maternal HFD by itself can change the insulin pathway and whether it is involved in liver alterations that turns offspring more susceptible to effects of fructose in the liver is under investigation. These data indicate that maternal HFD can contribute to development of metabolic diseases in response to excessive fructose intake in adolescents.

Fructose • High-fat diet • Programming

Poster | Wednesday 7th 17:40-18:40 hrs.

B20133
Basic Science
Maternal Nutrition and Gestational Disorders

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INCMNSZ, México

Probiotic intervention in obese pregnant rats: benefits in maternal and offspring metabolism

Obesity during pregnancy and lactation produce maternal and offspring metabolic dysfunction. While the mechanisms underlying these problems are unclear, high fat diets dramatically alter intestinal microbiota. To counteract these effects, recent studies suggested that probiotics might be a novel approach in the treatment of maternal obesity (MO). Modification of gut microbiota by probiotics during pregnancy and lactation has the potential to reduce the risk of immune-mediated and metabolic disease in both the child and the mother. We aim to evaluate the effects of maternal intervention in obese rats, prior and throughout pregnancy and lactation, with a probiotic of the genus Leuconostoc obtained from the aguamiel of Agave salmiana, in both maternal and offspring metabolism

From weaning throughout pregnancy and lactation female Wistar rats ate chow (C; 5% fat) or high energy obesogenic diet (MO; 25% fat). Half the C and MO mothers received a daily dose of probiotic orally (1 x 1010 CFU/mL) one month before mating and throughout pregnancy and lactation (CP and MOP). Offspring were weaned onto C diet. Glucose, insulin, triglycerides, cholesterol and leptin serum levels were determined in both mothers (at the end of lactation) and offspring (postnatal day 110). At the end of lactation, body weight gain, serum glucose and triglycerides, were higher in MO compared to C mothers. Probiotic intervention in MOP mothers reduced body weight gain, serum glucose, cholesterol and triglycerides levels compared to MO. Body weight, serum leptin, insulin and triglycerides were higher in MO offspring compared to C, maternal probiotic intervention in MOP reduced all these parameters compared to MO offspring.

Maternal probiotic intervention before and during pregnancy improved maternal metabolism and prevented offspring comorbidities associated with obesity. Designing effective interventions will prevent adverse effects of negative programming. This intervention presents opportunities to prevent or ameliorate negative offspring outcomes due to maternal obesity. This work was support by SEP-CONACyT-2016 (287912).

Obesity • Pregnancy • Probiotic

Oral | Wednesday 7th 15:20-16:20 hrs.

B20133

B20140
Basic Science
Maternal nutrition and gestational disorders

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Maternal protein calorie restriction reduced expression of TLR4 in offspring associated with lower LPS-induced lung inflammatory response

Inadequate nutrition in pregnancy results in consequences for fetus. This condition is associated more susceptibility to infectious diseases in offspring life as a result of alterations in the immune response. Respiratory diseases are common by world but lung has mechanisms to fight immunogen such as ciliated epithelium, production of mucus, resident macrophages in airways, pattern recognition receptors present in cells surface trigger innate immune response. However fetus immune system response caused by maternal protein calorie restriction during pregnancy is a few known. This work we examined the acute lung inflammation of C57Bl6 mice borned in protein calorie restriction environment during pregnancy.

In this study pregnants C57Bl6 females were separated into two groups: Control Group (CG) and Restrict Group (RG). The CG female were fed ad libitum chow and RG females RG were fed same chow at 30% of CG female intake. After parturition ever dams received ad libitum chow. The male offspring mice with 100 days of age received lipopolysaccharide LPS (45ug) or saline (intranasal). After 6 hours the animals were euthanized and collected lavage bronchoalveolar (for total cell count and neutrophils) and pulmonary tissues to analyse the expression of the TLR4 and production proinflammatory cytokines. In RG mice when stimulated with LPS has been observed a reduction in inflow of inflammatory cells, diminished TLR4 expression and increased production proinflammatory cytokines compared to the CG mice in same conditions.

In this study we observed that LPS failed in activate TLR 4 pathway in RG mice causing a reduced phagocytes migration to inflammatory site. This way immunogen has not been fought with same efficiency of CG mice and consequently its presence maintain the production proinflammatory cytokines like IL 1b and TNF a. Our results indicate intrauterine protein-calorie restriction decreased the immune response in these animals.

Fetal disorder • TLR4 • Inflammation

Poster | Friday 9th 11:10-12:10 hrs.

B20140

B20156
Basic Science
Maternal nutrition and gestational disorders

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Low birth weight rats have reduced NFkB pulmonary expression with alterated acute lung inflammatory response by LPS stimulus

Intrauterine growth restriction (IUGR) due to maternal food restriction during gestation is a condition to occur several long-term commorbities, probably in consequence of alterations in organs and systems functioning. Data from our group have demonstrated reduced allergic lung immune response in low birth weight rats induced by maternal caloric-protein restriction, with less leukocyte migration, cytokine release and adhesion molecules expression. The acute lung injury (ALI) caused by bacterial lipopolissacharide (LPS) is permeated by inflammatory proccess involving TLR4 receptor activation with consequent gene transcriptions by the action of NFkB. The aim of this study was to evaluate the possible changes in innate immune response related to ALI in this model of IUGR.

Females Wistar rats (12-16 weeks old) in estrus were mated and, after confirmed the presence of spermatozoa in vaginal swab, were divided into two groups: G1- fed with normal diet (commercial pellets) and water ad libitum; G2 - 50% food restriction and free water access. Offspring G1 of normal birth weight (NBW) and offspring G2 of low birth weight (LBW). Male offspring with 12-week-old were anesthetized and received LPS i.n. to induce ALI. After 6h the rats were euthanized, the bronchoalveolar lavage was performed for total and differential leucocyte count and lung tissue collected for: histopathological analysis, cytokines and MIP-2 quantification, ICAM-1 gene expression, TLR4 and NFkB protein expression. LBW rats presented a natural alveolar epithelium thickening, increased TLR4 and reduced NFkB expression. After LPS instillation in LBW rats was observed a reduced neutrophil infiltrate into lung and no increasing in ICAM-1; IL-6 and MIP-2 had a less increasing in relation to NBW, whereas IL-1b and TNF-a increased, however, no difference was observed between the groups.

IUGR due to 50% maternal caloric-protein restriction reduced the acute lung inflammatory response against an infectious stimulus by lower neutrophil infiltration, IL-6 and MIP-1 release. This innate imune system response was accompanied by less increasing in ICAM-1 6h after LPS instillation, which may be impairing the neutrophil transmigration. Although TLR4 receptor is increased in LBW

rats lung, NFkB expression is reduced before and 6h after LPS instillation. The reduced NFkB expression may implicate in lower release of proinflammatory mediators and as consequence, reduced neutrophil chemoattraction. (2017/02042- 3 and 2012/51104-8), CAPES and CNPq

IUGR • Inflammation • Innate immunity

Poster | Wednesday 7th 17:40-18:40 hrs.

B20167
Basic Science
Maternal nutrition and gestational disorders

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Organogenesis in a dish: hormone modulation of ventral prostate development from undernourished animals

Adverse conditions during pregnancy may lead to irreversible changes in the fetus by the fetal programming mechanism. Changes can be induced by maternal protein malnutrition (MPM), creating an imbalance of androgen levels thus directly influencing the morphophysiology of dependent structures, such as the prostate. Our project aimed to investigate the effects of maternal gestational protein malnutrition on the development of the rat ventral prostate (VP) by focusing on the rate of epithelial cell proliferation and androgen receptor expression associated with in vitro hormonal modulation.

Briefly, Sprague Dawley dams were distributed into two groups: control (NP; fed a normal diet containing 17% protein) or a low protein diet (RP, fed a diet containing 6% protein) during gestation. After birth, all males were euthanized and the VP dissected. RP animals showed reduction of testosterone plasma levels as well as lower body and glandular weights compared to NP control animals at birth. Some VP from NP and RP animals were submitted to morphological and molecular analysis. Others were grown in vitro for 7 days with/without 10nM testosterone diluted in medium culture. 4-hours before harvesting, 1nM of BrdU was diluted in culture medium to evaluate the proliferation rate. RP animals presented smaller VP with lower number of main ducts and a lesser ductal branch complexity. Testosterone alone was not able to recover the difference between VP from RP in relation to NP. There was no change on AR, however the proliferation rate and the levels of stemness genes were higher in the RP animals.

In summary, fetal programming by low protein diet promoted a delay in ventral prostate development. The proliferation/differentiation cell dynamic was impaired, leading to an increase in the number of basal cells and damaging their differentiation into secretory luminal cells. Testosterone alone was not able to restore the VP morphology suggesting the important involvement of other hormones.

Androgen • Low protein diet • Organ culture

Poster | Wednesday 7th 17:40-18:40 hrs.

B20167

B20170
Basic Science
Maternal nutrition and gestational disorders

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Circadian Cycle Rupture In Pregnancy Does Not Schedule Metabolic Dysfunctions In Adult Rats

Over time, organisms have developed a rhythmicity of physiological and behavioral processes related to environmental changes, such as the light-dark cycle, determining a circadian cycle. Mammals have the suprachiasmatic nucleus, a central coordinator located in the hypothalamus, in which occurs the coordination of the cycle through a feedback loop of clock genes that determine the rhythmicity of the peripheral tissues. During gestation, the rhythmicity arising from the mother is synchronized with the fetus, which is maintained after birth. Therefore, our goal was to assess if the rupture of the circadian cycle during pregnancy caused metabolic dysfunctions in female offspring during adulthood.

Female Wistar rats after pregnancy were separated into 2 groups: LD group (light-dark, normal cycle) and LL group (constantly exposed to light, 200 lx), both pregnancies were kept in a specific rack to study the circadian rhythms. At birth, all animals returned to the standard light-dark cycle and kept under controlled temperatures (23 Ã‚Â± 2 Ã‚Â° C). The litters were standardized: eight rats per mother. After 21 days, the animals were weaned. Weight and maternal food intake were recorded every 12 hours. The glycemic and lipid profile of milk and fat stores were also evaluated. In the female offspring, the evolution of body weight, fat stores, lipid profile and glycemic homeostasis were analyzed at 90 days of life. Data were expressed as average Ã‚Â± standard error of the average and analyzed by StudentÃ¢â‚¬â„¢s t test. The feeding behavior of the pregnant rats was altered, indicating a desynchronization of the maternal circadian cycle of the light-dark phase. LL animals in adulthood showed no change in glucose tolerance, fasting insulinemia and body fat stores. However, a small increase in weight at 90 days of life (2.74%) and decrease in total cholesterol (23.95%) was observed.

Exposure to constant light during pregnancy does not promote significant metabolic changes in adult rats. We suggest a possible resistance of the mother and/or fetus to a maternal dysynchrony of circadian cycle.

Pregnancy • Circadian • Metabolism

Poster | Thursday 8th 10:40-11:40 hrs.

B20170

B20205
Basic Science
Maternal nutrition and gestational disorders

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A maternal diet enriched in saturated fat induces intestinal alterations related to metabolic pathologies in the fetuses and offspring

Maternal diets enriched in saturated fat program metabolic alterations in the offspring. This is considered a cause for the worldwide increase in obesity. The intestine plays an important role in metabolic regulation. It synthesizes incretins, regulates the absorption of nutrients and the excretion of endobiotic and xenobiotic substances and precludes commensalist microbiota and small-inflammatory substances from entering the organism, thus preventing systemic infection and inflammation. Moreover, intestine integrity failure due to alterations in the epithelial barrier causes low-grade inflammation to enter the porta system, affecting the liver. Therefore, a proper intestinal function is important to prevent metabolic alterations.

The aim of our work was to evaluate intestinal expression of incretins and proteins involved in detoxifying function and epithelial barrier integrity in fetuses and offspring from rats fed with a saturated fat-enriched diet. Methods: Female Wistar rats were fed with standard or saturated fat diet (28% fat) since they were 6 week-old (SFD rats). After 8 weeks, they were mated with control males. Control and SFD rats were euthanized at 21 days of gestation or allowed to deliver and their offspring was euthanized at 140 days of age. The intestines from the fetuses and the offspring were obtained. mRNA levels of the incretin gastrointestinal peptide (GIP) and of the detoxifying channel multidrug resistance-associated proteins (MRP 2 and 3) were analyzed by RT-PCR. Protein levels and localization of Claudin-3 (Clau 3) were assessed by immunohistochemistry. We found a decrease in mRNA levels of GIP, MRP2 (20% $p<0.05$) and MRP3 (25% $p<0.05$) in the fetal intestine and of GIP (25% $p<0.05$), MRP2 (40% $p<0.01$) and MRP3 (25% $p<0.05$) in the offspring intestine from SFD rats. Clau-3 levels were reduced (30% $p<0.05$) in the intestine of the fetuses from SFD rats.

Maternal saturated fat-enriched diet induced a decrease in tight junction protein expression of the fetuses and a decrease in detoxifying channels and incretin mRNA levels in the intestines of the fetuses and the offspring. These results suggest that fat overload in maternal diet might be programming intestinal dysfunction, prompting the offspring to the development of metabolic pathologies.

Maternal diet • Intestine • Programming

Oral | Wednesday 7th 15:20-16:20 hrs.

B20205

B20222
Basic Science
Maternal nutrition and gestational disorders

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Epigenetic changes contribute to downregulate inflammatory response observed in the second generation of intrauterine malnourished rats

Adverse environmental factors in the prenatal period cause changes in the normal pattern of growth and development of the fetus. This can permanently affect the structure and physiology of several tissues and organs. This adaptive response includes changes in hemodynamics, metabolism, and production of hormones and their receptors, which predisposes the individual to cardiovascular, metabolic and endocrine diseases. In the present study we investigated the possible mechanisms involved in reducing the pulmonary inflammatory response induced by LPS in second generation (F2-UR) of F1 intrauterine undernourished rats, at 12 weeks of age. We also investigated whether possible epigenetic changes could be involved in the inflammatory response observed in these animals.

Male Wistar rats at 12 weeks/age were divided into 2 groups: nourished (NR) and F2 (ad libitum diet) obtained of F1 offspring from mothers receiving 50% of the nourished diet. Control group was given saline (i.n.). Experimental groups were given LPS (i.n.). 6h after instillation, the bronchoalveolar lavage (BAL) was collected to evaluate cellular infiltration. Lungs were harvested for measurement of the DNA methylation, histone deacetylase (HDAC) and HDAC1 by commercial kit. Western blot evaluate protein expression of Cyclooxygenase 2 (COX-2) and 5-lipoxygenase (5-LO). Malnourished group F2 (F2-UR) reduced cell infiltration in the BAL after LPS instillation compared to NR. Western blot assay showed that expression of COX-2 in LPS stimulated groups is decreased in F2-UR when compared to the NR. Only the NR group increased 5-LO expression. Basal methylation of the UR-F2 was increased compared the control NR, only the UR-F2 stimulated with LPS increased DNA methylation when compared to control. Activity of HDAC and HDAC1 was higher in the control NR when compared to the control F2-UR. There was no increase in HDAC activity after LPS stimulation in both groups.

Our preliminary results indicate the participation of epigenetic mechanisms contributing to downregulate inflammatory response observed in the second generation of intrauterine malnourished rats.
Animal Research Ethical Committee: CEUA 1408220915. Financial support: FAPESP (2012/51104-8, 2017/02042-3) and CNPq.

Undernutrition • Inflamation • Epigenetic

Poster | Wednesday 7th 17:40-18:40 hrs.

B20222

B20229
Basic Science
Maternal nutrition and gestational disorders

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Hypoproteic diet during pregnancy and/or lactation differentially affects the response of the offspring to an episode of acute kidney injury (AKI)

Protein restriction during pregnancy induces morpho-functional alterations related to deficient nephrogenesis. We studied the renal functional and morphological significance of protein restriction during pregnancy (Preg), lactation (Lact) or both, in the adult stage of the offspring and their repercussion on the AKI severity.

Female rats were randomly assigned to the following groups: C = standard diet, (SD) during Preg and Lact; CR = SD during Preg and protein restriction diet (PR) during Lact; RC = PR during Preg and SD during Lact and RR = PR during Preg and Lact. Three months after birth, at least twelve male offspring of each group underwent randomly to bilateral renal ischemia for 45 min (IR) or sham surgery. Thus, eight groups were studied 24 h after reperfusion: C, C+IR, CR, CR+IR, RC, RC+IR, RR and RR+IR. The CR, RC, and RR groups exhibited a significant reduction by Ã¯â€šÂ» 15% in the nephron number that was associated with a reduction in renal blood flow (RBF). In spite of this, glomerular hypertrophy was observed together with a significant reduction in endothelin, angiotensinogen and their receptors, as well as catalase and GPx mRNA levels. After renal ischemia, an increase in mRNA levels was found in angiotensinogen and ETA receptor in the CR and RC groups. The mRNA levels decreased for catalase and AT1 in all groups.

During basal conditions, the lesser nephrons observed in the offspring of protein-restricted mothers was associated with glomerular hypertrophy and reduced expression in vasoconstrictor factors. The ischemic insult in these groups induced a differential vasoconstrictor response that allowed a faster recovery in RBF, as compared to control group. These results suggest that CR, RC and RR groups respond better to an ischemic insult and most likely to the long-term consequences of AKI.

Hypoproteic • Ischemia • Pregnancy

Poster | Friday 9th 11:10-12:10 hrs.

B20229

B20236
Basic Science
Maternal nutrition and gestational disorders

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Evaluation of lipogenesis and lipolysis in rats submitted to dietary restriction during pregnancy

We investigated the processes of lipogenesis and lipolysis of adipose tissue in adult rats (12 weeks of age) submitted to intrauterine malnutrition, which causes low birth weight and hypercorticosteronemia.

Female Wistar rats (12-16 weeks of age) in estrus were mated and, after confirming the presence of spermatozoa in vaginal smear, were divided into two groups: G1 - fed with normal diet (commercial pellets) and water ad libitum; G2 - 50% food restriction and free access to water. G1 offspring of normal birth weight (NBW) and G2 offspring of low birth weight (LBW). These rats were euthanized, and gene expression and functional assays of lipogenesis and lipolysis were measured. Body weight (g) at 12 weeks old: NBW= 323,6-6,4 vs. LBW= 364,4-6,5*. Adipocyte volume (pL): NBW= 118,4-8,1 vs. LBW = 167,1-9,6*. Expression of lipogenesis genes are decreased in LBW (G6PDH, Malic, ATPcl and ACC) as well as the functional assay of glucose uptake into lipids (lipogenesis). Expression of the lipolysis related genes (LIPE, ADRB2, PLIN, AQP7 are decreased) as well as the release of fatty acids measured in functional lipolysis assay as well.

Our results indicate that adult rats that presented low birth weight as a result of maternal malnutrition throughout pregnancy reached higher body weight and higher adipocyte volume. Unexpectedly, we could observed that reduction in lipogenic response. Likewise, markers of lipolytic response were reduced in LBW rats. These preliminary results showed an imbalance in white adipose tissue. These alterations could contribute to increase in adipose mass presented by LBW rats submitted to intrauterine malnutrition. Supported by FAPESP-2012/51104-8, 2014/15210-3, 2017/02042-3 and CNPq

Undernutrition • Lipogenesis • Lipolysis

Poster | Thursday 8th 10:40-11:40 hrs.

B20236

B20248
Basic Science
Maternal nutrition and gestational disorders

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Transgenerational Impact of Maternal Over-Nutrition During Pregnancy on the Temporal Regulation of Core Body Temperature and Locomotor Activity in Rabbits

Metabolic parameters ranging from circulating nutrient levels and substrate utilization to energy expenditure and thermogenesis are temporally modulated by the circadian molecular clock machinery. It is possible that during critical developmental periods, epigenetic factors, such as maternal over-nutrition, alter key elements of molecular clockwork in different tissues associated to the generation of circadian rhythmicity, in such a way that compromises the expression of normal rhythmicity at birth. In order to address this issue, as a first approach we determine in a rabbit model whether the maternal over-nutrition, leads to alterations in the development of circadian rhythmicity at physiological and behavioral level in the offspring during lactation.

To this purposes, primiparous female rabbits were fed with a standard diet (SD) or with high fat and carbohydrates diet (HFCD) during gestation. At birth, newborn rabbits of both groups (n=31) were maintained under L:D cycle and nursed by foster mothers (fed with SD) once every 24 h. In postnatal day 8, rabbit pups were implanted with telemetry sensors for the continuous recording of core body temperature and gross locomotor activity, in 2 min bins. Rhythms were analyzed by the software SATYL, developed in our group. We found that HFCD pups exhibited conspicuous differences in the development of daily rhythm of temperature and locomotor activity, in comparison to the SD pups, such as: significant changes in the daily mean, an atypical temporal pattern characterized by a significant change in the time that temperature or activity remains above the average, shifts in the acrophase, a decrement in the duration and intensity of the anticipatory component and changes in the most energetic components of the rhythms.

These results clearly indicate that maternal over-nutrition alters offspring the circadian system. It is possible that this changes are associated to alterations of the canonical molecular clock. Further studies are needed to determine with accuracy if this alteration in the expression of rhythmicity are associated to changes in the machinery of the molecular circadian clock of central and peripheral oscillators. This work was supported by CONACYT-Fronteras de la Ciencia 398 and PAPIIT IN212516.

Over-nutrition • Temperature • Activity

Poster | Wednesday 7th 17:40-18:40 hrs.

B20248

B20250
Basic Science
Maternal nutrition and gestational disorders

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Association between FGF21, it´s FGFR1 receptor and ?-Klotho coreceptor expressed on Leukocytes of peripheral blood in Gestational Diabetes

Gestational Diabetes (GD) is the most frequent complication in pregnancy and FGF21 could have a key role on metabolic regulation. Recent reports indicate that pregnant women coursing with this pathology have transitory elevated blood levels of FGF21, which decrease at the end of gestation. FGF21 requires both the receptor FGFR1 and coreceptor ?- Klotho for its activation, where the last one acts as both an anchor and a necessary element for FGF21 to realize its endocrine function. Our objective is to demonstrate the relation between expressed FGF21, it's receptor FGFR1 and coreceptor ?-klotho in woman with Gestational Diabetes.

In our study 30 pregnant women between 18 and 43 years old were included. The total of participants were divided in two groups following the ADA criteria for GD classification: 15 normoglycemic and 15 GD patients. FGF21, its receptor FGFR1 and its coreceptor ?-klotho where measures using flow cytometry with a BD Canto II cytometer and analyzed by FACS DIVA8 software. Our results demonstrate that intracellular FGF21 levels are increased in patients with GD compared with normoglycemic pregnant woman (MFI, mean: 2977±215 vs 1147±589; p= 0.037). We determine that this molecule is expresed by leukocytes, more especifically neutrophils, wich was not especified in the literature. When comparing the expressed levels of FGFR1 receptor there was no estatitistically significant difference between the groups. Nevertheless, the expresion of coreceptor ?-klotho was diminished in the woman with GD compared with those normoglycemic (MFI mean: 1938±544 vs 3804±758; p= 0.044).

Our data suggest that inflammation in GD inhibits the expression of ?- klotho diminishing the FGF21 signaling, leading to an increase of its intracellular production as a compensatory mechanism. This is the first study that describes the interaction between FGF21, its receptor FGFR1 and coreceptor ?-klotho, as well as their expression on peripheral blood neutrophils in GD.

Gestational DM • Pregnancy • FGF21

Poster | Thursday 8th 10:40-11:40 hrs.

B20250

B20252
Basic Science
Maternal nutrition and gestational disorders

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Alterations In Cognitive Processes And Behavioral Patterns In Juvenile Rabbits Associated To Maternal Over-Nutrition During Gestation

Several studies associate the metabolic state of the mother during pregnancy to physiological and metabolic impairments, as well as cognitive deterioration and changes in behavioral patterns in the offspring. This bring to light the relevance to elucidate whether the intake of a high lipids and carbohydrates diet during pregnancy, affect the cognitive processes and behavioral patterns of the offspring.

In order to address this issue, a Food Preference Test (FPT) and a Novel Object Recognition Test (NOR), were performed in juvenile European rabbits obtained from females fed with a standard diet (SD) or with a high fat and carbohydrates diet during gestation (HFCD). In order to asses if the HFCD rabbits had a predisposition for unbalanced food, FPT was performed with a total of 47 rabbits. In order to evaluate the effect of the nutritional status during embryonic development on short-term declarative memory of offspring, the NOR test was performed with 40 rabbits. Differences between genders were analyzed. In the FPT, animals from the HFCD group ingested significantly more food respect the CON group. HFCD males required more time to choose one of the diets. However, the sequence of behaviors associated with food consumption was similar in both groups, with exception of grooming, that showed a significant increase in the frequency in the HFCD animals. The grooming and urination frequency were greater in males than in females. In the NOR test, the HFCD rabbits exhibited a significant increase on the latency of exploration of the novel object.

Preliminary results from the FPT indicate that the subjects obtained from over-nourished females exhibit hyperphagia, however, they did not show a preference for high fat/carbohydrates diets, as suggested in studies in other species. The significant increase in the grooming behavior presented by the rabbits of the HFCD group, in the FPT test, may be considered as an indicator of the presence of stereotyped and/or compulsive behaviors. In addition, the HFCD rabbits require more time to exhibit a proper response to novel objects. Further studies are needed to determine with more accuracy the effects of maternal nutrition on cognitive processes. This work was supported by CONACYT-Fronteras de la Ciencia 398 and PAPIIT IN212516.

Pregnancy • over-nutrition • cognitive

ORAL | Wednesday 7th 15:20-16:20 hrs.

B20252

B20254
Basic Science
Maternal nutrition and gestational disorders

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Changes in the diurnal profile of plasmatic lipids and carbohydrates associated to maternal over- nutrition in rabbits

Mammalian metabolism present circadian variations that are controlled by the molecular clock machinery. The clock genes that generate rhythmicity, also function as mediators that regulates both circadian and metabolic functions. Perinatal period is a critical time window in which the coupling between the chronostatic and homeostatic regulation can be altered by the maternal milieu, such as in maternal over- nutrition. It is possible that such disturbances, may translate in alterations in the expression of normal rhythmicity and the development of metabolic disease in adulthood. In this study we determined the effect of a maternal over-nutrition, on the temporal profile of metabolites of the offspring in adulthood.

To this purpose, European female rabbits were fed with a standard diet (SD) or a high-fat and carbohydrates diet (HFCD), does of both groups were mated by males fed with SD. At birth, pups were nursed by foster mothers fed with SD diet, and after weaning were fed with SD diet. At 250 days old, were characterized the pattern of metabolites in serum glucose (GLU), cholesterol (CHOL), high-density (HDL) and low-density lipoproteins (LDL), free fatty acids (FFA) and triglycerides (TAG) in fasting. In addition, the differences between genders were analyzed. Rabbits of the HFCD group showed a significant increase on the daily average of plasmatic GLU and a phase advances in the rhythm, in comparison to the SD rabbits. Significant changes associated to the maternal nutrition were evident in the diurnal pattern of CHOL, LDL, AGL and TAG in the HFCD group, that range from changes in the acrophase to the loss of 24-h rhythmicity. In addition, the alterations were different between females and males.

This is the first experimental evidence that demonstrated that in rabbits the maternal over- nutrition during pregnancy produce spontaneous metabolic and chronostatic alterations in offspring in adulthood. In addition, these alterations in the 24-h metabolic profile differs between genders. This work was supported by CONACYT-Fronteras de la Ciencia 398 and PAPIIT IN212516.

Rhythms • over-nutrition • metabolism

POSTER| Friday 9th 11:10-12:10 hrs.

B20254

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
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B20274
Basic Science
Maternal nutrition and gestational disorders

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México

Resveratrol intervention in obese pregnant rats partially prevents the increase in oxidative stress and metabolic dysfunction

Obesity in pregnancy causes maternal and offspring metabolic dysfunction associated with increase oxidative stress. Nutritional interventions during pregnancy offer a critical therapeutic window with potential benefit for both mother and child's health. Resveratrol (Res), a polyphenol compound found in certain plants and in red wine, has a wide-range of possible benefits to health, including its antioxidant capacity. The aim of the study was to evaluate the effects of maternal resveratrol intervention on biomarkers of oxidative stress and metabolism in obese pregnant rats.

At weaning (day 21) female Wistar rats were assigned to either chow (C- 5% fat) or a high-fat diet (MO-25% fat). One month before mating (day 90) and during pregnancy, half of the rats in each group were treated with 20 mg/kg/day of Res orally (Cres and MORes) and maintained on their respective diets. At 19 days of gestation, dams were killed, and serum was obtained to evaluate glucose, insulin, HOMA, cholesterol, triglycerides (TG) and leptin concentration; retroperitoneal fat was excised to determine adipocyte size; liver was removed to evaluate reactive oxygen species (ROS) and superoxide dismutase (SOD) activity. MO pregnant rats had higher insulin, TG and leptin serum levels and HOMA index compared with C. Adipocyte size was increased, liver ROS levels and SOD activity was augmented in MO compared to C. Res treatment reduced insulin and TG serum levels, improved HOMA index and lowered liver ROS levels in MORes compared to MO dams; liver SOD activity in MORes was similar to

C, whilst serum leptin levels and adipocyte size were unaffected in MORes. Glucose and cholesterol were similar across all groups. Res intervention in C dams (CRes) reduced l

Obesity during gestation leads to maternal metabolic dysfunction and dysregulation of oxidant/antioxidant homeostasis. Resveratrol intervention reduced the adverse metabolic outcomes of obesity in pregnancy. Oxidative stress represents a likely candidate mechanism by which maternal obesity programs offspring metabolic outcomes, and resveratrol may present a novel therapeutic agent. This work was supported by the Newton Fund RCUK-CONACyT (Research Councils UK – Consejo Nacional de Ciencia y Tecnología) I000/726/2016 FONCICYT/49/2016.

Maternal Obesity • Oxidative Stress • Resveratrol

POSTER | Wednesday 7th 17:40-18:40 hrs.

B20318
Basic Science
Maternal nutrition and gestational disorders

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MATERNAL NUTRITION
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México

Development of diseases such as obesity, type 2 diabetes, hypertension and premature birth in children of overweight or obese mothers during gestationals

Pregnancies in obese mothers have increased risk for complications including gestational diabetes, hypertensive disorders and preterm birth. Children born to obese mothers are at increased risk of obesity and metabolic disease and are susceptible to develop neuropsychiatric and cognitive disorders. Changes in placental function not only play a critical role in the development of pregnancy complications but may also be involved in linking maternal obesity to long-term health risks in the infant. Maternal adipokines, interleucina 6 and adiponectin link maternal nutritional status and adipose tissue metabolism to placental function. Adipokines and metabolic hormones have direct impact on placental function. Dr. Backer realized that children with low birth we.

METHOD Systematic review based on the Medline, Lilacs, Embase and Cochrane library databases between 1996 and 2016. Population Overweight pregnant women with a dyslipidemic profile, aged 18 years or older, and preterm NBs. Participating mothers underwent a 75-g oral glucose tolerance test (OGTT) between 24 and 32 weeks' gestation, maternal anthropometric measurements (height, weight and mean arterial pressure) and cord blood plasma sample. RESULTS Of the 5,789 articles initially selected between March 1996 and July 2016, only 32 were in accordance with the established criteria. Of these, 28.12% discussed risk factors of prematurity; 37.50%, metabolic alterations and gestational dyslipidemia; 21.87%, dyslipidemic complications in preterm birth; and 12,50%, lipid metabolism, glycemic and placental transfer. During pregnancy, investigators found an increase in the levels of high-density lipoprotein cholesterol and very-low-density lipoprotein cholesterol. That study provided guidelines as to when a physiological indicator may be associated with pregnancy diseases and/or disorders. Most notable was the association of maternal BM.

The investigation allowed to know that the diet, the state of health and lifestyle of the mother has an important influence on the health of the newborn as in adulthood is more likely to develop a chronic disease. There is a reduced adaptation of obese pregnant women to the metabolic changes of gestation. This favors dyslipidemic intercurrences in the mother, which, directly or indirectly, suggests the occurrence of premature births and high lipid transfer to the fetus. Therefore, preterm newborns, whose mothers were dyslipidemic during pregnancy, have greater risk

of epicardial fat, both in early (first year of life) and in later (adult) phases of life. Previous studies in the HAPO cohort and other cohorts have demonstrated that the combined effect of maternal obesity and gestational diabetes mellitus (GDM) on newborn size at birth is greater than either obesity or GDM alone. Maternal BMI and glycemia are associated with different components of the newborn metabolome, consistent with their independent effects on newborn size at birth. Maternal BMI, is associated with a newborn metabolic signature characteristic of insulin resistan.

maternal BMI • Obesity • Premature Birth

POSTER | Friday 9th 11:10-12:10 hrs.

B20344
Basic Science
Maternal Nutrition And Gestational Disorders

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Maternal Diet Enriched In Olive Oil Regulates Lipid Levels And PPAR Target Genes Expression In Fetal Livers From Gestational Diabetic Rats

Gestational Diabetes Mellitus (GDM) Is A Prevalent Disease That Increases The Risk Of Adverse Fetal Outcomes. We Have Previously Characterized A GDM Model Obtained Through Adverse Intrauterine Programming In The Offspring Of Pregestational Diabetic Rats. In The Fetal Liver From GDM Rats, We Found Sex-Dependent Alterations In The Levels Of Peroxisome Proliferator Activated Receptors (Ppars), Master Regulators Of Lipid Metabolism. The Aim Of This Work Was To Evaluate Triglycerides And Perilipin 2 (PLIN2) Levels And The Expression Of Target Genes Involved In Lipid Accretion (Fas, Scd-1) And Lipid Oxidation (Aco, L-Cpt-1) In The Fetal Liver From GDM Rats, As Well As The Capability Of Diets Enriched In Olive Oil To Prevent Possible Alterations In These Parameters.

Pregestational Diabetic Rats (F0) Were Obtained Through Neonatal Streptozotocin Administration (90 Mg/Kg). The Offspring From Control (C) And Pregestational Diabetic Rats Were Mated With Healthy Males. GDM Was Induced By Intrauterine Programming In The Offspring (F1) Of Pregestational Diabetic Rats. The Fetal Livers From C And GDM Rats Were Explanted On Day 21 Of Pregnancy. In The Liver Of Male Fetuses From GDM Rats, We Found An Increase In The Triglycerides And PLIN2 Levels (53% And 32%, Respectively; $P<0.05$ Vs C), And Fas And Scd-1 Mrna Levels (Fold Change 1.44 And 1.58, Respectively; $P<0.05$ Vs C). These Alterations Were Prevented By The Diet Enriched In Olive Oil ($P<0.05$ Vs GDM). In Contrast, Livers Of Female Fetuses From GDM Rats Showed Reduced Triglyceride Levels (66% $P<0.01$ Vs C) And Unchanged PLIN2 Levels Compared To Controls. Livers Of Female Fetuses From GDM Rats Showed Increased Expression Of Aco And L-Cpt-1 (Fold Change 1.53 And 3.26, Respectively; $P<0.01$ Vs C), Alterations Prevented With The Maternal Diet Enriched In Olive Oil ($P<0.001$ Vs GDM).

In This GDM Model Induced By Intrauterine Programming, The Altered Lipid Deposition In The Fetal Liver Is Sex-Dependent And Possibly Related To Changes In The Expression Of The Different PPAR Target Genes. In Addition, A Maternal Diet Enriched In Olive Oil Prevents The Increased Expression Of Enzymes Of Lipid Metabolism In The Fetal Liver From GDM Rats, Probably Improving The Liver Function In The Fetus And Also In The Offspring S Later Life.

Gdm • Programming • Maternal Diet

Poster | Wednesday 7th 17:40-18:40 Hrs.

B20344

B20349
Basic Science
Maternal Nutrition And Gestational Disorders

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Maternal Exposure To Glyphosate Alters Hepatic Steatosis In Adult Offspring Mice Submitted To High-Fat Diet-Fed

Glyphosate Leavings Have High Risk To Liver Functions By Altering Levels Of TG And CHOL And Inhibiting Liver Fatty Acid Oxidation Enzymes, Likely Resulting From Diversion Of Fatty Acids Away From Oxidation And Toward Other Lipid Pathway. Thus, The Aim Of This Work Was To Evaluate The Effects Of Maternal Exposure To Glyphosate In Hepatic Lipid Metabolism On Adult Mice Offspring High-Fat Diet-Fed.

The Pregnant Female Mice Were Randomly Divided In Control Group (CTL, N=7), Which Received Pure Water Ad Libitum, Or Glyphosate Group (GF, N=9), Which Received Water With 0.5% Of GF (Roundup Original DI®). At 60th Postnatal Day, The First Generation Of Male Offspring Was Divided In: CTL-LF-F1 (N=12), CTL-HF-F1 (N=9), GF-LF-F1 (N=8) And GF-HF-F1 (N=5) Group. Male Offspring Received LF Or High-Fat (HF) Diet For 90 Days And The Euthanasia Occurred At 150 Days Of Life. At 150 Days, GF-HF-F1 Had Body Weight 21% Lower Than CTL-HF-F1, But Similar To GF-LF-F1. The GF Increased Liver Weight In GF-LF-F1 When Compared To CTL-LF-F1 And In GF-HF-F1 To Compare To CTL-HF-F1. Liver Total Lipids Content And Triglycerides (TG) Were 32% Lower In GF-HF-F1 When Compared To CTL-HF-F1, Without Influencing The Liver Cholesterol (CHOL) Content. The HF Diet Increased The Liver Total Lipids Content (21%), CHOL (49%) And TG (42%) In CTL-HF-F1 When Compared To CTL-LF-F1. The Liver Of CTL-HF-F1 And GF-HF-F1 Presented Steatosis (Score 3 And 1, Respectively) And Fibrosis. All The Treatment Groups Had Lobular Inflammation, Microgranulomas And Large Lipogranulomas.

Our Study Shows That Glyphosate Exposure In Pregnancy And Lactation Period Prevented Body Weight Increasing In Adult Male Offspring Mice With High-Fat Diet-Fed Due To Possible Herbicide Effects, Or Its Metabolites, At Their Neuronal Center, Possibly In Hypothalamus. Treatment With High Doses Of Glyphosate Cause Alteration In >60 Distinct Lipid Species Including Several Neutral Lipids As Monoacylglycerols, Diacylglycerols, TG And Increased Fat Storage And CHOL Esters In Mouse Liver. We Show That Maternal Exposure In Low Doses Increased The Liver Weight, CHOL And TG Content In Male Offspring That Receives LF Diet. However, When Offered HF Diet To These Mice, We Observed A Reduction In Their Liver Weight, Liver Total Lipids Content And TG, Without Influencing CHOL Content. The HF Diet Was Not Effective To Elevate The Lipids Levels, Due To Previous Altera-

tion In These Pathways Caused By Glyphosate Exposure. These Alterations Can Be Observed In Lower Steatosis Grade And Presences Of Fibrosis And Inflammation On Their Liver. Nonetheless, More Studies Need To Be Done To Understand The Toxicological Mechanisms Associated With Glyphosate In Liver Of Mice Submitted To Different Diets.

Roundup • Liver • Programming

Poster | Friday 9th 11:10-12:10 Hrs.

B20373
Basic Science
Maternal Nutrition And Gestational Disorders

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Mouse blastocysts sense maternal nutrition quality via isoleucine availability to regulate trophectoderm endocytosis level, a survival mechanism

We have shown mouse maternal low protein diet during the preimplantation period with normal diet thereafter (Emb-LPD) causes chronic cardiometabolic and neurological disease in adult offspring. Emb-LPD causes depletion of branched-chain amino acids (BCAA) in maternal uterine luminal fluid and insulin in serum, recognised by embryo nutrient-sensing mechanisms, leading to compensatory responses including increased endocytosis in the blastocyst trophectoderm (TE), thereby increasing uptake of nutrient-rich maternal fluids. This study aimed to determine the role of individual BCAA and insulin depletion in stimulating endocytosis in TE using an in vitro embryo culture model.

2-cell embryos were cultured to the blastocyst stage (48 hours) in KSOM medium supplemented with BCAA and insulin at normal concentrations (control; as found in well-fed mice) or with individual BCAA (isoleucine, valine or leucine) and/or insulin depleted by 50%. After culture, blastocyst fluorescent markers for lysosomes and endocytosed/processed BSA were analysed using confocal microscopy and VOLOCITY imaging. Blastocysts cultured in depleted isoleucine (with normal insulin) but not other depleted BCAAs showed increased lysosome number and digested BSA per TE cell compared to controls (50% and 60% respectively, $P<0.05\%$). These lysosomal changes were accompanied by increased expression of both cathepsin B, a marker for lysosomal activation, and clathrin, a marker of endocytosis, but not of the endocytic receptor, megalin. Depleted isoleucine medium also promoted blastocyst TE nuclear delivery of transcriptor factor EB (TFEB), the lysosomal gene expression regulator, in an mTORC1-dependent process to enhance lysosomal vesicle number per cell. Embryos cultured in the same conditions from 2-cell until morula stage (36 hours) showed no changes in lysosome num.

Isoleucine availability has been identified a specific role in embryo nutrient sensing at the blastocyst stage. Preimplantation embryos sense isoleucine deficiency in vitro through mTORC1 which causes TFEB to translocate to the nucleus, promoting lysosome gene expression and biosynthesis. This compensatory response in vitro leads to increased endocytosis (requiring clathrin for coated vesicles) and increased lysosomal activation (requiring cathepsin B). These responses are activated in a temporally regulated mechanism at the morula- blastocyst transition. The isoleu-

cine-sensing enhanced endocytosis phenotype characterised here in the blastocyst is the earliest 'biomarker' of poor maternal nutrient provision so far identified and shown to lead ultimately to increased cardiometabolic risk in adulthood. If present in human embryos (current objective), it may facilitate protection against adverse developmental programming in clinical IVF treatment through both improved patient nutrition and culture medium composition. Funded by Rosetrees Trust and University of Southampton.

Endocytosis • Isoleucine • Blastocyst

POSTER | Thursday 8th 10:40-11:40 hrs.

B20401
Basic Science
Maternal Nutrition And Gestational Disorders

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Proteomic Analysis To Identify Molecular Biomarkers Of Prostate Carcinogenesis In Young Offspring Rats Submitted To Maternal Low Protein Diet.

Adverse Condition During Intrauterine Development Can Drive The Origin Of Different Diseases In Offspring During Postnatal Life, A Condition Known As Fetal Programing (FP). Among The Most Prevalent Are Obesity, Diabetes, Cardiovascular Disease And Even Some Types Of Cancer. The Intrauterine Exposure To Low Protein (LP) Diet Is One Of The Most Studied Rodent Model Of FP. Results From Our Group Show That Maternal LP Diet Can Be Associated Prostate Cancer In Adulthood, However, The Molecular Mechanism Involved In This Process Is Far To Be Elucidate. Here, We Aimed To Investigate The Changes In Proteomic Profile Induced By Maternal Exposure To LP Diet During Gestation And Lactation In 21-Day-Old Rat Offspring That Could Be Considered Potential Biomarkers Involved With Prostate Carcinogene.

Male Sprague Dawley Rats Were Divided Into A Control Group (CT, N = 4), Born From Mothers Fed Normal Diet (17% Protein) Or Born From Dams Fed A Low Protein Diet (6% Protein) During Gestation And Lactation (GLLP, N = 4). The Rats Were Euthanized On Postnatal Day 21 And The Ventral Prostate Was Processed For Proteomic Analysis. The Results Were Compared And Analysis In Silico On Gene Ontology And Survexpress With Datasets From The Cancer Genome Atlas (TCGA) And Galsky Oh. Mass Spectrometry Identified 77 Up-Regulated Proteins That Were Submitted To Gene Ontology To Identify Their Involvement With Regulation Of Tumor Necrosis, Regulation Of Metabolic Process, Cellular Response To Stress And Heat Shock Family. We Also Used Survexpress Database To Define Prognostic Value Of The Targets In Patients With Pca. The Elongation Factor 1 Alpha 1 (EEF1A1), Heat Shock 70 Protein 1 (HSPA1A), Endoplasmic Reticulum Chaperone (HSPA5), Protein Disulfide-Isomerase A3 (PDIA3), Calreticulin (CALR) Was Identified In TCGA As A Group Of Proteins Related With Poor Prognostic And Reduction Of Survival Of These Individuals. Galsky Oh Identified Only HSPA1A Associated With Poor Prognosis In High-R

These Results Highlighted The Role Of Maternal LP Diet In Disrupting Normal Prostatic Development, Altering Molecular Pathways That Promote Slow-Growing Prostate Carcinogenesis With Aging. Moreover, In Silico Analysis Can Be Useful Tools To Characterize Potential Biomarkers And Molecular Pathways Involved In Rodent And Human Pca.

Fetal Programmin • Prostate Cancer • Proteomic

POSTER | Thursday 8th 10:40-11:40 Hrs.

B20401

B20402
Basic Science
Maternal Nutrition And Gestational Disorders

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Morphology • Unesp
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Gestational low protein diet exposure causes microRNAs alterations in young offspring that can be the origin of prostate carcinogenesis in adulthood.

Over the past decades, it has been observed an increase in the incidence of cancer in the population. Studies show that cancer can originate from insults suffered by individuals during the intrauterine life, a condition known as Fetal Programming. The perinatal period is characterized by ability of the embryo/fetus to adapt to environmental changes by altering gene expression by post- transcriptional mechanisms. Recently, we demonstrated that maternal protein restriction promotes prostate carcinogenesis in aging offspring rats; However, there is lack of information on the molecular mechanism involved in this process. Thus, we aimed to identify the microRNAs deregulated in young programed rats and localize its possible targets associated with prostate carcinogenesis.

Male Sprague Dawley rats born to dams fed standard diet (17% protein) or low protein diet (6% protein) during gestation and lactation were euthanized on postnatal day 21 and the ventral prostate were processed by next generation sequencing (HigSeq-2500 Illumina) to determine the microRNome prolife. We identified 15 altered microRNAs (10 up regulated and 5 down regulated). In silico analysis were performed to identify the prediction of mRNA regulated by both up and down differential expressed microRNA. These mRNAs were analyzed in the Geneontology to identify their involvement in proliferation, apoptosis, morphogenesis and oxidative stress pathways. These analyses were performed in CBIOPortal and Survexpress database. In silico analysis identified 2 up regulated mRNA: DNA (cytosine 5) methyltransferase 1 (DNMT1) and receptor- interacting protein kinase 2 (RIPK2), and 6 down regulated mRNA: Phosphatase and tensin homolog (PTEN), Fibroblast growth factor receptor 1 (FGFR1), Secreted Frizzled Related Protein 1 (SFRP1), clusterin (CLU), FYN, Forkhead box protein O1 (FOXO1). Both up and down regulated mRNAs are related to worse prognosis in patients with prostate cancer.

Our results demonstrated that maternal low protein diet interfere with the expression of microRNAs involved in the development of prostate carcinogenesis in young offspring. These changes can be associated with intrauterine origin of prostate cancer observed in older offspring submitted to maternal protein restriction; reinforcing the “Gardner hypothesis” that PCa can be originate from in utero.

Fetal Programmin • Prostate Cancer • MicroRNAs

POSTER | Wednesday 7th 17:40-18:40 hrs.

B20402

B20406
Basic Science
Maternal Nutrition And Gestational Disorders

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Prenatal Testosterone Excess Induces Ectopic Lipid Accumulation and Greater Beta Cell Area in the Pancreatic Islets of the Female Sheep

Prenatal exposure to excess testosterone (T) causes peripheral insulin resistance, hyperinsulinemia, and lipotoxicity in the liver of adult female sheep, a model for polycystic ovary syndrome. Co-treatment with insulin sensitizer prevents the peripheral hyperinsulinemia by insulin-dependent programming while co-treatment with antiandrogen does not. Studies in rodents show that chronic infusion of lipids enhances beta cell insulin production. Whether hyperinsulinemia in prenatal T-treated sheep is the result of increased pancreatic insulin secretion stemming from excess lipid accumulation in the pancreas is not known. Therefore, we hypothesized that excess prenatal T, in an insulin- dependent manner, induces lipid accumulation and increases insulin production in the pancreas.

Pancreas from control (n=6), prenatal T- (100mg T propionate twice a week from days 30- 90 of gestation, n=6), prenatal T plus androgen antagonist, flutamide (15 mg/kg/day, n=11), and prenatal T plus insulin sensitizer, Rosiglitazone (0.11 mg/kg/day, n=5)- treated female sheep were studied at 24 months of age. Pancreatic islet lipid content was assessed through oil red O staining of cryosections while pancreatic triglyceride content was assessed using a colorimetric assay. Pancreatic beta cell area was determined using immunofluorescent staining for insulin in paraffin-embedded tissue sections by calculating the ratio of insulin stained area to the total pancreatic islet area. Data was analyzed using Cohen's effect size to determine magnitude of difference between control versus prenatal T, and prenatal T versus intervention groups. Prenatal T- treatment induced large magnitude increases (Cohen's d=>0.8) in oil red O staining, triglyceride content, and beta cell area. Increase in beta cell area was prevented by both prenatal interventions with large magnitude effects, while there was no prevention evident from oil red O staining and triglyceride assay.

Results from this study provide evidence that prenatal T excess compromises pancreatic function. The finding that intervention with androgen antagonist and insulin sensitizer prevents the prenatal T-programmed increase in beta cell area but not pancreatic lipid accumulation suggests that the programming of increased beta cell area involves both androgenic and metabolic pathways. While the significance of excess pancreatic lipid accumulation remains to be determined, failure of both interventions to prevent this increase raises the possibility of estrogenic programming due to aromatization of T to estradiol. Supported by NIH PO1HD44232

Programming • Testosterone • Pancreatic Islet

POSTER | Friday 9th 11:10-12:10 hrs.

B20406

B20453
Basic Science
Maternal Nutrition And Gestational Disorders

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Maternal programming by cafeteria diet leads to aberrant brain structural plasticity and anhedonia-like behaviour in male offspring

Maternal overnutrition predisposes to metabolic dysfunction and behavioral defects in offspring. We identified if maternal nutritional programing leads to defects in motivation for natural rewards, and if these changes correlate with brain plasticity alterations in male offspring.

Female Wistar rats ate a cafeteria diet (CAF) for 9 weeks (before, during pregnancy and before weaning). Metabolic profile characterization was determined by ELISAs kits. Motivation behavior in offspring was identified at two month old by addressing: 1) operational conditioning by the Skinner box, preference to sucrose, open field and novel suppressed feeding. Brain plasticity changes were analyzed by Magnetic Resonance Imaging (MRI) and Western blot and immunohistochemistry (NMDA and AMPA receptor markers and synaptophysin), respectively. Maternal programming leads to changes in plasma glucose, leptin and insulin sensitivity and fat accumulation, which correlates with defects in motivation behavior evidenced by: a) decrease in incentive lever presses in the Skinner box, b) decrease in preference to sucrose, and c) delay in the novel suppressed feeding test. MRI analyzes showed that maternal overnutrition promotes structural volume brain changes in the striatum, hippocampus and cortex. Also, we found anatomical changes in the hippocampus and striatum, and an increase in the GluR2 subunit (AMPA receptor) expression in the hippocampus.

Our findings reveal that maternal programming by CAF diet leads to metabolic compromise which correlates with defects in motivation for natural rewards such as anhedonia-like behaviour in the offspring. Behavioral defects associate to changes in the macro and microstructural plasticity of selective brain regions in the reward system.

Maternal program • Neuroplasticity • anhedonia-like b

ORAL | Thursday 8th 09:40-10:40 hrs.

B20453

B30015
Basic Science
Environmental health and neurodevelopment

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Dirt environmental monitoring and the metabolic programming for health and disease

The chronic exposure to environmental contaminants, as the bisphenol A (BPA), the particulate matter air pollution and organophosphorus pesticides, among others, may affect central neural tissues, as the hypothalamus, and peripheral tissues, as the endocrine pancreas, promoting inflammation and apoptosis, with direct, and later, implication to mammalsÃ¢â‚¬â„¢ metabolism. The Developmental Origins of Health and Disease (DOHaD) concept articulate events in developmental phases of life, as intrauterine, lactation and adolescence, to later life metabolism and health. These developmental phases are more susceptible to environmental changes; as those caused by environmental contaminants, which may predispose individuals to obesity and cardiometabolic diseases in later lif.

Alterations in the epigenome are explored mechanisms to demonstrate the programming effects on the metabolism, with key genes for metabolism functions being up and downregulated, according to the environment. Studies show that environmental contaminants may affect the epigenetic pattern in mammals, especially when exposed during the developmental phases of life, which leads to metabolic disorders in later life. In this review, we discuss the role of the environmental contaminants in the central and peripheral programming for obesity and metabolic syndrome.

In the current work it has been shown evidences and clues to Improve the environmental monitoring may affect directly the quality of life for the population and future generations

DOHaD • dirtenvironment • obesity

POSTER | Friday 9th 11:10-12:10 hrs.

B30015

B30021
Basic Science
Environmental Health And Neurodevelopment

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Environmental Enrichment prevents cognitive impairment and improves stress-reactivity in Prenatally-Stressed mice.

The stress suffered by a mother during pregnancy can induce adverse effects on the offspring, such as cognitive impairments, alterations in the hypothalamicÃ¢â‚¬â€œpituitaryÃ¢â‚¬â€œadrenal (HPA) axis and the stress response, and an increased vulnerability to the development of behavioral disorders later in life. Previous studies suggest that this effect may be sex-dependent. Research in animals has shown that early environmental enrichment (EE), a housing condition enriched with tactile, visual and social stimuli, increases hippocampal neurogenesis, and improves both spatial memory and stress reactivity. Our aim is to assess the efficacy of an early EE treatment in preventing or preventing the deleterious effects of Prenatal (PS) Stress on Balb/C mice.

Pregnant dams were divided into Control (C) and PS groups. The latter were subjected to restraint stress 2h/d, from PD14 until delivery. Offspring was weaned at PN21, and subjects from both groups were then randomly assigned to either Standard Housing cages or EE ones, resulting in four groups. At PN90, animals underwent behavioral testing, using a battery comprised of an Open field test, and an Object in Place (OIP) task. PS animals presented a significant increase in anxiety-related behaviors in the Open Field when compared to controls, with an increase in locomotion, but a decrease in the time spent exploring the center of the arena. This difference was not present in the PS+EE group. PS subjects also displayed an impairment in contextual-spatial memory. EE housing significantly prevented this effect, with PS+EE animals OIP score being more similar to their EE counterparts. After behavioral testing, animals were sacrificed and hippocampus samples were collected. PS animals presented a significant increase in hippocampal Glucocorticoid Receptors (GR), hinting at an HPA-axis alteration. This increase was not found in PS+EE animals, whose levels were more similar the C group.

PS mice showed a clear impairment on spatial memory. While a tendency regarding sex-differences was observed, the impact of prenatal stress on the Object-In-Place was not significantly different in males and females. Results in PS+EE mice suggest that an EE treatment can revert the effects of PS in contextual spatial memory. The increase of stress-related behaviors in the Open Field, such as rearing and center-avoidance, suggests that PS increased stress reactivity. This is supported by the increase in GR in PS animals, which may imply an alteration of the HPA-axis regulation. PSÃ‚Â¬+EE animals were again more similar to control and EE animals, suggesting that EE can prevent some of the negative effects of PS, both at neurochemical and behavioral levels.

Prenatal Stress • Enriched Housing • Behavior

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30021

B30038
Basic Science
Environmental Health And Neurodevelopment

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Short-term modulation of offspring astrocyte population by maternal obesity: potential implications for orexigenic neurons development

Strong evidence show that maternal obesity is associated to the modulation of offspring metabolism, impacting on weight gain, glucose homeostasis, adiposity and other physiological conditions during adulthood. So far, a small number of studies have addressed the role of maternal obesity on the hypothalamic structure/activity of the offspring both on short and long terms. The hypothalamus responds to nutrients and hormones as well as integrates the resulting signals in order to balance caloric intake and energy expenditure, which affects directly the whole body energy homeostasis. Thus, the current project aimed to investigate if maternal obesity could impact on the development of hypothalamic neurons, generating long term abnormalities, and to elucidate potential underlying m.

We used a mouse model of maternal diet-induced obesity. Female C57Bl/6J mice were fed either a control or a high fat diet diet from three weeks prior to mating and during pregnancy and lactation. Only male offspring were studied to avoid the confounding influences of sexual dimorphism. Offspring born from control and obese dams were studied at different time points: i, immediately after weaning; and ii, at 8 weeks of age (both litters weaned onto a balanced Chow diet until complete 8 weeks of life). Obese dams presented increased body weight before and during pregnancy. Also, there was a considerable increment in adiposity and brown adipose tissue (BAT) temperature as well as hyperglycemia and hyperinsulinemia at both pregnancy and lactation. Male offspring born from obese dams presented decreased body weight at birth. Three weeks of age male offspring from obese dams presented increased GFAP (astrocytes) staining in the arcuate nucleus. In addition, 8 weeks siblings born from obese dams presented hyperinsulinemia and increased gene expression of Tnf-alpha, Interleukin-6 and the orexigenic neurons, NPY and AgRP, in hypothalamus.

The set of results revealed an impaired development of hypothalamic neural circuits modulated by maternal obesity. Our findings suggest that adult offspring from obese dams presented increased levels of important orexigenic and pro-inflammatory components in hypothalamus. Apparently, such outcomes are preceded by an increase in astrocyte population, which control inflammation and neuronal stress, at very premature stage for these animals. As hypothalamus provides many physiological roles involved in feeding and metabolism, the enhanced stress response short term (and possibly continued) may be favoring the upregulation of NPY and AgRP neurons population long term. Supported by SÃ£o Paulo Research Foundation (FAPESP), 2016/07361-7

maternal obesity • hypothalamus • astrocyte

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30038

B30060
Basic Science
Environmental Health And Neurodevelopment

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HPA axis dysfunction and ANS imbalance mediate obesity in MSG-rats

Recent evidences suggest that, imbalanced autonomic nervous system (ANS) output and defects in the hypothalamic-pituitary-adrenal axis (HPA) axis, allowing high glucocorticoids levels, is linked to obesity and cardiometabolic diseases onset. The HPA axis exert important catabolic peripheral effects and influence ANS mediated processes. Impaired negative feedback control /or reduced sensitivity to HPA axis feedback and altered ANS activity seems to be associated with the development and maintenance of obesity. In the present study, therefore, we examined the hypothesis that central HPA axis is dysregulated favoring ANS disbalance in obesity.

We used monosodium L-glutamate (MSG)-induce rat obesity. Adult MSG- obese rat was treated with corticotrophin-releasing factor (CRF) and synthetic Dexamethasone (DEXA) given intracerebroventricular (ICV) injection for 3 days. Metabolic parameters, glucose homeostasis and ANS electrical activity was evaluated. Adult MSG-obese rats presented fasting hyperinsulinemia, insulin resistance, glucose intolerance, hypercorticosteronemia, hyperleptinemia and ANS activity unbalanced. CRF ICV caused decrease in food intake. DEXA ICV injection induced, increase fasting insulin and glucose levels, associated to insulin resistance. As expected, central CRF caused decrease of parasympathetic and increase in sympathetic activity; while, DEXA induced opposite effects, in control rats. In contrast, MSG-rats appear to be unresponsive to the central injections, mostly in ANS electrical activity.

Our study supports evidence that glucocorticoids participate, using HPA axis, as a signal to central nervous system-periphery communication, including changes in ANS activity and glucose levels; which allow maintaining metabolic homeostasis. Activity of the HPA axis is increased in MSG-obese rats; however, reduced sensitivity to HPA axis is observed after central DEXA or CRF infusion, which can be involved in obesity and metabolic syndrome onset

MSG-obese rats • glucocorticoids • autonomic nervou

POSTER | Thursday 8th 10:40-11:40 hrs.

B30060

B30061
Basic Science
Environmental Health And Neurodevelopment

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Insulin secretion induced by glucose and autonomic nervous system neurotransmitters is adjusted to glycemic control in msg-obese rats

There are evidences that unbalance of autonomic nervous system (ANS) activity is involved with the onset of obesity; which sympathetic is decreased and parasympathetic is increased. In the current work it was tested whether in obesity programed by postnatal administration of monosodium L-glutamate (MSG) in pup rats, the ANS is unbalanced.

The effect of acetylcholine (Ach) and Î±2 â€“ adrenergic agonist oxymetazoline (Oxy) on insulinemia and glycemia during the intravenous glucose tolerance test (ivGTT) in MSG-rats is investigated. Insulin release from isolated pancreatic islets stimulated by glucose, carbamylcholine (Cch) or epinephrine (Epi) was measured. MSG-obese rats presented tissue huge fat accumulation, basal normoglycemia and hyperinsulinemia. Glucose intolerance and hyperinsulinemia were observed in MSG-rats. Insulinogenic Index (âˆ†insulinemia/âˆ†glycemia) calculated from ivGTT was 2 fold higher in MSG-rats when compared to control. Exogenous Ach decreased glycemia and increased insulinemia of control rats; however, no changes were observed in MSG-rats. Treatments with Oxy caused decrease in insulinemia and increase in glycemia in both groups; however, the effect was pronounced in MSG-rats. Islets of the MSG - rats were more responsive to glucose; however, they presented low response to Cch e high to Epi when compared to controls.

Hypothalamic obese MSG-rats show disarranges in glycemic control, which might be caused by an ANS activity modified.

insulin release • obesity • ANS

POSTER | Thursday 8th 10:40-11:40 hrs.

B30061

B30081
Basic Science
Environmental Health And Neurodevelopment

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Neuroprotective Effect of Maternal Physical Exercise on Offspring against Amyloid-Î² Neurotoxicity

Alzheimerâ€™s disease is the main neurodegenerative disorder, in which amyloid-Î² peptide (AÎ²) oligomers are neurotoxic. Considering that disease course- modifying treatments are challenging, we propose the use of maternal physical activity as a prospective non- pharmacological therapy. Practicing exercise has emerged as a potential brain health enhancer, improving cognition of the practitioner. In addition, exercise promotes metabolic adaptations, even during pregnancy, benefiting the fetus early and later in life with the ability to modify offspringâ€™s disease susceptibility in adulthood. Our objective was to investigate the potential neuroprotective role of maternal swimming against AÎ² neurotoxicity in the adult offspring.

Female rats swam one week before and throughout pregnancy (30 min/day). At postnatal day 60, male littermate received a single intracerebroventricular injection of AÎ² 1-42 peptide oligomers (500 pmol/rat), and 14 days after injection behavioral and neurochemical analyses were performed. AÎ²- injected rats exhibited learning and memory deficits, which was accompanied by hippocampal brain-derived neurotrophic factor levels reduction. Furthermore, AÎ² peptide1-42 oligomers reduced synaptophysin immunocontent and increased mitochondrial fission protein Drp1 in the hippocampus. Strikingly, offspringâ€™s behavioral alterations elicited by AÎ² peptide oligomers and also hippocampal synaptophysin and Drp1 alterations were prevented by maternal exercise, which promoted augmentation of functioning mitochondria indicated by increase of mitochondrial mass and membrane potential and cytochrome c oxidase activity. These findings might be explained by the upregulation of brain mitochondrial function elicited by regular maternal swimming during pregnancy.

The evidences of programmed mitochondrial function by maternal exercise during pregnancy persisting at adult offspringâ€™s life, thus conferring resistance against AÎ² neurotoxicity, highlighting the metabolic programming as a promising approach to prevent chronic pathologies, such as Alzheimerâ€™s disease.

mitochondria • maternal exercis • memory

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30081

B30102
Basic Science
Environmental Health And Neurodevelopment

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Effects of maternal bisphenol a (bpa) exposure on body composition and hormones profile in neonate and adult rats of both genders

Bisphenol A (BPA) is an endocrine disruptor used in numerous industrial applications. In humans, BPA was detected in both placenta and milk and its exposure during perinatal life was already related to metabolic alterations in infants such as sexual dysfunction and obesity. We aimed to study the short and long- term effects of BPA exposure exclusively during pregnancy and lactation on body composition, food intake and hormone profile of young and adult rat offspring.

After pregnancy confirmation, female Wistar rats were divided into: control- CON (vehicle), BPA10 (10ÃŽÂ¼g/kg/day) and BPA50 (50ÃŽÂ¼g/kg/day). Ethanol 0.1% was used as vehicle for BPA and administered by gavage to CON and BPA dams from gestation until the end of lactation. Euthanasia occurred at weaning (dams and part of the pups of both genders) and adulthood (remaining male and female offspring). At the end of lactation, dams of BPA50 group showed hypercholesterolemia. At weaning, female pups of BPA10 group had hypercholesterolemia and hypertriglyceridemia. Male pups of BPA10 group showed lower plasma T3. Female and male pups of BPA10 group had higher plasma progesterone, testosterone and estradiol levels. In PN180, females of BPA50 group showed lower fat mass, higher lean mass and lower corticosterone levels, while the females of BPA10 group had lower T4 levels. Female offspring of both BPA groups had lower food intake and higher plasma insulin. Adult male offspring of BPA10 group showed lower estradiol and T4 levels, whereas the BPA50 group had lower food intake. Both BPA groups presented lower visceral fat, lower progesterone and testoster

Therefore, our data suggest that maternal exposure to BPA exclusively during gestation and lactation, even in low dose, induces changes in life-long reduction adiposity in the progeny associated with sex hormone, T4 and corticosterone deregulations.

bisphenol • gestation • lactation

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30102

B30105
Basic Science
Environmental Health And Neurodevelopment

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Post-weaning and long-term exposure to high-sucrose diet accelerates dementia and motor impairments via hippocampal ER stress-related apoptosis in rats.

Metabolic syndrome (MS) is a worldwide public-health concern defined as a set of metabolic alterations related to increased risk of cardiovascular diseases and type 2 diabetes. The raise of MS to epidemic proportions has been correlated to the exponential increase of added sugar consumption, especially among children. Notwithstanding, MS dysfunctions have also been associated to cognitive impairment and early development of dementias, although the mechanisms by which these interactions occur are still unclear. In this context, our study hypothesized that endoplasmic reticulum (ER) stress-activated pathways underlie the interconnection between long-term MS-dysfunctions and neurofunctional impairments.

Weaned Wistar rats were fed with high-sucrose diet (HSD) until 90 and 180 days of life (young and adult, respectively) and compared to both age-matched control (CTR) and middle-aged lean rats (OLD; 20 months old). Were assessed in these groups: MS-development; redox profile; cognitive, behavioral and motor functions; and hippocampal gene/protein expressions for ER stress adaptive (UPR-sensors Ire1?, Perk, Atf6; and chaperones Grp78, Grp94, Pdi A2, Calnexin, Calreticulin) and apoptotic pathways (Bcl2, Chop, Caspase, Parp1), as well as neuronal plasticity (Bdnf), antioxidant defense (Nrf2) and senescence (p53, p21). The post-weaned and prolonged HSD exposure induced MS-phenotype deepened with increased follow-up period marked by central obesity, hyperglycemia, dyslipidemia, steatosis, IR and oxidative stress. Besides, HSD showed motor deficit, anxiety and cognitive impairment similar to OLD rats. Noteworthy, HSD presented hippocampal ER stress characterized by failure of all-tested markers of adaptive signaling and increased expression of precocious cell death, as well as reduced plasticity and antioxidante defense, and accelerated senescence, a panorama similar to that found in OLD.

Our data reinforce the metabolic programming concepts, which establish that nutritional insults in the early stages of life (post-weaning, i.e.), increasing the predisposition for late development of chronic noncommunicable diseases, such as MS and dementias. Collectively, data herein presented successfully show that post-weaned and prolonged intake of sucrose leads to MS and oxidative stress, deepened by continuity of exposure, which in turn disrupt the ER homeostasis in hippocam-

pus and triggers the ER stress. In fact, the hippocampus of HSD young animals (3 months old) presented a transition from UPR-adaptive to pro-apoptotic signaling, while adult rats (6 months) had an ER stress pattern, marked by failure of any adaptive signaling and presence of apoptotic markers. That ER stress-derived apoptosis was related to hippocampal damages and directly contributed to accelerate neuronal aging and subsequently, cognitive, motor and behavioral impaiments. Finally, we established a relationship between cognitive decay and MS-driven hippocampal ER stress, shedding light into novel mechanistic pathways and opening up new venues for dietary interventions to prevent premature aging MS-caused.

ER stress • Early dementia • Sucrose diet

ORAL | Friday 9th 15:30-16:30 hrs.

B30110
Basic Science
Environmental Health And Neurodevelopment

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Maternal low-protein diet in pregnancy and lactation increase depressive behavior, glucocorticoid secretion and amygdala oxidative stress in male rat offspring

Suboptimal intrauterine environments predispose offspring to lifelong health complications. Maternal protein restriction during pregnancy and lactation, negatively affects offspring anxiety, learning and motivation; but few studies have addressed depressive behavioral outcomes. We evaluated effects of a maternal low-protein in pregnancy and lactation on male offspring depressive behavior, glucocorticoid production, and oxidative stress parameters in the amygdala.

Pregnant rats were fed with isocaloric diets during gestation and lactation and randomly assigned to two groups: Control (CC-20% of casein) and Restricted (RR-10% of casein). Around postnatal day 110, males were tested for two days (15 minutes first day and 5 minutes second day) in the Forced Swimming Test (FST).At the end of the test, serum corticosterone (CORT), ACTH and malondialdehyde (MDA) were measured. Oxidative stress biomarkers: MDA, reactive oxygen species (ROS), total superoxide dismutase (SOD) and glutathione peroxidase (GPx) were determined in the limbic system (amygdala). Statistical analysis by t-test ($P<0.05$). In the FST, the RR group exhibited a depressive type behavior characterized by increased immobility and decreased swimming behavior. Climbing behavior were similar between groups. CORT, ACTH and MDA serum levels were higher in RR vs CC. The amygdala from RR rats showed a significant increase in MDA and ROS as well as a higher SOD and GPx activity as compared to CC.

Maternal malnutrition during critical periods of development increases oxidative stress and negatively programs offspring behavior. The increased ROS productionmay lead to alterations in brain structures associated with cognitive and mood behaviors. We conclude that maternal low-protein diet during pregnancy and lactation results in depressive type behavior in male offspring. The increase in oxidative stress in the amygdala and glucocorticoid production may play a mechanistic role in the progression of behavioral deficits.

Drepession • Forced swimming • Oxidative stress

POSTER | Thursday 8th 10:40-11:40 hrs.

B30110

B30138
Basic Science
Environmental Health And Neurodevelopment

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Cognitive And Motor Decline In High-Sugar Diet-Induced Metabolic Syndrome In Postweaning Rats
Brasil

Premature cognitive and motor decline in male rats with metabolic syndrome induced by post- weaning high-sucrose diet intake.

Metabolic syndrome (MS) is characterized as a set of metabolic dysfunctions which are directly related to type 2 diabetes and cardiovascular diseases. Premature and prolonged consumption of added sugars has been associated to onset of several deleterious metabolic outcomes, likewise atrophy and electrophysiological changes in diverse brain areas, especially the hippocampus, resulting in cognitive and behavioral impairments. In this context, the present study aimed to investigate whether post-weaning intake of high-sucrose diet (HSD) is capable to promote late-in-life cognitive and motor declines, as well as assess the involvement of endoplasmic reticulum (ER) stress as an underlying mechanism.

Post-weaned Wistar rats were randomized into two groups: control (CTR, n = 6), which were fed a regular chow (10% sucrose, Nuvilab®); and obese (HSD, n = 5), which received a sucrose-rich diet (HSD, 25% sucrose). Both groups were followed up until 12 months old. To identify the MS development, the morphometry, biochemical/hormonal profile and insulin resistance were assessed. Additionally, motor and cognitive functions were respectively assessed in rotarod and water maze. Finally, the hippocampal expression of genes related to ER stress, apoptosis and senescence were performed. Our results showed that post-weaning and sustained exposure to HSD induce central obesity with visceral fat accumulation, dysglycemia, hypertriglyceridemia, glucose intolerance, insulin resistance and hepatic steatosis. HSD animals also presented motor and cognitive impairment (learning and memory) when compared to CTR. In addition, HSD rats showed ER stress characterized by increased expression of UPR-sensors (Ire1? and Perk) and decrease of chaperones (Grp78). Besides, the HSD rats showed reduction of anti-apoptotic gene (Bcl2) and increased senescence characterized by augmented P21 gene expression.

Our study was designed to mimic the nutritional environment, to which the current child population are exposed, where, as a rule, they have early and continuous access to added sugars throughout their life, which in turn could be related to increased predisposition for late development of chronic noncommunicable diseases, such as MS and dementias. Collectively, our data showed that sustained sucrose consumption initiated in early stages of life (post-weaning, e.g.) induces a

set of metabolic alterations, such as central obesity, dysglycemia, atherogenic dyslipidemia, insulin resistance and hepatic steatosis. Those metabolic alterations disrupt the ER homeostasis in hippocampus and lead to the ER stress, marked by apoptotic and senescence pathways. Moreover, that ER stress-derived apoptosis accelerated neuronal aging are directly associated to subsequent motor impairments and early dementia. In summary, our study originally established a relationship between cognitive decay and MS-driven hippocampal ER stress, shedding light into novel mechanistic pathways and opening up new venues for dietary interventions to prevent premature aging MS-caused.

High-sugar diet • ER stress • Cognitive decay

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30146
Basic Science
Environmental health and neurodevelopment

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Aspartame intake during adolescence cause depressive-like behavior and decrease hippocampal neurogenesis in male Wistar rats

Exposure to food additives, such as artificial sweeteners, during childhood and adolescence, has been increasing in recent years. However, the safe use and benefits of these products have been questioned. During these development phases, the nervous system has an intense ability to modify its morpho-functional organization in response to the environment. Thus, early interventions may contribute to long-term effects and can alter the susceptibility to psychopathologies. Based on this context, the main idea of this study was to investigate the effects of the chronic use of sweetened beverages, such as sucrose or aspartame (artificial sweetener), from prepuberty to late adolescence, evaluating depressive and anxiety-like behaviors and hippocampal neurogenesis in male and female rats.

After weaning (21 postnatal days - PND), male and female Wistar rats were divided into three experimental groups, according to the solution they received in the drinking water: control (water), sucrose (45g / L) and aspartame (2g / L). The solutions were available ad libitum from 21 to 56 PND. At 45 days of age, behavioral tasks were performed to evaluate the anxiety and depressive-like behaviors (open field and forced swim tasks). The animals were killed at 56PND. The brains were coronally sliced and the dentate gyrus was marked with doublecortin (DCX) and NeuN antibodies. Two random areas per region of interest were quantified per animal and the integrated density value per unit of the area was obtained. Statistical analysis was performed by one-way ANOVA. This project was approved by the Ethics Committee of UFRGS (#32823). No differences were found in the open field task. However, aspartame male group increased the time [$F(2,29)=5.95$; $p<0.01$] and decreased the latency to immobility [$F(2,29)=3.48$; $p<0.05$] in the forced swim task. Additionally, in the dentate gyrus, a decrease of DCX was found in male aspartame group [$F(2,17)=4.38$; $p<0.05$] with no differences between female.

From these results, it was observed that the consumption of aspartame solution during development caused a depressive-like behavior in the late adolescence, and this effect was observed only in males. In addition, this effect is not associated with a decrease in locomotor activity, since no di-

fferences were found between the groups in the open field task. Moreover, the mechanisms underlying these behavioral effects may involve a decrease in the hippocampal neurogenesis. Thus, these findings suggested that the consumption of an artificial sweetener, as aspartame, in sensitive periods for neural plasticity can affect the susceptibility to depression and brain plasticity. In this way, this study contributes to understanding how early events, such as nutritional factors, in puberty and adolescence, cause behavior and neurochemical changes related to psychiatric disorders, such as depression. Keywords (3): aspartame; adolescence; depression.

Aspartame • Adolescence • Depression

POSTER | Thursday 8th 10:40-11:40 hrs.

B30189
Basic Science
Environmental health and neurodevelopment

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Impact of different neonatal stress protocols on feeding behavior and mechanisms involved in weight control

The relationship between mother and offspring is important for mammals, thus the importance of maternal care and attachment in the first days of life. Traumatic events during this period may impair physiological and psychological development. Recent studies have demonstrated an important role of neonatal stress (NS) in controlling body weight (BW). Different pathways are possibly activated in distinct protocols of NS, contributing to different encephalic changes related to the control of BW and food intake. These changes may involve mechanisms related to appetite control and eating behavior. We investigated how different NS protocols alter behavior and mechanisms involved in appetite, eating behavior and BW, considering sex-specific differences for all aspec

The study was submitted to the Animal Research Ethics Committee (UFES 26/2017). A total of 75 Wistar rats were submitted to Maternal Separation (MS; rats separated from the maternal presence from 2nd to 14th postnatal days (PND), for 3 h/day) or a Maternal Deprivation (MD; rats separated from the maternal presence during two 24-hour periods in 9th and 11st PND). Control animals were kept under minimal manipulation. In the 21st PND, animals were weaned and submitted to standard housing conditions. In 60th PND, behavioral tests were applied: elevated plus maze, open field, consumption of palatable food (PF) and standard food (SF). The BW was measured once a week. After the behavioral tests, the animals were euthanized, and the amygdala dissected to analyze serotonin (5-HT) and its metabolite 5-HIAA using HPLC. We observed an effect of NS decreasing BW of males and females and increased anxiety related behaviors only in males. We also observed an altered SF intake, and an effect of MS increasing consumption of PF of males and females. NS decreased amygdalar 5-HT content in males, leading also to an increased 5- HIAA/5-HT ratio, but no cha.

Male rats were relatively more vulnerable to NS than females. These results confirm our hypothesis that different NS protocols can cause different changes in the body weight of animals, and that these results vary according to sex. Also, we confirmed that body weight changes are related to food consumption, which could be related to the increase in anxiety-related behaviors. In addition, we observed changes in the serotonergic content, which may be directly related to the results found on food consumption, in both sexes. Currently we are evaluating mechanisms related to appetite control, including neuropeptides and their receptors involved in the control of the appetite in the hypothalamus.

neonatal stress • body weight • appetite control

POSTER | Friday 9th 11:10-12:10 hrs.

B30189

B30256
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Environmental health and neurodevelopment

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Maternal docosahexaenoic acid (DHA) intervention prior and during pregnancy and lactation improves spatial learning and memory in male rat offspring

Obesity in pregnancy has short- and long-term implications for maternal and child health. Children born to obese mothers are at higher risk to develop obesity, behavioral and cardiometabolic alterations in adult life. DHA is a long-chain polyunsaturated fatty acid which is part of the neural membrane phospholipids, and impacts brain structure and function. Few studies have evaluated the effects of DHA intervention in pregnant obese women in offspring behavioral alterations. We hypothesized that maternal DHA intervention in obese pregnant rats before and throughout pregnancy and lactation would improve spatial learning and memory in male offspring.

From weaning throughout pregnancy and lactation female rats ate Control (C – 5% fat) or obesogenic diet (MO – 25% fat). At postnatal day (PND) 90, one month before maiting and during pregnancy and lactation, half of the females from each group were treated with 400 mg/kg/day of DHA orally; and kept with their respective diet. After weaning, offspring ate C diet. At postnatal day 130, male offspring were tested for two days (first- acquisition test and second- retention test) in the Morris Water Maze. In the acquisition test, no differences were observed in MO in comparison with C group. Escape latency to locate the platform area after 24 hours of learning was higher in MO vs C. MO group decreased number of entries to target zone as compared to C. No differences

were observed in time and distance in target zone among groups. Maternal intervention in the MO group (MO+DHA) decrease the escape latency in comparison with MO.

Maternal obesity impairs spatial memory retention without changes in the acquisition. DHA intervention improves spatial memory retention. Further studies are needed to evaluate the mechanism involved. This work was supported by ANR-CONACyT 2015-16-273510

Maternal Obesity • Offspring • Spatial Memory

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30263
Basic Science
Environmental health and neurodevelopment

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Distinctive changes in heart period and heart rate variability provoked by fetal gross movements and fetal breathing movements

The manifestation of fetal gross movements (FGM) or fetal breathing movements (FBM) has long recognized as a developmental milestone during pregnancy. Both type of movements are quantified to assess the biophysical profile and fetal well-being. Yet, the adaptive concomitant changes that these movements provoke in other variables such as the fetal heart-period (FHP) or the fetal heart rate variability (FHRV) are rarely considered as potential biomarkers. The objective of this study was to determine whether FGM or FMB introduce distinctive changes in FHP and FHVR regardless of the fact that both movements involve somatic activity and the recruitment of skeletal muscles.

Short-term transabdominal ECG data of low-risk gestations were collected at mid (from 23 to 34 weeks, N=12) and late gestation (from 35 to 40 weeks, N=22). Simultaneously, US B-mode recordings were obtained to identify fetal motor activity manifested either by FGM or FBM. Gestations ended at term, fetuses showed no complications along pregnancy and all presented > 2500 g and < 3800 g as newborn weight. The fetal ECG data were processed in coincide with FGM or FBM and also akinesia (A), when none of these movements were identified during 5-minute segments. FHP was quantified as the RR interval, and the Hilbert-Huang transform was used to quantify the FHRV. In comparison with A, fetuses at mid gestation presented a reduction of the FHP only during FGM ($p=0.032$), showing no significant differences in FHRV neither in FHP and FHRV during FBM. Yet, fetuses at late gestation did show a reduction of the FHP ($p<0.0002$) accompanied by differences in the amplitude of high-frequency components of FHRV ($p=0.002$) during FGM, and an increment of the FHP ($p<0.0001$) together with differences in both the amplitude of high- ($p=0.002$) and low-frequency components ($p=0.0003$) of FHRV during FBM.

Our main findings are that at late gestation fetuses already exhibit distinctive changes in FHP and FHVR in relation to FGM or FBM, whereas this distinction is not identified at mid gestation. Such changes suggest that the hemodynamic adjustments and autonomic adaptability, demanded by both type of movements, involve different regulatory responses mainly expressed by either an increased parasympathetic (cholinergic) modulation in case of FBM or a sympathetic activity (adrenergic) in case of FGM. The manifestation of FGM and FBM is identified as early of 7 to 8 and 10 to

11 weeks of human gestation, respectively. However, here we are reporting that the regulatory responses that these movements provoke are integrated latter in gestation, after 34 weeks, which could be then considered as potential developmental biomarker of the fetal autonomic adaptability. This adaptability is increasingly recognized as a key physiological mechanism to face challenges in the perinatal period and latter in life.

Fetal well-being • Autonomic system • Biomarkers

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30285
Basic Science
Environmental health and neurodevelopment

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MCGILL
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Differential susceptibility to positive environments influences childhood emotional eating according to genetically determined DRD4 gene expression on the PFC

Obesity has become a major global health problem and to better address this issue, it is crucial to understand how maladaptive feeding behavior develops during ones life. Genetic differential susceptibility states that individuals may vary both by exhibiting poor responses when exposed to adverse environments, and disproportionally benefiting from positive settings. Therefore, ones gene expression can moderate the influence of environmental variables on behavioral outcomes that lead to development and maintenance of obesity. Possible candidates are the dopamine-related genes, that affect neurocognitive outcomes and behavioral responsiveness to the environment, including the dopamine D4 receptor gene (DRD4).

We analyzed the interaction between a) a score for postnatal environmental buffer, that accounts for positive outcomes (adequate birth weight and gestational age, good maternal mental health, income, family function, secure attachment, no marital strains, presence of breastfeeding) and b) the genetically regulated gene expression of prefrontal DRD4, computed using a machine learning prediction method (PrediXcan), that estimates the component of gene expression determined by the genetic profile, imputing gene expression from the genotype information. The outcome measure was the emotional eating domain from the Child Eating Behavior Questionnaire at 48 months of age. The interaction between the positive environment and the predicted prefrontal DRD4 gene expression was significant (estimated beta= neg. 0.403, p=0.02), in which the high gene expression group had more or less emotional eating according to the exposure to lower or higher environmental support respectively, showing evidence of differential susceptibility criteria according to Roisman, since regions of significance were inside the range of the environmental variation (cross over point=3.4, PoI=0.52,PA=0).

This study provides data that shows how the genetic differential susceptibility, by means of predicted DRD4 gene expression, can moderate the impact of different environmental exposures on the onset of maladaptive feeding behavior, especially the impact of the positive postnatal environment. Adopting a differential susceptibility framework allows us to go beyond the diathesis-stress view, accounting for not only how vulnerable an individual is to adversity, but also how much it will benefit from supportive environments. This has implications for the development of several important health outcomes, including growth, obesity and metabolic alterations. Applying this novel approach to the developmental origins of health and disease agenda guides the elaboration of more efficacious and cost effective interventions, targeting individuals that would benefit the most from interventions.

Emotional eating • Gene expression • Environment

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30374
Basic Science
Environmental health and neurodevelopment

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Titulo Maternal protein restriction during gestation and the preimplantation period is associated with adult offspring sex specific long-term memory deficits and alt

Background Maternal protein malnutrition throughout pregnancy (LPD), the preimplantation period (Emb- LPD) and lactation compromises brain development in late gestation and after birth, affecting structural, biochemical, and pathway dynamics with lasting consequences for motor and cognitive function. Our group has previously shown that Emb-LPD and sustained LPD reduce neural stem cells (NSCs) in the fetal brain. Moreover, Emb-LPD causes remaining NSCs to upregulate neuronal differentiation in com- pensation beyond control levels and increase cortex thickness and neuron ratio, leading to short-term adult memory deficits. However, the importance of nutrition during pregnancy on long term hippocampal dependent memory and the glial populations is still widely unknown.

Metodos Female mice were fed different diets from conception: normal protein diet (NPD), low protein diet throughout pregnancy (LPD), or only the preimplantation period (Emb-LPD: LPD for 3.5 days, NPD thereafter). Offspring were maintained on standard chow after weaning at 3 weeks. Adult offspring (16 weeks old) underwent the alternating t-maze task. Mice were then sacrificed and brains removed for immunohistochemistry for astrocyte (GFAP) and microglia (IBA1) markers and hippocampi samples underwent RNA seq analysis. Both male and female Emb-LPD offspring showed decreased long-term memory, whilst only LPD males showed decreased memory with LPD female offspring being unaffected. Immunohistochemistry showed that LPD females present an increase in astrocyte density in the CA1 and dentate gyrus regions of the hippocampus ($p<0.001$) and a reduction of astrocyte density in CA3 region of the Emb-LPD female offspring hippocampus ($p<0.01$). Microglia density was also decreased in both Emb-LPD and LPD male and female offspring dentate gyrus and CA1 of the hippocampus ($p<0.0001$). Further RNA seq analysis on whole female hippocampus extracts showed LPD adult offspring had significant 4-fold incre

Conclusion The role of astrocytes in memory formation is highly debated, but recently hippocampal astrocytes in the CA1 have shown that astrocytic activation can dramatically potentiate synaptic transmission, promote memory allocation, and improve memory performance. Our data shows an increase in astrocytes in the LPD female CA1 and dentate gyrus. This increase in astro-

cytes coupled with the increase in BACE-2 expression in the female LPD hippocampus, which studies have shown over expression has neurocognitive protective role, could explain why the female LPD offspring have a normal long-term memory compared to their male counterparts and the Emb-LPD offspring. This data provides new evidence that neurodevelopment can be perturbed as early as the pre-implantation period with consequences which persist into adulthood. It also shows the LPD females have efficient compensatory mechanism to provide a normal long-term memory phenotype.

neuroscience • nutrition • behaviour

POSTER | Wednesday 7th 17:40-18:40 hrs.

B30411
Basic Science
Environmental health and neurodevelopment

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Hydroethanolic extract of azadirachta indica ameliorates metabolic and neurobehavioral parameters of rats with metabolic syndrome induced by high sucrose di

The excessive consumption of added sugars directly contributes to the epidemic Metabolic Syndrome (MS), which is associated with late- in-life cognitive decline, neurobehavioral changes and severe motor impairment. In order to prevent these damages, complementary therapies, including several medicinal plants, have been extensively investigated. In this context, we hypothesized that the hydroethanolic extract of Azadirachta indica leaf (HEAL), whose chemical composition confers it hypoglycemic, antioxidant and anti- inflammatory activities, has the potential to delay or prevent metabolic, cognition, behavioral and motor deficits in MS rats.

Weaned Wistar rats were randomized into 2 groups: Control (CTR), fed a standard chow, and High-Sucrose Diet (HSD), fed a high-sucrose diet. At 150 days of life, each group was split into 2 new groups, resulting in 4 groups: CTR, CTR-T, HSD and HSD-T, where T means those animals were orally treated with (300 mg/Kg/day) for 30 days, meanwhile their controls received tap water (1 mL/Kg/day). At the end of the treatment, morphometric profile (body weight, fat deposition, Lee index, food intake), insulin resistance (TyG), cognition (Morris water maze test), motor (rotarod) and behavioral parameters (forced swimming) were assessed. HSD induced a MS phenotype, which was characterized by central obesity, hypertriglyceridemia and insulin resistance. HSD animals also showed significant motor deficit without cognitive impairment. HEAL treatment promoted significant reduction of periepididymal, mesenteric, retroperitoneal fat pads, as well as attenuated hypertriglyceridemia of HSD-T animals, meanwhile no effect was observed in CTR-T group. Notwithstanding, HEAL treatment completely restored the performance of HSD-T rats on rotarod, suggesting an important neuromotor protective

This study reinforces that childhood consumption of high-sucrose diet leads to late-in-life metabolic alterations in parallel with severe motor damage. The treatment with HEAL promoted lipolytic activity, attenuation of hypertriglyceridemia as well as significant neuromotor protection. In part, these biological actions are attributed to the mixture of polyphenols found in the leaf of A. indica, supporting the use of this plant species as a complementary therapeutic tool

metabolic • neuroprotection • neem

POSTER | Friday 9th 11:10-12:10 hrs.

B30411

B30467
Basic Science
Environmental health and neurodevelopment

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B-estradiol 17-valerate as a possible endocrine reproductive disruptor in fish.

B-estradiol 17-valerate (EV) is a synthetic estrogen widely used in combination with other steroid hormones in hormone replacement therapy drugs and has been detected in natural waters. Although EV is known as an estrogenic chemical, few studies have focused on the developmental and reproductive toxicity of EV in aquatic species, such as fish. Studies with EV in fish has been conducted mainly on sensitive life stage of fish like sexual differentiation or embryonic stage. The aim of this study was to determine whether a exposure to different concentrations of EV would cause detectable endocrine disruption to adults Astyanax altiparanae, a small characid fish widely distributed in South America.
A total of 40 adult males were used for this study. Fishes were divided into four tanks of 10 individuals (5 males and 5 females). Three tanks were dosed with EV at 10, 800 and 8000 ng/L and one tank control. After 14 days of exposure, animals were euthanized, and gonads were fixed in Bouin's solution, paraffin-embedded, sectioned, and H&E stained and submitted to histological analysis by light microscopy. Some EV-exposed male at concentration of 800 and 8000 ng/L had an occurrence of intersexuality, in which vitellogenic oocytes scattered throughout testicular tissue were observed. No histological differences were observed in female gonad sections.
This study evaluated the effects of EV on adult-life. Under our experimental conditions, the presence of intersex male fish demonstrated that EV can be an endocrine disruptor of the reproductive system in fish acting in a short time of exposure. Studies of the effects of EV over longer periods of exposure and other phases of development may provide a more definitive answer as to the endocrine impacts of EV exposure and any impacts on reproduction. In addition, complementary studies, such as demonstrating the expression of vitellogenin in males' liver, will be conducted for a better understanding of the mode of action of EV.

B40012
Basic Science
Life style and perinatal nutrition

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Newborn offspring from obese-resistant mice are partially protected from the metabolic disturbances that may be driven by hepatic Let7 modulation

Recent studies indicate that Let7 may be involved in energy homeostasis, and an in silico analysis revealed that Prkaa2, the gene that encodes AMPK, is a predicted target of this microRNA. AMPK is an essential cellular energy sensor and, when activated in the liver, this protein decreases hepatic glucose production as well as TG content, by increasing oxidation and inhibiting SREBP1c lipogenic activity. Changes in nutritional status at critical developmental phases may lead to a phenomenon known as metabolic programming, which, in turn, can be triggered by epigenetic mechanisms. Thus, this study aimed to investigate the potential role of Let7 in regulating AMPK levels and its consequences for the metabolic disturbances observed in the newborn offspring from high-fat diet fed mice.

Female Swiss mice were fed chow (C) or an HFD for an adaptation period before mating. HFD females were classified into 2 groups: obese prone (OP) or obese resistant (OR), according to their weight gain. OP females presented elevated fasting glucose, insulin and NEFA prior to delivery. Male newborn offspring from OP dams (OP-O) showed lower body weight, but higher serum glucose and insulin, when compared to offspring from C dams (C-O). Oil Red and PAS staining revealed higher lipid and lower glycogen content in the liver of OR-O and even more pronounced altered phenotype in OP-O, suggesting that insulin resistance may be present as early as birthday in offspring from obese HFD fed dams. Let7 expression was upregulated in the liver of OP-O in comparison to OR-O and C-O. Lin28a, an RNA-binding protein that controls Let7 expression, was found to be downregulated in OP-O at transcriptional and protein levels. mRNA and protein content of PI3K were also lower in the liver of OP-O. Moreover, AMPK mRNA and protein levels were lower, while SREBP1C and FAS content were upregulated in the same group. Furthermore, preliminary in vitro inhibiting of Let7 lead to higher AMPK content.

It had been already showed that early exposure to nutritional overload leads offspring to metabolic disturbances that may be driven by epigenetic mechanisms, such as miRNAs expression. Nevertheless, this is the first study to show that maternal consumption of an HFD in the absence of obesity does not disturb the metabolic homeostasis of newborns at the same level of when obesity is ins-

talled. Furthermore, we showed that AMPK may be a direct target of Let7 and that these molecular changes may be involved with the programmed phenotype of offspring from obese-prone dams. In summary, our results demonstrate that hepatic AMPK modulation may be driven by the microRNA Let7, which can lead to metabolic disturbances at different levels in newborn offspring from obese-prone and obese-resistant mice.

maternal diet • offspring health • microRNAs

ORAL | Thursday 8th 09:40-10:40 hrs.

B40022
Basic Science
Life style and perinatal nutrition

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Naringin supplementation during pregnancy alters offspringÃƒÂ¢Ã¢â€šÂ¬Ã¢â€žÂ¢s redox homeostasis and mitochondrial function in prefrontal cortex

Naringin is a flavonoid glycoside mainly found in citrus fruits as rough lemon and grapefruit. Several studies using animal models of cognitive dysfunction have been demonstrating the beneficial effects of naringin supplementation on improving brain cognitive health through its antioxidant capacity. Nevertheless, these studies use adult animals and do not consider the effects that naringin supplementation during pregnancy might trigger in the offspring, especially in the central nervous system. Thus, in our work we evaluated the effects of naringin supplementation to pregnant rats on redox homeostasis and mitochondrial function in female offspring prefrontal cortex and the performance of male offspring in a memory task.

Pregnant Wistar rats were separated into two groups: control (vehicle) and naringin (100 mg/kg), treated by oral gavage during pregnancy. On postnatal day (PND) 1, 7, and 21, female pups were euthanized and prefrontal cortex was dissected for biochemical essays. Data was analyzed by Studentâ€™s t test or Mann Whitneyâ€™s test and considered significant when $p<0.05$. The project was approved by a ethical commission (CEUA-UFRGS nÂ° 31397). It was observed increased nitric oxide levels on PND1, but no alterations on PND7 and 21. We found increased superoxide dismutase and decreased thyoredoxin reductase activity on PND1 along with no alterations on the other ages evaluated here. However, catalase activity was increased only on PND7, but not on PND1 and 21. Thiol and carbonyl levels were both increased on PND1, but unaltered on PND7 and 21 along with no alterations on GSH content. Mitochondrial mass and membrane potential were both decreased on PND1, unaltered on PND7, and only mitochondrial mass was increased on PND21. Only complex II was increased on PND7, with no other alterations on the other mitochondrial enzymes. No alterations were found in t

Our work demonstrated that naringin supplementation to pregnant rats disrupted offspringÃƒÂ¢Ã¢â€šÂ¬Ã¢â€žÂ¢s redox homeostasis and mitochondrial function. On PND1, it seems that a negative modulation of the redox network occurred in the prefrontal cortex with a progressive decline in the number of alterations observed on PND7 and PND21. This shift might indicate a possible recovery of the programming effects triggered by maternal naringin consumption. Moreover, despite the biochemical alterations found in female offspring prefrontal cortex we did not find

any cognitive alterations concerning the male offspring submitted to the open field and object recognition tests. Thereby, our findings demonstrate that caution needs to be taken when considering naringin supplementation during pregnancy and evidence the need to further clarify how this phytochemical impacts offspringÃƒÂ¢Ã¢â€šÂ¬Ã¢â€žÂ¢s health and how long these alterations might last throughout adult life.

prenatal • programming • naringin

POSTER | Wednesday 7th 17:40-18:40 hrs.

B40023
Basic Science
Life style and perinatal nutrition

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Effect of Naringenin Supplementation and/or Exercise Practice during Pregnancy on Offspring Postnatal Overnutrition: Brain Redox Homeostasis at Weaning

Prenatal and early postnatal environments have major influence on health in adult life. Early overnutrition enhances the risk for the development of chronic diseases, while maternal intake of flavonoids or exercise practice during pregnancy seem to cause metabolic adaptations that bring health benefits to offspring. Our objective was to evaluate if maternal exercise practice allied or not with naringenin supplementation during pregnancy could protect against possible postnatal overnutrition insults induced by reduced litter size during lactation.

Female Wistar rats were divided into four groups during pregnancy: (1) sedentary allied to vehicle intake, (2) sedentary allied to naringenin intake, (3) swimming exercise allied to vehicle intake, and (4) swimming exercise allied to naringenin intake. One day after birth, the litter size was adjusted to control (8 pups) or overfed (3 pups). Offspring was euthanized at weaning, when plasma, fat tissue and brain structures were collected. Plasma glucose, total cholesterol, and triglyceride levels were measured, and redox parameters evaluated on pupsâ€™ cerebellum, hippocampus, and hypothalamus. Experiments approved by the local Ethics Commission, number 31307. Litter size reduction cause higher body weight and fat mass, that was reduced by maternal exercise and naringenin supplementation. Maternal interventions when isolated also cause reduced glucose plasmatic levels in offspring nurtured in control litters. In cerebellum, reducing the litter size caused decreased activity of thyoredoxin reductase, which was prevented by maternal supplementation with naringenin. Hippocampus and hypothalamus showed augmented in antioxidant enzymes activities in resp

Postnatal early overnutrition leads to higher weigh gain and fat mass at weaning, which was partially reduced by the maternal exercise practice or naringenin supplementation during pregnancy. The positive effect of these maternal interventions was also demonstrated by the reduced pupsâ€™ glycaemia. As we hypothesize, when maternal exercise during pregnancy was allied to naringenin supplementation, the offspring presented similar results to those born from sedentary mothers, demonstrating the abolition of the effects. In summary, exercise or naringenin supplementation during pregnancy can be important interventions for combating the increasing rates of overweight and related disorders, and more in-depth studies are required to assess the exact mechanism behind the effects of pre and postnatal interventions.

metabolic progra • redox status • polyphenol

POSTER | Wednesday 7th 17:40-18:40 hrs.

B40023

B40024
Basic Science
Life style and perinatal nutrition

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Moderate Caloric Restriction In Pregnant Rats Affects Mitochondrial Biogenesis And Redox Homeostasis In The Pupsâ€™ Prefrontal Cortex

Caloric restriction (CR) is known as the best strategy to promote health and life span in adult animal models, promoting redox homeostasis and increasing mitochondrial biogenesis. When applied during pregnancy, it seems to promote negative alterations in pupsâ€™ health, which develop the thrifty phenotype. However, most studies apply gestational CR without malnutrition prevention. Considering the over nutrition and sedentary behavior of laboratory rats, we aim to show the beneficial effects of 20% gestational CR in pupsâ€™ prefrontal cortex from birth to adulthood with responsibly malnutrition prevention by balancing micronutrients consumption between groups. This is an important strategy to be studied, since 1 of 5 pregnant women is overweight or obese.

Female Wistar rats underwent 20% gestational CR supplemented with micronutrients by gavage. Control received ad libitum food and the vehicle. Pups were euthanized in postnatal day (PND) 0, 7, 21, and 60; prefrontal cortex was dissected. Dichlorofluorescein (DCFH) oxidation, mitochondrial superoxide (Oâ€¢âˆ’2), nitric oxide (NOâ€¢), mitochondrial mass and membrane potential were analyzed by flow cytometry. Superoxide dismutase, (SOD), catalase (CAT), glutathione peroxidase (GPx), glutaredoxin (Grx) activities and protein oxidation by spectrophotometry. Reduced glutathione (GSH) by fluorimetry. Vitamin C and lipid oxidation by HPLC. Data analysys: multiple t tests, $p<0.05$ considered significant; presented as meanÂ±S.E.M. Ethics comission approval (CEUA): 30044. On PND0, DCFH oxidation was increased, Grx activity and GSH were decreased. Mitochondrial mass and membrane potential were increased. On PND7, DCFH oxidation was decreased, NOâ€¢ was increased, CAT activity was increased and lipid oxidation decreased. On PND21, NOâ€¢ and lipid oxidation were decreased. On PND60, mitochondrial mass and membrane potential, SOD, CAT, Grx, TrxR, GSH and vitamin C were

Pups born to restricted dams had increased mitochondrial biogenesis, increased oxidants content, and decreased enzymatic and non-enzymatic antioxidant defenses, namely Grx and GSH, at birth. On PND7, Grx returned to control levels and CAT was activated promoting DCFH oxidation decrement and protecting pups against lipid oxidation despite NOâ€¢ increment. On PND 21, most parameters were unaltered (except NOâ€¢ content and lipid oxidation, which were decreased). On PND60, the pups show incredibly increased redox profile and mitochondrial biogenesis. Enzymatic

and non-enzymatic antioxidant defenses were vastly activated in this age and lipid oxidation remained decreased. Most works showing detrimental effects of gestational CR correlate these effects to reduced weight at birth. We believe that our model promoted brain protection because the moderate restriction protocol associated to malnutrition prevention did not reduce birth weight in pups despite promoting reduced weight in dams. We further state our concern on laboratory animals over nutrition and absence of malnutrition prevention on CR protocols.

Mitochondria • Redox status • Restriction

POSTER | Thursday 8th 10:40-11:40 hrs.

B40073
Basic Science
Life style and perinatal nutrition

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Early tobacco exposure alters corticosterone levels and ACTH receptor in adult rats by sex-dependent manner: effects on lipogenesis

Maternal smoking is related to obesity and metabolic dysfunctions in both childhood and adulthood; however, mechanisms are unknown. In a rat model of postnatal tobacco exposure, we have reported overweight and higher central fat depot in the adult offspring of both genders. Cortisol is altered during stress and may contribute to an obesogenic phenotype, since this hormone is associated with increased adipogenesis and lipogenesis in visceral adipose tissue (VAT), and also with lipogenesis in liver. We tested if maternal smoking during lactation causes alterations in glucocorticoids levels, metabolism and action as well as in ACTH receptor and contribute to alterations in protein expression related to adipogenesis and lipogenesis in VAT and liver of adult rat offspring from both genders.

Experiment was approved by Animal Care and Use Committee. To mimetizing the maternal smoking, at PN3, dams and offspring of both sexes were exposed to a smoking machine, 4x/day/1h (S). Control animals were exposed to ambient air. Offspring were evaluated at PN180. Plasma corticosterone was measured by RIE. Protein expression was determined by Western Blot: type 2 melanocortin receptor (MC2R) was evaluated in adrenal gland; type 1 11Î²-hydroxysteroid dehydrogenase (11Î²-HSD1), glucocorticoid receptor (GR), acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS) and peroxisome proliferator-activated receptor gamma (PPAR-Î³) were measured in VAT and liver. Corticosterone was lower in male (-33%) and higher in female offspring from S group (+1.5 fold). In adrenal, we found higher protein expression of MC2R in both genders from S group (+52% male; 1.3 fold female). We did not find changes in GR and 11Î²-HSD1 in VAT and liver in both genders. However, ACC and FAS contents were higher in VAT only in male of S group (1 and 1.3 fold, respectively). In liver, PPAR-Î³ and ACC content were higher in male S offspring (+2.4 fold; +33%, respectively), while in female only ACC was higher (1.1 fold

Tobacco exposure during suckling phase induces overweight in both genders by distinct mechanisms. We suggest that both male and female present a HPA-axis dysfunction instead of changes in glucocorticoids metabolism and action. We also evidence that lipogenesis in VAT and liver are more influenced by postnatal smoke exposure in the males than in females.

Tobacco • lipogenesis • sexual dimorphis

POSTER | Wednesday 7th 17:40-18:40 hrs.

B40073

B40075
Basic Science
Life style and perinatal nutrition

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Short And Long-Term Effects Of Bisphenol S (Bps) During Pregnancy And Lactation On Biochemical And Hormonal Profile In Rats

Babies are exposed to bisphenol A by placenta and milk, and this endocrine disruptor was already related to future metabolic diseases. Nowadays, based on several adverse effects on health, bisphenol A has been replaced by its analogue, the bisphenol S (BPS), although little is known about its effects. Additionally there are no data on the short and long-term effects of BPS exposure in critical windows of development. Here we studied the effects of maternal BPS exposure during gestation and breastfeeding on the biochemical and endocrine profiles of dams and offspring.

All the experiments were approved by Animal Care and Use Committee (CEUA/016/2017). Female Wistar rats were divided into three groups: BPS10 (10ÃŽÂ¼g/kg/day), BPS50 (50ÃŽÂ¼g/kg/day) and control - CON (vehicle). BPS was diluted in ethanol 0.1% (vehicle) and administered by gavage to CON and BPS groups throughout gestation and lactation. Dams were euthanized at weaning and offspring at PN21 and PN180. At weaning, male pups of BPS50 group had hypotriglyceridemia and hyperthyroxinemia, whereas the females of BPS50 group showed higher 25(OH)D levels. Adult male and female offspring of BPS-treated groups presented a lower food intake, despite no change of body weight. Males from BPS-treated groups showed lower visceral fat mass, while females had normal visceral fat. At PN180, males of BPS50 group had higher serum triglycerides and lower serum T3. Concerning the female offspring, both BPS-treated group showed lower serum T4. Females of BPS10 group had lower progesterone, while females of BPS50 group had higher serum 25(OH)D.

Our data evidence that BPS, despite being BPA substitute, promote biochemical and hormonal changes in offspring of both genders when administered at critical periods of development, suggesting their participation in late metabolic dysfunctions. More research is needed due to a shortage of literature regarding this compound and to explain the mechanism underlying the difference in visceral fat mass of both genders and the role of vitamin D.

imprinting • bisphenol •hormones

POSTER | Wednesday 7th 17:40-18:40 hrs.

B40075

B40078
Basic Science
Life style and perinatal nutrition

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Early low-protein treatment programs weaning rat pups to weak cholinergic-muscarinic activity

Malnutrition in early stages of life development implicates several metabolic disruptions that leads to long-term consequences in metabolism. Metabolic dysfunctions such as type 2 diabetes is one of the most common long-lasting diseases on that issue. Herein, we aimed to assess the muscarinic-cholinergic pathways, as well as metabolic parameters in weaning male rats that were malnourished during the first two third of lactation.

Lactating dams were fed a low-protein (4%, LP group), while control dams were fed a normal-protein diet (20.5% NP group). At weaning, a batch of rat offspring underwent a surgery to isolate and records superior vagus nerve tonus. Another batch of fasted rats were submitted to an intraperitoneal glucose tolerance test (ipGTT, 2 g/kg). Blood samples, visceral fat pad and pancreatic islets were removed to evaluate biochemical, biometrical and functional parameters. LP-rats showed reduced body weight (Ã¢â‚¬â€œ41.1%, P<0.001), mesenteric (Ã¢â‚¬â€œ24.5%, P<0.01) and retroperitoneal fat pads (Ã¢â‚¬â€œ68.1%, P<0.001). In fast condition LP-rats were hypoglycemic (Ã¢â‚¬â€œ19.4%, P<0.01) and hypoinsulinemic (Ã¢â‚¬â€œ57.1%, P<0.01). In comparison to NP-rats, glycemia from LP-rats increased by 58.8% (P<0.001) during the ipGTT. Insulinotropic response in LP-rat islets were decreased in 46% by glucose 8.3mmol/L and in 21% by acetylcholine 10Ã‚Âµmol/L (P<0.05). The use of 4-DAMP 10Ã‚Âµmol/L, a selective antagonist for muscarinic receptor subtype M3 reduced insulin secretion by 63.4% in NP- and by 6.7% in LP-rat islets (P<0.01). Vagus nerve tonus decreased by 30.

Low-protein diet in suckling phase disrupts cholinergic pathways controlling glucose-insulin metabolism in male rat offspring, which can contributes to high risk to type 2 diabetes onset as long-term consequence.

Malprogramming • insulinotropic • pancreatic islet

POSTER | Friday 9th 11:10-12:10 hrs.

B40078

B40096
Basic Science
Life style and perinatal nutrition

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Post-weaning exposure to high-sucrose diet gradually downregulates hepatic ER stress adaptive pathways and potentiates de novo lipogenesis in male mice

Non-alcoholic fatty liver disease (NAFLD) is an emerging metabolic syndrome-related disorder characterized by abnormal intrahepatic triglyceride accumulation (steatosis) in the absence of chronic alcoholism and other liver diseases, predisposing people to severe hepatic diseases, such as cirrhosis and hepatocarcinoma. NAFLD onset is intimately associated with sugar overfeeding, which leads to increased de novo lipogenesis (DNL) and decreased insulin sensitivity in the liver. The molecular mechanisms involved in NAFLD progression are still elusive, although evidence has proposed a role for the endoplasmic reticulum (ER) stress. Thus, the present study aimed to investigate the role of disrupted DNL and ER stress on NAFLD development induced by high-sucrose consumption.
Post-weaned Swiss mice were fed a high-sucrose diet (HSD) for 30, 60 and 90 days and compared to those fed a regular chow. Metabolic syndrome (MS) development, liver fat content, histological analysis and hepatic gene expression of DNL and ER stress markers were assessed. Exposure to HSD promoted MS development in a time-dependent manner marked by central obesity, hyperglicemia, dyslipidemia and insulin resistance (IR). Moreover, these animals presented increased fat liver content and microvesicular steatosis. After 30 days of nutritional intervention, it was found a balance between fatty acid synthesis (Chrebp and Scd1) and oxidation (Ppar?) markers, as well as upregulation of ER stress adaptive pathways featured by increased gene expression of UPR sensors (Ire1?, Perk and Atf6), chaperones (Grp78 and Pdi A1) and antioxidant defense (Nrf2). However, from 60 days on HSD, there was marked increase in gene expression of DNL transcription factors (Chrebp and Srebp-1c), exponential raise of fatty acids synthesis (Scd1), and ER stress response moving toward a pro-apoptotic pattern, characterized by gradual increase of Chop gene expression.
Exposure to sucrose-rich diet after weaning and for short period (30 days) triggered metabolic changes and UPR-adaptive signaling to reach a balance between the synthesis and oxidation of fatty acids in the liver, keeping the steatosis onset under control. However, upon exposure for longer periods (60 – 90 days), it was observed the establishment of an obesogenic profile marked by dyslipidemia and IR, accompanied by upregulated expression of genes related to fatty acid synthesis and ER stress apoptotic pathways. That uncontrolled lipogenesis associated to ER stress

were crucial to microvesicular steatosis development, a precursor stage for more severe liver diseases. Considering the elevated consumption of added sugars, especially among children, our set of data reinforce the concepts of metabolic programming, which establish that insults in the early stages of life (for example, post-weaning) impact on individuals geno- and fenotype, increasing the predisposition and posterior aggravation of chronic non-communicable diseases, such as MS and NAFLD.

ER stress • NAFLD

ORAL | Thursday 8th 09:40-10:40 hrs.

B40114
Basic Science
Life style and perinatal nutrition

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Sympathetic hyperactivity in undernourished rat at lactation can be blocking obesity onset

It has been known that nutritional insults during perinatal life impair energy metabolism and autonomic nervous system in later life. Given that, obesity is one of the most common metabolic dysfunction observed in later life, and considering that brown adipose tissue (BAT) is the main thermogenic tissue controlling energy expenditure, we hypothesized that sympathetic hyperactivity may be preventing obesity in rat- offspring whose dams underwent food restriction in lactation.

The control dams were fed ad libitum throughout lactation, whereas food restricted group (FR50 group) received just 50% of diet offered to control dams until the day 14th of lactation. At 21-day-old, rat- offspring was weaned and the body weight and food intake assessed each two days until 100-day-old. Food intake at dark-cycle (6 PM to 11 PM and 6 PM to 6 AM) was evaluated. Body weight and mesenteric fat pad, as well as the extensor digitorum longus (EDL) muscle were used to assess the body composition. The weight of BAT was quantified, as a marker for sympathetic nervous activity. When compared to control rats, the assessment of area under the curve (AUC) of body weight gain from FR50 rats displayed a decreased of 9%, while the AUC of food intake was increased by 10% (P<0.01). The food intake of FR50 rats, at dark-cycle, was equal in the first 4h and 13% higher in overnight (P<0.01). In relation to control group, the body composition markers in FR50 rats were reduced (mesenteric fat pad, Ã¢â‚¬â€œ36%, P<0.05; and EDL, Ã¢â‚¬â€œ52%, P<0.01). By other hand, BAT was 38% higher in FR50 rats (P<0.001) than control ones.

Calorie-restriction just at the first phase of lactation implies a lean phenotype, even associated with a paradoxically hyperphagia, or in other words Ã¢â‚¬Å“obesity resistanceÃ¢â‚¬Â”. It might be due to high BAT that implicates hyperactivity of the sympathetic nervous system that blocks body weight gain.

Malprogramming • **thermogenesis** • **food-restriction**

POSTER | Wednesday 7th 17:40-18:40 hrs.

B40114

B40118
Basic Science
Life style and perinatal nutrition

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Soy beans isoflavone recovers Î²-cell function and preventing type 2 diabetes

The prevalence of diabetes has become a serious public health challenge around the world. Type 2 diabetes is typically accompanied by obesity and insulin resistance. Nutritional studies with humans and animal model suggest that the ingestion of soy isoflavones reduces insulin resistance and improves glucose control. Soy beans products containing isoflavones have been highlighted a potential dietary component to preventing type 2 diabetes and metabolic dysfunction.

To test this hypothesis male Wistar rats at postnatal day 3 (P3) were programmed to metabolic dysfunction by small litter animal model (SL). At P30 the animals were gavaged with soy beans isoflavone (300mg/day) or water vehicle. At P90 all the groups were examined to observe the effect of isoflavone treatment in biometric and biochemical parameters, in vivo and in glucose insulinotropic response in isolated pancreatic islets. The results showed that SL rats presenting metabolic dysfunction, such as, high fasting plasma glucose and insulin, insulin resistance, increased body weight, adiposity. On the other hand isoflavones treatment inhibited metabolic dysfunction in SL rats. Interestingly glucose insulinotropic response was enhanced by isoflavones in isolated islets. Isoflavones also was able to increase insulin release in islets from rats previously treated with soy beans isoflavones.

The current results suggest that soy beans isoflavones long-term supplementation improve pancreatic Î²-cell function and can be preventing type 2 diabetes and obesity.

Isoflavones • Type 2 diabetes • Î²-cell function

POSTER | Thursday 8th 10:40-11:40 hrs.

B40118

B40121
Basic Science
Life style and perinatal nutrition

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In vitro amino acid restriction programs pancreatic beta-cell to changes in heat shock protein response when challenged by glucolipotoxicity.

Amino acid restriction in neonatal period decrease cell proliferation in pancreatic islets and increase cellular apoptosis, which in the future may leads to development of type 2 diabetes at adulthood. Proteins called heat shock proteins (Hsp) are one of the primary cellular protection responses, which play a key role both during the synthesis, assembly, folding and degradation of proteins, and in preserving cell survival under adverse environmental conditions. The Hsp70 interacts directly with elements of the apoptotic pathway and inhibited the cascade of events that culminate in cell death by apoptosis. We aimed to investigate the effects on Hsp70 and Hsp90 protein content in amino acid restriction on INS-1E cells challenged by glucolipotoxicity exposure.

INS-1E were treated for 48 hours in RPMI 1640 medium supplied with 5% FCS and 11 mmol/l glucose, with 100% (Control-C) or 25% (Malnutrition-M) of amino acids solution (RPMI 1640 Amino Acid Solution 50x R7131/ Sigma) at 37 celsius degrees in a humidified atmosphere of 95% O2 and 5% CO2. After 48 hours of amino acid restriction (Malnutrition), we treated the cells with glucose (25mM) and palmitate (500nM) for 6 hours (Control Glucose+Palmitate - C+GP or Malnutrition Glucose+Palmitate - M+GP). We evaluated the Hsp70, Hsp90, Hsp90 alpha and beta and Bax/Bcl-xl ratio protein content by Western Blot. The results were expressed as mean Ãƒâ€šÃ‚± SEM. Statistical significance was determined using Student t-test, p<0.05 was considered significant. We observed that, amino acid restriction followed by glucolipotoxicity exposure, reduced Hsp70 protein content in M+GP (3.87 Ã‚± 0.85, p<0.05) when compared to C+GP cells (7,08 Ã‚± 1.06, p<0.05), despite no changes were observed in Hsp90 and Hsp90 alpha and beta. However, we observed statistical significance reduction in Bax/Bcl-xl ratio in M+GP (0.84 Ã‚± 0.59, p<0.05) when compared to C+GP cells (2.68 Ã‚±

According to these results, we observed that the cellular machinery which protecting against apoptosis is altered in pancreatic beta cells and Hsp70 could be one of the protein modified by the amino acid restriction and may leads cell death when exposed to glucolipotoxicity.

amino acids • programming • Beta cells

POSTER | Thursday 8th 10:40-11:40 hrs.

B40121

B40128
Basic Science
Life style and perinatal nutrition

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Estradiol increases the insulin sensitivity in protein restriction animal model through estrogen receptor alpha.

Perinatal protein restriction increases insulin sensitivity in peripheral tissues and reduces insulin secretion by pancreatic beta cells in mice. Estradiol (E2) is a steroid hormone involved in the control of energy balance and glucose homeostasis. Estrogen receptors (ERs) are implicated in insulin biosynthesis and secretion, as well as, insulin sensitivity. The aim of this study was to assess the role of ERs on glucose homeostasis of protein restriction mice and the effect from 17-beta-estradiol in them.

Post-weaned Swiss male mice were fed with low protein(LP;6%) or control(C;14%) diet during 8w. We analyzed body weight(bw), and insulin, protein and albumin plasma levels to confirm the malnourishment phenotype. Also, we verified insulin sensitivity(IS) and the effect of 10ug/KgE2 on LP mice by hyperinsulinemic-euglycemic clamp, and Western blot in peripheral tissues. Data were expressed as mean and analyzed using T-test. LP diet reduced bw($p<0.001$), plasma insulin($p<0.01$), albumin($p<0.05$) and protein($p<0.05$). The hypersensitivity to insulin was demonstrated by the higher glucose infusion rate(GIR) in LP than in C group during clamp. The stimulation with E2, in the clamp, increased the GIR in LP compared with C group($p<0.01$). In addition, E2 increased the glucose uptake on peripheral tissues($p<0.01$). To verify if these effects were produced by ER, mice were treated(500ug/Kg/day) with ICI and MPP, ER antagonists, during 4d. In these mice, the effect of E2 on GIR and uptake were absent. MPP, an ERa antagonist, also prevented the effect of E2 to enhance IS. We observed an increased activity of insulin pathway, represented by a higher pAKT in LP muscle

This data shows a greater impact from E2 in LP mice improving the insulin sensitivity in muscle tissue. Based on these data, we conclude that the effect of estradiol enhanced the insulin sensitivity on malnourished mice was produced by estrogen receptor alpha, through an increased (serine) AKT phosphorylation in muscle. This work was supported by FAPESP CEPID-OCRC.

malnourishment • estradiol • estrogenreceptor

POSTER | Friday 9th 11:10-12:10 hrs.

B40128

B40142
Basic Science
Life style and perinatal nutrition

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Litter Size Reduction Induces Hyperphagya And Obesity When Expose To High Calorie Diet In Adult Life

Obesity and protein-restricted lactating dams affect body weight and hormonal states of neonates, via milk, inducing metabolic programming to offspring. This effect becomes more evident when these animals are exposed to an abundant food environment. The objective of this study was to evaluate the effect of animals from a reduced litter that were exposed to a high glycemic diet.

: Male rats were mated with nulliparous rats in the polygynous mating system (3 females for each male), both aged 70 to 90 days. The female rats were separated into individual boxes after the visual confirmation of the pregnancies. Thus, 24 litters were obtained, which were distributed into 2 experimental groups, defined by the number of offspring during the lactational period. The Normal Litter group (NL) was maintained with 9 pups/ dam and the Small Litter (SL) group was maintained with 3 pups/ dam. These groups were divided into 2 more group: NN-CAF (n-12) animals that received cafeteria diet and SL-CAF (n=12) animals that received cafeteria diet for 30 days until 90 days of life. The animals SL showed increase of food intake when compared to NL, the group exposed to cafeteria diet showed an expressive increase of food intake more evident in SL group.

Animals that were expose to cafeteria diet increased 37% when to compare SL-CON group and 7% to NL-CAF. This profile was similar in body weight, mesenteric depot and retroperitoneal depot. The reductions in litter size during lactation stages promote changes in offspring, this change was evident when the offspring was expose to high calorie diet. Promoting hyperphagia and increases in fat depot

litter size • programing • cafeteria diet

POSTER | Thursday 8th 10:40-11:40 hrs.

B40142

B40176
Basic Science
Life style and perinatal nutrition

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Transgenerational Effects Of Chronic Maternal Exposition To High Sugar/Fat Diet And Physical Training

Pregnant individuals who overfeed are more likely to expose their fetus to the development of metabolic disorders in their adulthood. Physical training is a mechanism for the prevention and treatment of these disorders, since it improves metabolism and body composition. This study evaluated the protective effect of physical exercise against possible metabolic changes in generations F1 and F2, whose mothers were submitted to a high sugar/fat (HS/F) diet.

Wistar rats belonging to generation F0 were grouped in four groups (n=10): CSed and CExe; DSed and DExe. From 21 days of age until the end of the lactation period, CSed/CExe animals received standard feed, and DSed/DExe animals received HS/HF diet. Animals from groups CExe/DExe underwent physical training from 21 to 120 days of age. Males and females in generations F1 and F2 received normocaloric feed and did not perform physical training, being clustered into four groups (n=10) according to the maternal generation which they belonged to. In generation F0, there was an increase in body weight, adiposity, glucose and lipidic profile; the exercise reduced the biochemical parameters between groups DSed/DExe. Maternal exercise had an effect on future generations, reducing adiposity as well as plasma glucose and triglyceride concentrations.

Maternal overfeeding increased health risks both for mother and offspring, showing that HS/F diet consumption promotes metabolic alterations in offspring. However, physical training performed by generation F0 proved to be protective against such effects.

Maternal Overfee • Transgenerationa • Offspring health

POSTER | Thursday 8th 10:40-11:40 hrs.

B40176

B40211
Basic Science
Life style and perinatal nutrition

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Cardiometabolic and behavioral effects of caloric restriction during puberty in adult rats

Environmental and nutritional disorders during the perinatal period cause metabolic dysfunction in the progeny and impairs health, which is observable in the Small Litter experimental model. Therefore, severe caloric restriction has the potential of affecting several organic systems through the same epigenetic mechanisms, and its effects in metabolically programed animals need elucidation. The objective of this work was to determine whether the caloric restriction would impact small litter and normal litter animals equally if at all, and what that would entail on the obesity prognosis.

At delivery, female Wistar rats (CEUA protocol 52/2017) were separated in small litter (3 pups) and normal litter (9 pups) groups, their offspring in turn were subjected to caloric restriction (50% restriction when compared to controls) or left with free access to chow during the puberty period (from 30 to 60 days). These animals were then subjected to non-anaesthetized recording for the evaluation of cardiovascular parameters, open field (OF) and elevated plus maze (EPM) tests for behavioural analysis, then glucose and insulin tolerance tests. In addition, their body weight and food intake were monitored throughout the experimental period. SL and SLR offspring were overweight, developing obese phenotype, showing insulin resistance and glucose intolerance during insulin and glucose tolerance tests in relation to NL and NLR offspring ($p<0.05$). Differences in mean arterial pressure were also observed, when comparing small litter control animals with the rest of the groups ($p<0.05$). In addition, SL and SLR offspring showed a tendency for anxiety-like behaviour during the OF and EPM tests ($p<0.05$).

The present study showed that early overnutrition caused obesity, anxiety-like behaviours and impairments in glucose homeostasis. Also, the animals subjected to food restriction showed no improvement in the behavioural tests, however the non-obese animals showed similar impairments in behaviour. There was also a tendency for high blood pressure observed in the obese animals, and a tendency for the attenuation these levels in obese animals that were subjected to food restriction.

Small Litter • Food Restriction • Obesity

ORAL | Thursday 8th 09:40-10:40 hrs.

B40211

B40245
Basic Science
Life style and perinatal nutrition

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Role of dysfunctional white adipose tissue on the progression of non-alcoholic fatty liver disease induced by postweaning high-sucrose diet intake in male m

Non-alcoholic fatty liver disease (NAFLD) is the major chronic liver disease in Western countries. NAFLD can evolve from simple steatosis to non-alcoholic steatohepatitis (NASH), which is an independent risk factor for cardiovascular diseases. NAFLD has been associated to chronic ingestion of carbohydrate-based diets. However, the mechanisms involved in the onset and progression of high-sugar diet-induced NAFLD remain unclear. Thus, in the present study we sought to characterize metabolic, as well as inflammatory factors involved in NAFLD progression in weaned mice fed a high-sucrose isoenergetic diet (HSD).

Weaned male Swiss mice were fed with HSD (25% sucrose) or regular chow (10% sucrose, CTR) for 8 or 12 weeks. Obesity, glucose homeostasis and serum biochemistry were determined of each time point. At the end, white adipose tissue (WAT) function was assessed through ex vivo lipolytic assay at basal and stimulated conditions (isoproterenol and insulin). Liver samples were also collected for histology, gene expression and cytokines quantification. 8-week fed HSD mice showed increased WAT fat pads (53%), triglyceridemia (47%), serum free fatty acids (FFA, 30%), as compared to CTR, but no change in fasting glucose. At both time points, WAT dysfunction, insulin resistance and NAFLD were found. However, 12-week fed HSD mice showed greater fat accumulation (66%) and additional insulin resistance in WAT, which coincided to fasting hyperglycemia, higher triglyceridemia (106%), increase of serum FFA (62 %) and more than twice hepatic gene expression of lipogenic transcription factors SREBP1c and ChREBP. Finally, 12-week fed HSD mice presented NASH characterized by hepatic leukocyte infiltration and consequently increased levels of hepatic cytokines TNF-? (38%), IL-6 (16%) and IL-10 (19%).

First of all, this study ratifies the importance of diets nutritional composition than its energetic content in NAFLD development. But, mainly, it consistently supports the onset of insulin resistance in the dysfunctional white adipose tissue as a capital switch factor for the progression of NAFLD toward NASH in high-sucrose isoenergetic-diet-induced metabolic syndrome since weaning.

High-sucrose die • Adipose tissue • NASH

POSTER | Friday 9th 11:10-12:10 hrs.

B40245

B40434
Basic Science
Life style and perinatal nutrition

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Can a postnatal sugar consumption change the maternal low-protein diet effects in male offspring rats?

Maternal insults during the intrauterin and postnatal life can alter some organs morphology in the offspring, including genital system. Female rats that received a low protein (LP) diet during gestational and lactation periods can impairs the prostate morphogenesis and causes an increased incidence of prostatic disorders in age animals. Besides, LP diet is associate with the increasing of metabolic syndromes and this effests can be enhanced by sedentary life and an increased of sugar consumption. The aimed of this study was to investigate if sugar intake, after weaning until postnatal day (PND) 90, amplified the negative impact of maternal LP diet in Sprague dawley male offspring at adult age.

Pregnants female received eigther control (CTR, 17% protein) or LP diet (6% protein) during perinatal period. After offispring weaning the male rats were divided in 4 groups: Control (CTR; normal water); Control+sugar (CTR+SUG; 10% sugar in water); Gestational and Lactational LP (GLLP; normal water); GLLP+SUG (10% sugar in water). At PND90 the ventral prostate (VP) was collected to avaluated morphophysiological parameters and antioxidant enzymes, and blood was collected for a metabolic profile serum (MPS). The body weight and anogenital distance were lower in both GLLP groups. The PV morphology showed a smaller acini size, an increased on the epithelial height, pleated on the epithelium and in the stromal collagen fibers in both GLLP groups. Epithelial cell proliferation and sulfiredoxin immunostaining were increased in GLLP groups. Western Blotting for Glutathione-s-transferase, Sirt-1 and sulfiredoxin showed no changes among the groups. And MPS, total proteins, triglycerides and glucose levels were not differents too. Oxidative stress enzymes analysis showed that superoxide dismutase was not altered, but catalase and glutathione were increased in GLLP group when com

These results demonstrate that postnatal consumption of sugar associated or not with maternal LP diet causes alterations in biometric parameters and impairs disorders prostatic such as the increase on the epithelial proliferation, a chronic inflammation and alteration in antioxidant enzymes.

Ventral prostate • sugar intake • Low protein

POSTER | Friday 9th 11:10-12:10 hrs.

B40434

B40451
Basic Science
Life style and perinatal nutrition

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Obesity in early life is an important risk for Non Alcoholic Fatty Liver Disease (NAFLD) in Chilean adolescents (648)

We assessed steatohepatitis using elastography with controlled attenuation parameters (CAP) in all participants with NAFLD. The association between NAFLD and anthropometric data was assessed annually from birth to 5 yrs; these included (weight, length, BMI (Kg/m2), % fat mass and abdominal circumference (cm). We also considered maternal BMI before conception and weight gain during pregnancy. Yearly abdominal ultra-sound served to identify fatty liver after birth and define the presence of NAFLD (non-alcoholic fatty liver).

1200 participants of the early growth and obesity development study (EGOS); a longitudinal cohort of ~ 1400 children born 2002-03 followed longitudinally from mid gestation (1000 born 2002-3 followed yearly from 2006; relevant information on growth and development during gestation and infancy 2016-2018 was collected. 398 adolescents (65,7% male) with a mean age of 14.6 yrs were assessed;41 presented evidence for NAFLD(10,3%), no differences were observed in adolescents with or free from NAFLD birth weight (3.55 ± 0.44 kg vs 3.61 ± 0.43 kg), nutritional status at birth (78% NB AGA vs 75,3% NB AGA) nor in the prevalence of macrosomia (17,1% vs 11,9%). No difference in pre-gestational maternal BMI (25.8 ± 4.2 kg/m2 vs 24,3 ± 4,5 kg/m2, p:0.074) nor in weight gain during gestation (13,7 ± 7,0 kg vs 14,6 ± 7,0 kg, p:0.538). The presence of obesity at 1 yr of age was unrelated to NAFLD in adolescence (OR= 1,32, IC 95% -1,25 – 3,89). However we noted that after age 2 yrs, the obese children had a greater chance for NAFLD in adolescence; this was significant with ORs of 3.97 (IC 95% 1.66 – 6.29), 3.96 (IC 95% 1.63 – 6.30), 5.57 (IC 95% 3.54 – 7.61) y 5.71 (IC 95% 3.45 – 7.98) at 2,

We must now add “risk of NAFLD” to the increased of cardiovascular, diabetes and obesity in the off-spring derived from maternal obesity. We must now include the risk to develop non- alcoholic fatty liver NAFLD starting in childhood followed by progression to cirrhosis in adolescence and adult life. The results support a call to act early in the life course to prevent diet related chronic diseases. Control of maternal obesity and excess weight gain during pregnancy need to be stressed; the earlier the better; before conception would be optimal. Mothers must consider not only their own risks but the key role their obesity plays in marking multiple health outcomes that will affect their offspring and their children for generations to come. Prevention and control of maternal obe-

sity should start before conception and be maintained during pregnancy; to avoid the risks of obesity related chronic diseases from the time of conception and offer the infant conditions for a healthy start. (500 total words)
CONICYT-PFCHA/MagísterNacional/2018- 22180234 Fondecyt 1161456

early obesity • fatty liver • Cirrhos

POSTER | Thursday 8th 10:40-11:40 hrs.

B50032
Basic Science
Perinatal infection and programming

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Low Insulin Levels During Lactation In Rat Offspring Can Protects Against Obesity In Adult Life

Obesity has become, over time, a worldwide public health problem. The DOHaD concept, through clinical and preclinical studies, suggests a strong association between environmental damages occurred in the fetal or perinatal life and the emergence of chronic diseases in adult life. The Central Nervous System is easily affected at critical stages of development, such as in lactation. Hyperinsulinemia in early life has been associated with an obese phenotype in adult life. In opposition, hypoinsulinemia in the perinatal phase is related to a lean phenotype. Cholinergic terminals activity into pancreatic beta-cell has been associated to those phenotype-early low-insulin levels. Therefore, our aim was to investigate whether the short-term treatment with a buscopan, could pre

After birth, male Wistar rats received intraperitoneal injection of scopolamine butylbromide, 0.5 mg/Kg body weight/day during the first 12 days of lactation (Treated Group; T) or saline 0.9% (Control Group; C). At 60-days-old, the offspring from both group consumed normal fat diet (NF) or high fat diet (HF:35% of fat) by next thirty days. At 90-days- old body weight, food intake, fat tissue accumulation, glucose tolerance, insulin tissue sensitivity and fasting glucose and insulin blood levels were evaluated. T group presented lower body weight than C group until 60-days-old ($p<0,0001$) associated to a lower food intake ($p<0,05$). At 90-days-old, T-HF group showed low body weight compared to C-HF ($p<0,0001$). The T-HL animals presented increased fasting glycemia and insulinemia 23% ($p<0,05$) and 60% ($p<0,001$) lower than the C-HF group, respectively. The T-HF group had greater insulin sensitivity by the HOMA index, compared to C-HF control. T groups presented lower fat tissue accretion (T-NF 30%;T-HF 14%; $p<0,05$) compared to C-NF and C-HF respectively. During intraperitoneal glucose tolerant test, the T-HF animals presented lower glucose levels than C-

Therefore, we conclude that treatment with a cholinergic antagonist, which allows low insulin levels during lactation protects the animals against metabolic dysfunction and obesity onset later in life; at least in part this resistance can be attributed to improvement of insulin action and secretion.

Lactation • Hypoinsulinemia • Obesity

POSTER | Friday 9th 11:10-12:10 hrs.

B50032

B50036
Basic Science
Perinatal infection and programming

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Metformin treatment in early life protected for insulin resistance in adult life

Metformin is worldwide the most used drug for the treatment of type 2 diabetes and metabolic diseases. Perinatal phases are known as window to program adulthood metabolism. Therefore, the aim of this study was verified whether metformin treatment during lactation could attenuate later metabolic dysfunction caused by obesity induced by high fat diet exposition in adulthood.

At Wistar rat birth, all litters were adjusted to 9 pups for each dam and divided in two experimental groups. Saline (S) pups received a 0,9% saline solution in the first to the twelfth day of life via an intraperitoneal injection, while the other group received metformin (M) (100mg/kg body weight (bw)/day) in the same period of life. At sixty days of age, offspring from S and M groups were fed with a normal fat diet (4.5% of fat; NF) or high-fat diet (35% of fat; HF) until ninety day-olds. Thus, the four experimental groups used were: S-NF: saline offspring with NF, M-NF: metformin offspring with NF, S-HF: saline offspring with HF, and M-HF: metformin offspring with HF. The early metformin treatment did not change bw and food intake in rats with 60 days old. High-fat diet consumption at adulthood resulted in increased bw in both groups, S-HF and M-HF; although they had a lower food intake compared to groups NF. The S-HF animals presented a higher final weight compared to S-NF. The fat pad mass was higher in the rats were fed with HF. Fasting glycemia was higher in M-HF rats compared to M-NF rats, although the treatment with

Metformin treatment in early life not prevent weight gain and the increase of fat pad mass caused by a high-fat diet in adulthood, however, this treatment protected the animals for insulin resistance.

Metformin • overweight • high-fat diet

POSTER | Thursday 8th 10:40-11:40 hrs.

B50036

B50246
Basic Science
Perinatal infection and programming

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Characterization Of B-Cells In Amniotic Fluid Of A Mouse Model Of Preterm Birth Induced By A Systemic Injection Of Bacterial Lipopolysaccharides.

Perinatal infections (PNI) are the main cause leading to preterm birth (PTB). Our laboratory has developed a mouse model of PTB induced by a systemic injection of bacterial lipopolysaccharides (LPS) to gain a better understanding of the mechanisms involved in this pathoogy. While diverse components of the innate immunity have been found in amniotic fluid (AF), we found the presence of immature (CD19+B220- IgM-) and more mature (CD19+B220+IgM+) B-cells. However, the characterization of B-cells in the context of a PNI was not investigated so far. B- cells are classified in B1 and B2. B2 cells are continuously generated through the postnatal life and B1 cells are originated during embryonic life from precursors found in the yolk sac and fetal liver
The aim of this work was to make a phenotypic characterization of the AF B-cells of pregn

ant mice challenged with LPS. Therefore, C57BL/6 (H2b) females were mated with BALB/c (H2d) males and at day 15 of pregnancy, an experimental group was exposed to a dose of LPS (10 µg/ml) capable to induce preterm birth and, another group was injected with PBS. After 5 h females were sacrificed and AF was extracted from the same amount of embryos (6). AF cells were isolated and further stained with specific antibodies against CD19, B220, CD5 and H2d for phenotypic characterization using flow cytometry. Phenotypic analysis of AF isolated cells from both groups showed a decreased number of CD19+B220+ cells in the LPS compared to PBS control group (LPS: 46277± 14941*; PBS: 1267±406; Number of cells/ml AF; *p<0,05 vs PBS, t-Student test). Further characterization demonstrated that all CD19+ cells were also CD5+ in both groups (CD19+CD5+, ?98%). Importantly, all CD19+ B cells expressed H2b denoting fetal origin. There were no differences in the total numbers of cells in AF and in CD19+B220+ median fluorescence intensity (MFI) between groups.

These results demonstrate that the maternal exposure to perinatal LPS reduces the amount of mature B1 cells (CD19+B220+CD5+) in AF. A possible explanation to this finding, is the migration of these cells to diverse inflammation sites, such as decidua, were other authors demonstrated the presence of B1-Lymphocytes (Huang et al, 2017). Further studies need to be done to elucidate the involvement of embryonic AF B1 cells, as a first line of fetal defense in the context of a maternal infection.

Amniotic Fluid • B-Lymphocytes • Preterm Birth

ORAL | Friday 9th 15:30-16:30 hrs.

B50246

B50269
Basic Science
Perinatal infection and programming

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Neonatal treatment with hemin and melatonin reverts pulmonary vascular dysfunction in neonatal sheep with pulmonary hypertension born in chronic hypoxia.

Chronic hypoxia during gestation programs cardiopulmonary dysfunction and can lead to Neonatal Pulmonary Hypertension (NPH). This is a multifactorial syndrome with chronic hypoxia and oxidative stress being the main factors involved in pulmonary vascular dysfunction. We hypothesized that this pulmonary vascular dysfunction can be treated by using a combination of hemin as a vasodilator and anti-remodeling and melatonin as a vasodilator and antioxidant.

Twenty lambs gestated and born at 3600 m were studied, 5 received vehicle, 5 received melatonin (1 mg * kg-1. oral during 21 days), 5 received hemin (10 mg * Kg-1, SC, during 10 days) and 5 received melatonin + hemin (combined treatments). We monitored the in vivo cardiopulmonary status every morning until 1 month old. After 7 days of treatment termination, we evaluated vascular reactivity in pulmonary resistance arteries by wire myography; and protein expression in lung tissue by Western Blot. All procedures were approved by the Bioethics Committee (CBA # 0761 FMUCH). The combined treatment (hemin-melatonin) improved endothelium-dependent vasodilator function, enhancing pulmonary protein expression related to the nitrergic and prostanoid pathways, such as GCs-PKG and PGFIs-Ip. However, the smooth muscle-dependent vasodilatation by sodium nitroprusside (SNP) only increased in the independent treatments with melatonin or hemin. Finally, hemin induced the hemoxygenase system expression (HO-1 and HO-2) in lung tissue.

These results demonstrate that a combined hemin-melatonin treatment improved endothelial vasodilator function by increasing protein expression and activating the nitric oxide, prostacyclin and hemoxygenase pathways in the pulmonary circulation. These improved vasodilator mechanisms were maintained even after a week of the treatment termination. Melatonin and hemin have significant scavenger capacity against reactive oxygen species (ROS), increasing the nitric oxide (NO) bioavailability and inhibiting the prostanoid vasoconstrictor pathway. Further the increased HO system generates more carbon monoxide, a known pulmonary vasodilator. We believe that the combined treatment was able to revert the programming of endothelial dysfunction by perinatal chronic hypoxia and oxidative stress. Future studies should focus on potential epigenetic mechanisms affected by this treatment, enhancing the vasodilators pathways expression and decreasing the risk of developing NPH and further cardiovascular diseases later in life.

Chronic hypoxia • oxidative stress • pulmonary hypert

POSTER | Wednesday 7th 17:40-18:40 hrs.

B50269

B50347
Basic Science
Perinatal infection and programming

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Early metformin treatment programs pancreatic islets from adult rat offspring to reduce glucose-stimulate insulin secretion

Metformin, an antidiabetic drug is used worldwide to treat type 2 diabetes; improving tissue insulin sensitivity which attenuates insulin resistance allowing to decrease fasting hyperinsulinemia. Besides this mechanism, evidences suggest that metformin stimulates apoptosis, which nowadays metformin is used to treat cancer. Recently has been shown that metformin inhibited glucose- induced insulin release (GIIR) and provoked cell death in isolated pancreatic islets from mice. Our group showed that early metformin treatment blocked fasting hyperinsulinemia onset of adult obese without change pancreatic islets insulin secretion profile. In the present work we tested whether early metformin treatment changed GIIR of pancreatic islets from adult rat offspring.

Newborn pup Wistar rats were peritoneal injected with metformin, therapeutic dose 100mg/Kg body weight, from P1 to P12, early group. Adult rats also were metformin injected with dose as used in pups, from 60- to 71-days-old, late group. Controls were saline solution injected. It was measure body weight gain and fasting blood glucose levels of rats with 90 days old from early group and 120-days-old rats from adult group. Those rats were isolated pancreatic islet to test insulinotropic response with different glucose concentrations. There was no changes in body weight neither fasting glycemia to both group, early or late ones. While, using fasting glucose concentration 5.6 mM islets from animals early did not altered insulin release, increasing to 8.3 and 16.7 mM, post-prandial levels, islets from early group showed drastic insulin secretion reduction. Islets from late group did not showed any insulinotropic changes, eventough increasing glucose concentration, regarding their controls.

Early, but not late metformin treatment provokes decrease in glucose insulinotropic effect. Whether this programming is good or bad must to be evaluated.

metformin • early treatment • pancreatic islet

POSTER | Wednesday 7th 17:40-18:40 hrs.

B50347

B50382
Basic Science
Perinatal infection and programming

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Maternal High Fat Diet Consumption Causes Change In The Angiotensin Ii Receptor Expression (At1) And Cardiac Hypertrophy In The Female Offspring At Weaning

Besides to obstetric complications, obesity in women during gestation and lactation may predispose metabolic programming in the lineage, with the emergence of cardiovascular diseases in the adult progeny. Our research group showned that maternal consumption of high fat diet increased body mass, adiposity, hyperleptinemia in the offspring of rats at weaning, as well as impairment of systolic function at 30 days of age. The renin angiotensin system (RAS) expressed in the heart appears to trigger cardiac hypertrophy (CH), through the overexpression of Angiotensin II (Ang II) and activation of it's receptor, AT1. This study aimed to investigate whether the maternal consumption of a high fat diet promotes CH and correlate to change the cardiac RAS system expression in male and female offsprin

Forty Wistar rats received control or high fat diet (9% group C and 29% HF group, respectively) during gestation and lactation. At weaning, 21 days of life, the offspring were weighed and euthanized (?C=20, HF=19, ?C=22, HF=20). The heart and white adipose tissue (retroperitoneal, inguinal and perigonadal) were weighed. Histological analyzes (sections stained with HE and picrosirius) were performed using samples from the ventricles. Cardiac Ang II was measured by RIA analyzes and AT1 receptor expression was assessed by Western blotting using the left ventricle (LV). The body mass was higher in HF offspring (?=8%, ?=9%), as well as the depots of white adipose tissue (retroperitoneal:?=2,9x, ?=80%, inguinal:?=100%, ?=70% and perigonadal: ?=2,4x, ?=90%). The heart mass (?=8%, ?=7%) and the diameter of the cardiomyocytes of LV was increased (?=60%; ?=7%) in HF offspring. The presence of fibrosis was not observed. There was no difference Ang II among the offspring. The cardiac expression of AT1 was increased (50%) in female but was not altered in male HF offspring.

These results suggest that the maternal consumption of high fat diet promotes high body mass, adiposity, LV hypertrophy in offspring at weaning. Although male and female present the same phenotype of left ventricular hypertrophy, they have different signaling mechanisms. The alteration in AT1 receptor expression found in female suggests that RAS may be involved in LV hypertrophy observed in the female HF offspring.

Obesity • Heart • Angiotensin II

POSTER | Thursday 8th 10:40-11:40 hrs.

B50382

B50383
Basic Science
Perinatal infection and programming

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Human Placenta Susceptibility To Respiratory Syncytial Virus Infection

The human Respiratory syncytial virus (RSV) is a common respiratory virus that usually causes mild cold-like symptoms, but can be especially threatening for infants and older adults. Additionally, a study in an animal model, has reported its capacity for vertical transmission, suggesting a possible transplacental transmission and infection of some elements of the placenta, such as trophoblastic cells and chorionic villus stromal cells. In the present study, we demonstrate the susceptibility of human chorionic villus explants obtained of terminal human placenta and cell lines of trophoblast (BeWo and HTR-8/ Sv neo) to RSV infection.

Human chorionic villus explants were obtained of human placenta of Instituto Nacional de Perinatología; we characterized by immunofluorescence assay the identity of trophoblast cells by the hallmarks of cytokeratin 7 positive, vimentin negative. Them the explants were infected with the RSV and immunodetection of viral proteins (F protein) was evaluated by immunofluorescence. Therefore, two human trophoblastic cell lines of the first trimester HTR8 / Sv neo and BeWo cells, was used to characterization of viral cycle infection, by performed western blot and immunofluorescences assay and evaluate the detection of viral antigens, also performed RT-PCR assay to evaluated the expression of the viral gene (NS2) and determinates replication of viral genome in the cellular models of trophoblast. Finally, a plaque forming unit assay (PFU), was used to evaluated in supernatants of trophoblast cell lines infected with VSR the production of infectious viral particles.

In conclusion the results indicate that trophoblast cells of terminal placenta are not infected with RSV, but other cellular types of the placenta environment could be permissive. And we suggest that trophoblast cells of early gestation are more permissive to RSV infection, because cell lines like trophoblast cells support the cycle infection with RSV.

Human placenta • RSV • Trophoblast

POSTER | Thursday 8th 10:40-11:40 hrs.

B50383

B50388
Basic Science
Perinatal infection and programming

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Determination of Zika virus transport across human fetal membrane system

The spread of the current ZIKV epidemic and the severe manifestations of congenital ZIKV infection, it is crucial to learn the fundamental mechanisms of viral transmission from the mother to the fetus. The routes of access of the virus to the fetus are components of the manternal-fetal interface, as are the human fetal membranes. However, the ability to cross the barrier of fetal membranes intact by ZIKV has not evaluated. The present work aimed to determine the transport of ZIKV employing a compartmentalization system of human fetal membranes that permit evaluate the viral movement from the maternal side to the fetal.

Fetal membranes were obtained after delivery by elective cesarean section, cut at a distance of 2cm from the placental disc and placed in a Transwell chamber to form the independent chambers: the maternal or choriodecidual zone and the fetal or amniotic zone. To determine the viral transport, it was infected on the maternal side and the supernatants of the fetal side were recovered at different times (20 min,40 min,1 h,2 h,4 h,6 h and 10 h), using a control with crystal violet for ensure the integrity of the membranes. Subsequently, Vero cells were infected with supernatants recovered, and immunofluorescence was performed to demonstrate the presence of viral antigen, observing increase in the expression of viral protein at 2h p.i. and Vero cells was infected at 60 percent of the total of cells. Moreover, decrease between 4 and 6 h, and not observing infection in the following hours. In addition, viral titration assays were performed with the supernatants obtained to know the viral load in the fetal compartment and confirming the previously results.

At early times post-infection ZIKV can be the transported through the membranes, the diffusion of the crystal violet molecule at a much lower rate, indicating that the amount of virus transported could not be reached by passive diffusion through the intracellular spaces of the membranes, so it is suggested that there are mechanisms that allow the transport of the virus through the membranes. Nevertless, if the virus infects the membranes and manages to replicate in the cells of the different layers than the components, or if the viral passage is due to a transcytosis of internalized viral particles is still a subject of study. Our studies of ZIKV infection in the authentic tissues of the human maternal-fetal interface unveil a route of transmission whereby virus originating from the mother could reach the fetal compartment via efficient replication and with that in the future they will generate therapeutic targets.

Zika Virus • Fetal Membranes • Vertical infecti

POSTER | Friday 9th 11:10-12:10 hrs.

B50388

B50396
Basic Science
Perinatal infection and programming

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Higher frequencies of activated naive CD4+CD32a+ T cells in HIV-exposed infants

Actually, the risk of vertical transmission of Human Immunodeficiency Virus (HIV) has decreased with the implementation of perinatal cares. However, there are evidences that activated and memory differentiated T lymphocytes are able to migrate from maternal circulation to the fetus and could be responsible for the spontaneous appear of HIV copies during infancy in high risk children from HIV+ mothers. Recently has been described a competent proviruses reservoir in CD4+ T cells that express CD32a in HIV infected adult population, but it is unknown if these cells are present in children from HIV- infected mothers. The objective of this study was to determinate if CD4+CD32a+ T cells were present in blood of children from ART-treated

We used a multi- parametric flow cytometry analysis to quantify the frequencies of CD4+CD32a+ T cells in peripheral blood samples of HIV- exposed infants (n=42 2 to 13 months), and compared with samples of HIV-non exposed infants (n=7, 2 to 7 months old). In addition, we determinate the naïve/memory (CD45RA/CD45RO) phenotype according their antigenic experiences and the expression of CD69 as activation marker in the same cells. We show that percentages of CD4+CD32a+ T cells in HIV-exposed are significantly higher than in HIV-non exposed infants (7.1+/-4.5 vs 4.2+/-1.0, p=0.0347). In addition, in a longitudinal monitoring, the numbers and frequencies of CD4+CD32a+ T cells in HIV-exposed infants increased with the age reaching a peak at the third month of life. In addition, we found that the most of these cells have naive phenotype (74.4+/-16.8) and the expression of CD69 is significantly higher in comparison with their CD4+CD32a+ T cells counterparts (177.1+/-86.2 vs 80.7+/-20.8, p<0.0001).

In summary, higher frequencies of T helper CD32a+ cells are presented in peripheral blood of newborn and infants from HIV+ mothers. These cells represent possible HIV reservoirs, even though no viral load has been detected on the studied patients. The phenotype the T helper CD32a+ cells were predominantly naive and highly activated (evaluated with CD69 expression). Further studies should be performed to determine if these cells could be latently HIV- infected reservoirs.

Perinatal HIV • Immune cells • Reservoirs

ORAL | Friday 9th 12:30-13:30 hrs.

B50396

B60004
Basic Science
Maternal and fetal health

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HIF-1 alpha-induced placental differentiation is influenced by redox status and glycemia intensity

Hypoxia inducible factor (HIF) activity is required to regulate placental morphogenesis and fetal vascularization, and is also involved in the proliferation and differentiation of the trophoblast. Diabetes can impair placental activity by causing the accumulation of reactive oxygen species (ROS), which, in turn, modulate intracellular signaling redox-sensitive proteins such as HIF. Aiming at further understanding the role of HIF in placental development and embryofetal alterations, we used two diabetes different models (mild and severe) to assess the influence of glycemia intensity on oxidative stress status, and, consequently, on HIF-1 alpha activity.

Wistar rats were allocated into 3 groups: mild diabetes (MD), severe diabetes (SD), and control (C). Diabetes was induced by streptozotocin. At days 9.5, 10.5, 11.5, 18.5 and 21 of pregnancy, maternal blood samples were collected for determining glycemia and redox status. Ectoplacental cones (EC) and embryos were collected for HIF-1 alpha and antioxidant enzymes (SOD, CAT and GSH-Px) assessment, PCR-real time analysis, western blotting, and immunohistochemistry and enzymatic assays. At term pregnancy, maternal, placental and fetal samples were collected for redox status and fetal growth evaluation. MDA was increased in both MD and SD during the study. Reduced maternal blood antioxidant defenses were observed at least at one of the time points analyzed. HIF-1alpha gene expression was increased in EC at day 9.5 of pregnancy. Nuclear staining was observed in C and MD. At term pregnancy, maternal decidua area was reduced in MD and SD, while a decreased labyrinth area was observed in SD. Increased and decreased placental glycogen storage was visually detected in SD and MD, respectively. The proportion of fetuses small for gestational age was increased i

HIF1-alpha expression is influenced by glycemia level and redox status. HIF-1 alpha gene expression in EC was increased in both MD and SD. No changes in maternal-fetal exchange were observed in MD probably due to the presence of nuclear staining, which was seen in MD only. In SD, as HIF-1 alpha translocation to the cell nucleus did not occur, target genes were not activated. In consequence, placental differentiation and maternal-fetal exchange were impaired at the end of pregnancy. Furthermore, it is possible that different placental glycogen storage patterns may also contribute to IUGR in both mildly and severely diabetic rats.

diabetes • oxidative stress • rat

POSTER | Thursday 8th 10:40-11:40 hrs.

B60004

B60005
Basic Science
Maternal and fetal health

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Long-term effects of diabetes-induced fetal programming and postnatal high-fat diet exposure on glycemia

Intrauterine diabetic environments confer risk for diabetes and obesity in the offspring, both on the short and the long term. This study aimed at assessing the long-term influence of high-fat diet on glycemic responses in the offspring of diabetic rats.

We used 20 rats born via vaginal delivery to dams with streptozotocin- induced mild diabetes (experimental model characterized by glycemia similar to human glucose intolerance). From weaning onwards, 10 of the pups were fed a standard diet (SD), while the other 10 received a high-fat diet (HFD). At adulthood (115 days), all animals underwent oral glucose tolerance testing (OGTT) for both glucose and insulin assessment. The area under the curve was similar, but the behavior of the glucose curve differed between groups: HFD showed unexpectedly lower fasting glucose and insulin levels, similar glucose and insulin post-load levels, but higher glucose and lower insulin at the end of the experiment, compared with SD.

In this study, the combination of a diabetic intrauterine environment with a post-natal high-fat diet reduced insulin secretion at adulthood in rats born to diabetic mothers. Furthermore, our results indicate that fasting glucose levels may not reliably indicate impaired pancreatic insulin secretion in these animals.

offspring • high-fat diet • glycemia

POSTER | Friday 9th 11:10-12:10 hrs.

B60005

B60007
Basic Science
Maternal and fetal health

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Vitamin D improvement on glucose control, oxidative stress and reproductive outcomes in mildly diabetic pregnant rats

Although vitamin D effects on glucose metabolism and metabolic control during pregnancy have been shown to be positive, the influence of vitamin D on diabetic pregnancies remains uninvestigated. Since vitamin D stimulates pancreatic ÃŽÂ²-cell calcium (Ca2+) channels to promote insulin secretion, we tested whether it can improve the maternal diabetic metabolism and thus contribute to adequate fetal growth in rats.

Sprague-Dawley rats injected with Streptozotocin for diabetes induction at birth, were later mated and treated with either vitamin D alone, or Ca2+ alone or their combination during pregnancy. At term pregnancy, maternal blood samples were collected for metabolic profiling, oxidative stress measurement and fetal analysis. In the diabetic animals treated with vitamin D and Ca2+ combined or with vitamin D alone glycemia was decreased during glucose tolerance test (GTT) and the area under the curve (AUC) was reduced. TBARS concentrations in these animals were also decreased. On the other hand, no changes were observed in those receiving Ca2+ alone in these parameters. However, the treatment with Ca2+ alone or combined with vitamin D led to renal calcification. Both vitamin D and Ca2+ combined and vitamin D alone reduced embryo-fetal loss rates and increased the rate of fetuses classified as adequate for age of pregnancy.

Our results suggest that, due to its action on insulin secretion, vitamin D improves glycemic control and, consequently, decreases the production of lipoperoxides. Thus, the use of vitamin D may contribute to improving reproductive repercussions and fetal growth.

vitamin D • diabetes • pregnancy

POSTER | Friday 9th 11:10-12:10 hrs.

B60007

B60008
Basic Science
Maternal and fetal health

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Effects of Curatella americana treatment on complications of diabetic pregnancy

Hyperglycemia causes maternal and fetal complications, leading to metabolic and reproductive changes. As a complementary therapy, medicinal plants are indiscriminately used for the diabetes treatment. The literature shows that different preparations of Curatella americana presents anti-inflammatory, antimicrobial, antihypertensive and other effects. The population reports the use of this plant as anti-diabetic even in pregnancy. However, there is no scientific evidence of its effect on maternal glucose metabolism and maternal- fetal repercussions. Thus, the objective of the study was to evaluate if the aqueous extract of the C. americana leaves show anti-diabetic effect and its influence on maternal reproductive parameters and fetal development in rats with mild diabet

The female offspring received at birth vehicle (ND) and streptozotocin for mild diabetes (MD) induction (experimental model characterized by glycemia similar to human glucose intolerance). At adulthood, all animals underwent oral glucose tolerance test (OGTT) for glucose assessment as inclusion criteria. The adult rats were mated and distributed into (n=12 animals/group): ND, ND + plant treatment (NDT); MD; MD + plant treatment (MDT). The rats received 300 mg/kg aqueous extract of C. americana during pregnancy. OGTT was also performed on the day 17 of pregnancy. On day 21, the rats were killed for blood biochemical assessment, analysis of maternal reproductive performance, fetal development and malformations. The plant caused no glycemic changes during OGTT in NDT and MDT. A reduction in serum levels of triglycerides, total cholesterol and VLDL-cholesterol in the MDT was observed in relation to MD. The NDT group had decreased fetal and placental weights and an increased rate of fetuses classified as small for the age of pregnancy compared with ND group. The rates of embryofetal losses and malformations were not altered in both groups treated.

The plant treatment leads to intrauterine growth restriction in healthy animals, showing the need for care and caution of the indiscriminate use of plants without medical recommendation. Although the treatment with C. americana does not alter the glycemic metabolism of diabetic rats, it improves the maternal lipid profile and presents no change in maternal reproductive parameters and fetal development.

Curatella americ • Diabetes • Pregnancy

POSTER | Friday 9th 11:10-12:10 hrs.

B60008

B60010
Basic Science
Maternal and fetal health

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Maternal obesity, but not high fat diet alone, modulates hepatic microRNAs and alters metabolic homeostasis in offspring of the second generation.

MicroRNAs may exert great influence on energetic metabolism. In the liver, downregulation of miR122 leads to an increase in triglycerides synthesis, as well as a decrease in fatty acids transportation and oxidation. Let7 have been reported to be involved with insulin resistance and previous studies from our lab showed that offspring from obese dams presented increased Let7 and decreased miR122 expression in the liver. These microRNAs modulation are probably involved with the hyperglycemia, greater adiposity and fatty liver present in those animals. Therefore, this study aimed to evaluate whether HFD consumption at gestation and lactation would lead to transgenerational deleterious effects that could be triggered by hepatic microRNAs expression.

Female Swiss mice were classified into two groups: control (C) and HFD fed (HF), which were later subdivided into obese resistant (OR) or prone (OP), according to the weight gain presented during the 4 weeks of exposure to the experimental diet at the adaptation period. F0 females were mated with control males for F1 generation conception. After weaning, F1 females were fed exclusively a control diet until they were able to be mated with control males to originate the second generation (F2). F1 females from OP dams presented increasing in fasting and fed glycemia, serum cholesterol, serum triglycerides and body weight before mating. At the birth day, offspring from obesity prone grandmothers (F2 OP) had an increase in fasting glycemia, which was maintained until the 28th day of life, even though the body weight did not differ between groups. Furthermore, in d28, both F2 OP and offspring from obesity resistant grandmothers (F2-OR) showed an increase in liver fat content in comparison to offspring from control grandmothers (F2 C). F2 OP offspring showed a lower expression of hepatic miR 122 and, on the other hand, they presented higher levels of Let7 in th

Maternal nutrient imbalance during gestational and lactational periods leads to a phenomenon called metabolic programming, and it has been shown that the effects of the poor maternal nutrition can persist through future generations. miR 122 and Let 7 can be referred as predictors of metabolic disorders and, in the present study, we showed that the second generation of obese prone HFD fed dams present modulation at these microRNAs that may be, at least in parts, adjuvants of glycemia and fat storage in the liver. In summary, the results of the present study showed

that maternal diet induced obesity leads to transgenerational upregulation of Let 7 and downregulation of miR 122. These alterations may be related to the hyperglycemia and fat accumulation within the hepatocytes. These findings confirm the need for adequate nutrition and weight gain during the gestation and lactation periods for the good prognosis of the health of the newborns and the prevention of several chronic diseases across the generations.

obesity • epigenetics • microRNAs

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60011
Basic Science
Maternal and fetal health

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Pancreatic islet response to diabetes during pregnancy in rats

Pregnancy is a time when significant maternal adaptations occur to ensure an appropriate fetal development. During pregnancy, oxidative stress plays a leading role in fetal programming and the development of diseases such as diabetes. Thus, the objective of this study was to assess the mechanisms underlying pancreatic islet adaptation in diabetic mothers and their offspring. Additionally, the influence of pancreatic adaptations on maternal reproductive performance was also investigated.

Wistar rats were injected with Streptozotocin for diabetes induction at birth. At adulthood (115 days), all animals underwent oral glucose tolerance test (OGTT) for glucose assessment as an inclusion criterion. The animals were mated and killed at day 18 of pregnancy. Blood was collected to determine fasting insulin and glucagon concentrations. The pancreas was removed and processed for the immunohistochemical analysis of insulin, glucagon, somatostatin, Ki-67 (cell proliferation marker) and PDX-1 (Î²-cell function/survival marker), superoxide dismutase 1, glutathione peroxidase (GSH- Px) and malondyaldeyde (MDA). The pregnant uterus was collected for the evaluation of embryofetal loss. The diabetic rats showed increased glucose, serum glucagon and insulin concentrations, and embryofetal loss rates. They also showed reduction in pancreatic islets area and percentage of cells stained for insulin, increased percentage of non-Î² cells stained for Ki-67, glucagon and somatostatin. Moreover, the cells stained for somatostatin were spread across the islets and showed stronger staining for MDA and weaker staining for GSH-Px.

Diabetes during pregnancy leads to adaptive responses from the endocrine pancreas that especially involve non-Î² cells, modifying the mantle core structure. Nonetheless, these adaptations are not enough for glucose homeostasis and affect the maternal environment which, in turn, impairs fetal development.

hyperglycemia • gestation • pancreas

POSTER | Thursday 8th 10:40-11:40 hrs.

B60011

B60063
Basic Science
Maternal and fetal health

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Maternal Roux-in-Y Bypass Gastric induces brown adipose tissue changes in adult male offspring

Brown Adipose Tissue (BAT) is specialized in thermogenesis, a process dependent on uncoupling protein 1 (UCP1) to dissipate heat. According to metabolic programming concept, nutritional and hormonal insults in early phases of development, such as gestation and lactation, can exert effects on the offspring phenotype. Interestingly, maternal obesity in these phases reduces thermogenesis in offspring contributing to obesity installation in adulthood. Currently, the most effective treatment for fat loss is the bariatric operation (BO), being Roux-in-Y Gastric Bypass (RYBG) the most used surgery. Moreover, many obese women in gestational age are submitted to BO, but the effects on offspring health are unknown. Here we evaluated the effects of maternal RYBG on BAT of male offspring in adulthood

After weaning Wistar female rats received standard diet - Control group (CTL, n=8), or cafeteria diet - CAF group (CAF, n=12). At 18 weeks, the CAF group was submitted to sham operation (S, n=7) or RYBG (n=5). At 23 weeks the females were mated and their male offspring were studied in 3 groups (n=6 rats/groups): CTL(F1), CAF-RYBG(F1) and CAF-S(F1). The offspring received standard diet throughout life and was euthanized at 120 days. The BAT was collected and submitted to histological analysis and to UCP1 protein expression evaluation. From birth to adulthood CAF-RYBG(F1) rats presented a decrease in body weight in relation to CAF-S(F1) and CTL(F1) ($p<0.01$). The fat deposits were smaller (56%) in CAF-RYBG(F1) group than CAF-S(F1) rats, matching the CTL(F1) group. About BAT, the weight increased in the CAF-S(F1) (40%) and CAF-RYBG(F1) (60%) groups in relation to CTL(F1). The CAF-RYBG(F1) group showed an increase in the number nuclei (43%) and reduction in the size of lipid droplets (67%) in relation to CAF-S(F1), matching the CTL(F1) group. The expression of UCP1 increased 100% and 200% in the CAF-RYBG(F1) group in relation to the CTL(F1) and CAF-S(F1) groups, respectively.

According to the fetal overnutrition hypothesis, inadequate maternal nutrition in early life predisposes to adverse effects on the health of offspring, including reduction of thermogenesis process in BAT. For the first time, we have been able to show that Roux-in-Y Bypass Gastric performed in the obese women in gestational age modulates histological and molecular aspect in BAT of offspring,

reducing the accumulation of fat in the tissue and increasing cell proliferation as well as UCP1 expression. Taken together, these data suggest that the maternal RYBG can increase thermogenesis in BAT of the male offspring in adulthood, contributing to increasing the energy expenditure and avoiding obesity development.

maternal obesity • RYBG • thermogenesis

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60113
Basic Science
Maternal and fetal health

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Brazil

Assessment of adult offspring memory of breast-feeding Wistar rats treated with Valeriana officinalis

The postpartum period is critical for the development of the newborn. The maturation of the nervous system is completing and modifications may be responsible for upcoming physiological and behavioral changes in adult life. In this period, maternal anxiety is common, and pharmacological treatment is recommended due possible consequences of this disorder. Valerian is used as anxiolytic and mild sedative. Its effects derive from interactions with GABA metabolism and receptors, which is related to processes such as emotions and memory. It is known that the presence of psychoactive substances during lactation can alter the chemical and functional structure of the brain. Thus, it is important to verify if maternal treatment with Valerian can lead to changes in memory in adult life.

Approved by CEEA/UFJF (Protocol number 002/2017). After the birth of their pups, Wistar rats were randomized in 5 groups (n=15) that received treatment during the first 10 days of lactation by oral administration: control (1ml distilled water), vehicle (1 ml distilled water 20% glycerin) and three treated (500 mg/Kg/ day, 1000 mg/Kg/day, 2000 mg/Kg/day of Valerian). The offspring were kept under standard conditions. When adults, one male and one female from each litter were randomly selected and submitted to the step-down inhibitory avoidance task, to evaluate long-term memory. After data analysis, no significant changes were observed in the establishment of long-term memory between the experimental groups, in both male and female offspring.

These findings suggest that maternal treatment with Valeriana officinalis during lactation does not cause changes in long-term memory in adult offspring.

Maternal anxiety • Lactation • Memory

POSTER | Friday 9th 11:10-12:10 hrs.

B60113

B60115
Basic Science
Maternal and fetal health

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Maternal exposition to Glyphosate-Roundup programs the developmental of the reproductive system in male C57Bl6 mice

One of the most consumed pesticides in the world is glyphosate, the active ingredient in the herbicide RoundupÂ®. Despite its alleged safety due to its highly selective mechanism of action in plants, it has been shown that glyphosate acts as an endocrine disruptor. Exposure to these substances at critical times of development such as gestation and lactation, can lead to fetal programming and cause reproductive problems in adulthood. Reproductive toxicity of glyphosate is associated with inhibition of aromatase and alpha- reductase enzymes and decreased expression of androgen and estrogen receptors. Our hypothesis is that maternal administration of glyphosate during pregnancy and lactation will affect the development of reproductive organs leading to impair fertility in

Female C57Bl6 mice received 0.5% of glyphosate (Roundup Original DIÂ®) in the drinking water (Gly group) or pure water (CTL group) during the pregnancy (21 days) and lactation (30 days). After weaning male offspring were selected to compose the two experimental groups: Gly-F1 and CTL-F1which were named according to the maternal exposition to glyphosate or not. Both groups received standard diet and water ad libitum. At 150 days of life, the mice were euthanized and whole blood was collected to obtain the plasma. The epididymis was removed for sperm count with a hemocytometer. The plasmatic and intra-testicular levels of testosterone were measured by ELISA and LH and FSH was evaluated with the Milliplex Map assay kit. The level of significance was set at $p<0.05$. The Gly-F1 group showed a decrease in sperm number in epididymis cauda ($p=0.001$) and an increase in the intratesticular testosterone ($p=0.004$) and LH ($p=0.008$) levels compared to CTL animals. The levels of plasmatic testosterone and FSH did not show differences between the groups ($p= 0.281$ and $p=0.808$, respectively).

For the first time, we showed that the maternal administration to glyphosate RoundupÂ® Original DI during the entire pregnancy and lactation period alters the male reproductive system in adult mice. As this period is critical to development of male reproductive system, we suggest that glyphosate leads to fetal programming and, consequently, leads to changes in the fertility in adult mice. Also, our results reinforce the idea that glyphosate acts an endocrine disruptor due to changes in the hypothalamic-pituitary axis.

Pesticides • Testosterone • Programming

ORAL | Thursday 8th 12:00-13:00 hrs.

B60115

B60153
Basic Science
Maternal and fetal health

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Maternal protein restriction influences Src, Cldn-1 and NFÃŽÂºÃŽÂ² expression during epididymis development on male rats offspring

Early-life induced epigenetic changes can permanently alter the phenotype of the adult organism, making it susceptible to the development of several diseases. Protein restriction is one of the best characterized early growth restriction models studied until today. During pregnancy an increase in protein turnover is required to meet the embryos rapid growth requirements and adequate protein intake is important to attend the additional nitrogen demand required by the fetus. Maternal protein restriction causes sperm alterations on male offspring associated with epididymal functions such as sperm motility and viability. There are no studies explaining how these alterations occur and how protein restriction at an early stage of development affects epididymal development an

Pregnant females Wistar rats were distributed in two groups and fed ad libitum with normoprotein (NP group) or low-protein (LP group) diets during gestation and lactation. After weaning, at post-natal day (PND) 21, the male offspring received standard diet until the ages of 21, 44 and 120 days when they were euthanized and had their epididymis collected and divided into initial segment plus caput (IS+CP) and corpus plus cauda (CP+CD). Western Blotting analyses were performed to Src 416, Src 527, Cldn-1 and NFÃŽÂºÃŽÂ² expression evaluation in each epididymal part. Maternal protein restriction increased Src 416 expression in whole epididymis at PND 21, while at PND 44 and 120 these protein expression was decreased by low-protein diet only on IS+CP and CP+CD respectively. A decrease on Src 527 expression was observed only in IS+CP of LP animals at PND 21. Low-protein diet increased the expression of Cldn-1 on epididymis in all analyzed ages, despite this result had been significant only in CP+CD at PND 44. Finally, it was observed an increase on NFÃŽÂºÃŽÂ² expression only in CP+CD of 120-days animals whose mothers were submitted to protein restricti

Src pathway plays an important role in the earliest stages of epididymal development, acting on the growth and cellular differentiation of the organ, while in adulthood these proteins are directly related to sperm capacitation. Cldn-1 is a transmembrane protein that makes up the hemato-epididymal barrier and is therefore fundamental for the regulation of epididymal highly specialized lumen necessary for spermatozoa maturation. The aberrant activation of NFÃŽÂºÃŽÂ² pathway is part of epididymal inflammatory response, and may even trigger the appearance of adeno-

matoid tumors, the most common neoplasia of epididymis. We observed that maternal protein restriction, during gestation and lactation, altered the expression of Src, Cldn-1 and NFÃŽÂºÃŽÂ² in the epididymis of male offspring at important periods of this organ development and the sperm capacitation. Thus, the insufficient supply of proteins in early life permanent changed the structure and the functioning of epididymis, which may have contributed to the appearance of spermatic alterations already observed with this experimental model.

low-protein diet • epididymis • development

POSTER | Thursday 8th 10:40-11:40 hrs.

B60178
Basic Science
Maternal and fetal health

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Intrauterine malnutrition contributes to downregulate inflammatory responses via NF-kappaB and p38 MAPK signalling pathways in lung endothelial cells.

Low birth weight (LBW) rats exposed to intrauterine malnutrition present impaired lung inflammatory response and failure to increase circulating leptin levels. Based on this information, we proposed that this hormone might play an important role in immune response. To investigate it, we evaluated the activation of the p38 MAPK and NF-kB signaling pathways, involved in defense process, in pulmonary endothelial cells from these animals, also examining the expression of leptin receptor (ObRb) and its role in the production of lipid mediators and cytokines.

Lung endothelial cells were obtained from normal-birth-weight (NBW) rats or LBW, induced by intrauterine malnutrition. These cells were stimulated with leptin (10 ng/mL), LPS (lipopolysaccharide - 1 microgram/mL) or leptin plus LPS. Six hours after stimulation, the production of inflammatory mediators (PGE2, LTB4, IL-1 beta and IL-6) was evaluated using commercial ELISA kits; western blotting was performed to investigate p38 MAPK and NFkB activity and ObRb expression. In endothelial cells from NBW rats, LPS enhanced the production of IL-1 beta and IL-6 and Leptin increased IL-1 beta levels. LPS increased the levels of PGE2 and LTB4, in cells from both groups and leptin addition potentiated lipid mediator production induced by LPS, in NBW cells. The expression of leptin receptor was decreased in endothelial cells from LBW group. Both LPS and leptin administration stimulated activation of signaling pathways in NBW group. In addition, leptin did not potentiate the activation induced by LPS. However, none of the stimuli were able to activate NFkB and p38 signalling pathways in cells from LBW rats.

These results suggest that intrauterine malnutrition could contribute to attenuate inflammatory response of lung endothelial cells, inducing molecular changes that compromise expression of Ob-R and activation of NF-kB and p38 MAPK signalling pathways, also reducing the expression of inflammatory mediators and cytokines. Supported by FAPESP (2017/02042-3 and 2012/51104-8) and CNPq.

Malnutrition • Inflammation • Leptin

POSTER | Thursday 8th 10:40-11:40 hrs.

B60178

B60179
Basic Science
Maternal and fetal health

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Low-protein maternal diet deregulates ERK and c-SRC pathways during postnatal epididymal development: a catch-up attempt in male rat offspring.

The concept of Developmental Origins of Health and Disease defines as fetal programming the gestational conditions that determine changes in the fetus phenotype to adapt to the postnatal environment. This process impairs the individual development and some effects could be permanent. Low-protein diet during gestation and lactation is one of the most useful models to induce morphofunctional changes in different organs of offspring, which are a consequence of maternal malnutrition. Previous studies have shown that fertility of the male rat offspring is affected by maternal malnutrition. This result may have deleterious effects on the normal epididymal development. A better understanding of the mechanisms and signaling pathways that regulate the epididymis development is

The aim of this study was to investigate the effects of maternal protein restriction on the epididymal development of male rat offspring. Pregnant female Wistar rats were divided into two groups that received either normoprotein (17%; NP) or low-protein (6%; LP) diet ad libitum during the perinatal phase. At postnatal days (PND) 7 and 14, male pups were euthanized and the epididymis were collected to verify ERK, c-SRC, FGFR1 and FGFR2 protein levels by Western Blotting method. The protein levels of ERK, c-SRC and FGFR1 were higher in the LP group at PND 7 and 14. Conversely, the restricted animals showed a reduction in the levels of epididymal FGFR2 at PND7 and a significant increase was found at PND 14.

SRC, ERK, FGFR1 and FGFR2 proteins are considered of extreme importance in the earliest stages of epididymal development. They are closely related to the cell proliferation, differentiation and polarity. FGFRs act by signaling events during the formation of the mesonephric duct, among them FGFR1 is expressed in the mesenchyma and FGFR2 in the epithelium. SRC and ERK play an important role to regulate the transduction signal for cell growth and differentiation, mainly in the initial segment region of the epididymis. The present results suggest that the maternal diet deregulated these proteins at molecular level at both restricted ages. These changes, found in animals that grew in an adverse intrauterine environment, could be a possible catch up attempt at postnatal epididymal development promoted by low-protein maternal diet.

low-protein diet • epididymis • PND development

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60179

B60181
Basic Science
Maternal and fetal health

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Maternal exposure to glyphosate reduces body weight of adult offspring mice without impaired glucose homeostasis in adult life

Glyphosate (N-(phosphonomethyl)glycine) (GL) is a broad-spectrum systemic herbicide used to kill weeds. The excessive exposure to GL may be involved to the etiology and pathophysiology of metabolic syndrome and type 2 diabetes. Exposures to environmental chemicals in intrauterine life and during lactation can result in permanent changes in tissue and organ function, causing negative implications and diseases in adult life. Herein we evaluated the effects of chronic exposure to GL in pregnant mice and their male offspring.

During pregnancy and lactation (total 51 days), C57BL/6 mice received 0.5% of glyphosate (GL group) in drinking water while the control group (CTL) received only water. Ten days after weaning, the female mice were euthanized and body features and fasting glucose and insulin were verified. At 60 and 150 days of life, male offspring mice (CTL-F1 and GL-F1) were submitted to oral glucose tolerance test (OGTT). At 150 days, body features and fasting glucose and insulin levels were analyzed. Data are mean (SEM). Students t test, $p<0.05$. The body weight gain during pregnancy and lactation was lower in GL group. There was no difference in the number of offspring born in both female groups. GL group also showed lower water and food intake. The glycemia and insulinemia is similar in both female groups, although the white adipose content was higher in GL group. At 60 days and after glucose loading, GF-F1 group showed lower glycemia in the OGTT. But, at 150 days there was no difference in the OGTT in both male groups. Body weight was lower in GL-F1 group, without changing the white adipose content. Glycemia and insulinemia were similar in both male groups.

Pre- and postnatal exposure to GL impaired the body weight gain during pregnancy and lactation, without changing the number of offspring born, as well as, decrease water and food intake in GL group. Maternal chronic exposure to Roundup Original DI reduced the glycemia on the OGTT at 60 days of life, and impaired body weight gain on GL-F1 group. However, the glycemia was normalized during the adult life and insulinemia was not affected.

Pesticides • Toxicity • Glycemia

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60181

B60190
Basic Science
Maternal and fetal health

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Maternal obesity in the rat impairs offspring aging of the muscle function

Maternal obesity affects fetal skeletal muscle development, enhancing intramuscular adipogenesis and fibrogenesis in the offspring. These early changes in the muscle phenotype may have long-term negative consequences for the offspring aging. Physiological muscle aging is accompanied by the presence of skeletal muscle weakness and atrophy. We hypothesized that maternal obesity impairs prematurely offspring muscular function. To probe this hypothesis, we aimed to evaluate the progress of age-related muscle dysfunction at three ages in offspring from obese mothers.

From weaning throughout pregnancy and lactation, female Wistar rats ate chow (C group) or high-fat (MO) diets. Offspring (OFF) only ate chow diet. Forelimb grip strength (FGS) and Rotarod (RR) tests were performed in juvenile (postnatal day 70), young adult (220), and middle-aged (450) OFF. Data difference ($p<0.05$) of mean ± SEM was determined by 2-way ANOVA; n=6-12 rats/group. Similar body weight (BW) per age was observed in C and MO male OFF. BW was higher in young adult and middle-aged MO female OFF compared to C female OFF. Less FGS had young adult and middle-aged C and MO male OFF than juvenile rats; no FGS differences between C and MO male OFF were found. C and MO female OFF showed similar FGS at all ages. FGS decrease was found in young adult and middle-aged MO female OFF in comparison to C female OFF. Finally, achievement of execution was considered when tested rats remained 10 min walking in RR at 11 RPM. All juvenile MO and C male OFF (100%) executed the RR decreasing to 71% at young adult age and to 33% at middle-aged. No differences were found between MO and C male OFF. Differences of execution were found in middle-aged MO female OFF (83%) compared to C (100%).

Our findings suggest that physiological aging of muscle dysfunction may begin at middle age in the offspring of mothers fed with control diet. Maternal obesity promotes premature muscular weakness at young adult age, displaying a low performance of the enforced motor activity at middle age in the female OFF. Further studies with animals of median ages to those evaluated here could support these findings.

Maternal obesity • muscle dysfuncti • offspring aging

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60190

B60201
Basic Science
Maternal and fetal health

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Can prostate cancer originate in utero? Role of cancer signaling pathways in prostate carcinogenesis induced by maternal low protein diet in aging offspring

Background: Maternal exposure to low protein diet (LPD) increases susceptibility to prostate cancer (PCa) in older rat offspring. Although the imbalance of estrogen/testosterone ratio upon the developing prostate has been implicated with PCa, the molecular mechanisms of how maternal LPD elicits prostate carcinogenesis are still unknown.

Methods and Results: Here, we used male rat offspring born to dams fed control diet (CTR, 17% protein) or LPD (6% protein) during gestation and lactation periods. The animals were euthanized on postnatal day (PND) 21 and 540 and the ventral prostate was excised and processed for RNAseq (HighSeq-2500 Illumina) and mass spectrometry (LCMS/MS). We identified 14 microRNAs significantly altered between CTR and LPD on PND21 and 9 between CTR and LPD on PND540. Proteomic profile listed 78 altered proteins between CTR and LPD on PND21 and 282 between CTR and LPD on PND540. Enrichment analysis of biological processes and disease related pathways using miRtarget, Survexpress and CBioportal databases revealed cancer as the common signaling pathway associated with altered microRNAs and proteins. Among them, the top downregulated were the microRNAs miR-7a and miR-18a in LPD offspring on PND21 and 540, respectively, whereas the top upregulated protein was Calreticulin (CALR) in LPD groups in both age.

Conclusion: Maternal exposure to LPD disrupts the developing prostatic molecular homeostasis in young rats, creating a permissive microenvironment to slow-growing prostate carcinogenesis, which results in high incidence of PCa in older rat offspring. Moreover, our study highlights the application of Ã¢â‚¬Å“omicsÃ¢â‚¬Â” analysis combined with biological databases approach as a useful tool to characterize potential biomarkers and molecular pathways involved in rodent prostate carcinogenesis and human PCa.

Maternal LPD • Rat prostate • Carcinogenesis

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60201

B60223
Basic Science
Maternal and fetal health

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Effect of high intensity physical exercise during pregnancy in female Wistar offspring

Insults during early life can predispose individuals to long-lasting deleterious effects later in life. This phenomenon has been known as metabolic programming. Studies have shown that physical exercise during pregnancy is known to have beneficial effects on maternal health, decreasing the risk of preeclampsia and gestational diabetes. On the other hand, high intensity physical exercise during pregnancy in women can affect fetal health, inducing maternal hyperthermia, increased uterine contractility by hormone stimulation, fetal hypoglycemia and reduction in visceral and placental blood flow due to diverted blood to the working muscles mass and skin. Higher intensity exercise over a long duration during pregnancy can induce negative outcomes in human and rodent offspr

To test these hypotheses, pregnant female Wistar rats, 70 days-old were distributed into 2 groups: sedentary mothers (SM) and exercised mothers (EM). the exercised group performed high intensity physical exercise, on the rodent treadmill at 80-90% VO2Max during15 minute per session 3 times a week throughout pregnancy. At birth the female offspring were standardized in 9 pups per dam and distributed into 2 groups: sedentary mothers offspring (Sed-Mothers) and exercised mothers offspring (Exe- Mothers), the both groups were euthanized at P21. The offspring from maternal high intensity physical exercise shows low mesenteric fat pad stores and low abdominal and cranial diameter at birth, the results suggest that high intensity physical exercise during pregnancy, could be reduced placental blood flow and affected fetal nutrition and normal fetus development, suggesting intrauterine restriction growth. On the other hand, at 21 days old both groups showed a similar data to biometric and metabolic parameters, suggesting an catch-up of growth, that could be lead to metabolic chronic disease in an adult life.

In conclusion, the future studies are necessary to investigate the effects of maternal high intensity exercise exposition and the possible relation with metabolic chronic disease in offspring adult life.

High intensity • Exercise • Pregnancy

POSTER | Friday 9th 11:10-12:10 hrs.

B60223

B60291
Basic Science
Maternal and fetal health

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Optimal Characteristic Selection and Classification of Fetal Growth Restriction using AECG

Fetal Growth Restriction (FGR) is manifested in the first stages even when there is no evidence of hemodynamic alterations in the Doppler evaluation. Despite this, adverse perinatal outcomes are still identified, indicating the importance to explore the fetal physiological responses. An altered autonomic cardiac regulation has been associated with FGR. In this work several indices extracted from the analysis of the heart-period fluctuations, along with anthropometric information of the mother, were used for the classification of FGR using a Random Forest (RF) classification method. Also, an optimal characteristic selection was made using Genetic Algorithms (GA) in order to improve the classification result. An accuracy of 82.5% was achieved using o

The AECG recordings where obtained from 43 patients, seeking for simultaneous fetal breathing movements and detectable fetal QRS complexes. The mother weight, height, IMC and age were used along with 29 variability indices extracted from the ECGA signals were used for the classification FGR. Random Forest is a hybrid classification method that uses an ensemble of randomly trained decision trees with the same distribution, letting them vote for the most popular class. An accuracy of 55.0% was obtained using the 43 patients in the data base along with the 33 previously mentioned characteristics. Optimal characteristic selection is an important problem that may increase the outcome of the classification. GAs have been previously used in order to find the optimal features for classification in different research areas. Several runs of a simple GA were made to increase the outcome of the RF by reducing the number of characteristics used for the classification. The best results were obtained using only 5 of the 33 characteristics, obtaining an accuracy of 82.5%.

A simple GA along with a RF classification method were used in order to find the optimal characteristics that improve the outcome of the classification of FGR. An accuracy of 82.5% was obtained using the weight and age of the mother along with three variability indices, having a better outcome compared with the results obtained using all the 33 characteristics (Accuracy of 55%). The results show that the classification of FGR is possible using RF when a selection of optimal characteristics is made. The three variability indices correspond to the high frequency and low

frequency indices, in fact all of the simple GA runs choose the high frequency index obtained with the fast Fourier transform (parameter closely linked with fetal respiratory sinus arrhythmia, parasympathetic activity and to the autonomic fetal adaptability) as an optimal characteristic for classification, indicating that this characteristic has relevant information and should be taken into account for future studies.

Growth restricti • AECG • Random forest

POSTER | Thursday 8th 10:40-11:40 hrs.

B60296
Basic Science
Maternal and fetal health

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Regulatory mechanism of monocyte function in neonates from obese women through differential effects of leptin and FFAR4 on mTOR pathway

Offspring from women with pre-gestational obesity (pOB) are at high risk to develop immune-related chronic diseases. Recent data show that maternal obesity also results in an altered pro- and anti-inflammatory responses in pOB monocytes and macrophages compared with cells from offspring from lean women (pLE), along with increased leptin and decreased EPA/DHA levels in plasma. Considering the active role of leptin and EPA/DHA regulating pro- and anti-inflammatory responses, respectively, we hypothesize that monocyte function is differentially regulated by leptin and FFAR4 signaling, and that aberrant regulation in pOB monocytes leads to exacerbated inflammatory responses.

Monocytes were obtained from pOB and pLE umbilical cord blood. Monocyte DNA was isolated, converted with bisulfite for further microarray-based DNA methylation analysis. Differential DNA methylation in pOB monocytes was inspected by pathway enrichment analysis. pLE macrophages were obtained by differentiation with M-CSF for 7 days in presence or absence of leptin. Macrophages were activated with LPS+IFN? for 24 hours and mRNA expression of pro- and anti-inflammatory cytokines (TNF and IL-10, respectively) was assessed by qPCR. Monocytes from pLE were stimulated with DHA and levels of total and phosphorylated proteins of Akt/mTOR pathway were determined by western blot. Extended exposure of leptin during monocyte differentiation increased basal expression of TNF-? mRNA. Also, pre- treatment with leptin further increased TNF-? mRNA expression upon stimulation with LPS+IFN? in pLE macrophages. DHA treatment induced phosphorylation of Akt S473 by mTORC2, potentially mediated by the fatty acid receptor type 4 (FFAR4). DNA methylation analysis showed that pOB monocytes have differentially methylated CpG sites in genes involved in several pathways, including insulin and Akt/mTOR pathways.

Enhanced expression of TNF-? by leptin suggests that the increased levels of leptin in pOB blood might be involved in the programming of the fetal immune system, driving strong responses to pro-inflammatory stimuli. pOB monocytes exhibit changes in the methylation of several genes related with Akt/mTOR pathway which regulates cell growth, cell cycle and metabolism. The differential methylation on genes involved in this pathway might reflect that the M1-like function of pOB monocytes and macrophages is caused by a metabolic programming, induced by maternal obesity and mediated by leptin. Both leptin and FFAR4 signaling modulate the activity of Akt/mTOR. Chronic exposure to leptin might lead to increased mTORC1 activation and reduced Akt and mTORC2 activity. The activation of FFAR4 with DHA induces the phosphorylation of Akt S4[illegible]

which is mediated by mTORC2, suggesting that FFAR4 signaling could inhibit the pro-inflammatory response induced by leptin through regulation of the Akt/mTOR pathway. Understanding the role of the modulation of mTOR pathway by leptin and FFAR4 signaling could provide insight into the mechanisms of inflammation-related diseases after birth.

maternal obesity • fetal monocytes • programming

ORAL | Thursday 8th 12:00-13:00 hrs.

B60361
Basic Science
Maternal and fetal health

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Excessive gestational weight gain induces differential microRNAs expression in visceral fat: a link between maternal and fetal metabolic programming

Maternal metabolic adaptations during pregnancy assure an adequate fetal energy supply, and adipose tissue plays an important role in regulating mechanisms involved in fetal nutrition. Pre-gestational obesity and excessive gestational weight gain (EGW) are related to altered production of maternal adipokines, cytokines and oxidative stress that have been associated with a state of fetal overnutrition. MicroRNAs are post-transcriptional regulators of several physiologic processes including energy metabolism, and their expression profile in visceral adipose tissue during pregnancy it has not been described. Our aim was to characterize the effect of gestational weight gain over the microRNAs expression profile in mature adipocytes from maternal visceral adipose tissue.

Visceral fat biopsies (n=20) were obtained during cesarean section from healthy adult women with singleton pregnancies at term without labor. Pre-gestational weight was categorized according WHO criteria and gestational weight gain by IOM criteria: obese with EGW, obese with adequate gestational weight gain (AGW) and women without obesity with AGW. Mature adipocytes were isolated from fat by enzymatic digestion to extract total RNA (including microRNAs), and concentration, purity, integrity and microRNA content was assessed using a bioanalyzer platform. RT- qPCR microarrays were used to evaluate the expression of 84 microRNAs and in silico functional analysis was evaluated for significantly over expressed microRNAs. Results: Obese women with EWG showed a significant overexpression of mir-24-3p (3.97 fold change) and mir-128-3p (2.97 fold change) compared to women without obesity and AWG, as well as overexpression of mir-124-3p (13.13 fold change) compared to obese women and AWG. In silico analysis showed association of these microRNAs with pro- and anti-inflammatory responses, metabolism of folic acid and cholesterol, insulin resistance, and oxidative stress generation.

Maternal obesity with excessive weight gain during pregnancy promotes an unfavorable environment that generates changes in microRNA expression in adipose tissue, which probably regulate several signaling pathways linked with fetal nutrition. These findings open a new research field about the role of the maternal microRNAs in fetal programming. This study characterizes for the first time the expression profile of microRNAs in mature adipocytes of visceral fat.

Obesity • Weight gain • microRNA´s

ORAL | Thursday 8th 12:00-13:00 hrs.

B60361

B60364
Basic Science
Maternal and fetal health

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Characterization Of Upec Clinical Isolates In Pregnant Women.

Urinary tract infection (UTI) continues to be a public health problem in Mexico. It is characterized by the presence of bacteria in the urine (bacteriuria). UTI can be symptomatic or asymptomatic, complicating its diagnosis and treatment. E. coli is the main causa agent. When E. coli colonizes the urinary tract, it is called uropathogenic E. coli (UPEC). This bacterium has been associated with the development of neonatal sepsis, nosocomial outbreaks and with recurrent infections in pregnant women. In addition, this bacterium has high rate of antibiotic resistance. Therefore, the identification of the genetic profile of E. coli strains isolated from pregnant women, might lead us to establish their clonality and to relate them to clinical presentation and complications.

The E. coli clinical strains were obtained from urine culture samples collected in the INPer of women with urinary tract infection. The UPEC strains were selected by the detection of the fimH, iutA, fyuA, hlyA, traT, rpaI, papA and ibeA genes by multiplex PCR. For the classification of the UPEC in phylogroups, the methodology of Clermont and collaborators was used. The clonal characterization of the clinical isolates was carried out by PFGE, using the XbaI enzyme in the CHEF Mapper® XA system. The bioinformatic analysis was carried out in the Bionumerics 7.6 software. In 97% of the clinical isolates of UPEC, at least one of the 8 virulence factors were identified; the most frequently amplified genes were: fimH (70.1%), fyuA (82%), iutA (54%) and traT (54%), The genes that were in less than 50% of the isolates were: rpaI, ibeA, hlyA and papA. Regarding the phylogroups, it was found that 45% of the isolates belonged to phylogroup B2, 37% to phylogroup A, 12% to phylogroup D and 6% to phylogroup B1. PFGE analysis of 42 clinical isolates did not show a predominant group; but, two clones presented the same restriction profile. The frequency of antibiotic re

The fimH, fyuA, iutA and traT genes were the most frequently amplified genes and are useful as molecular markers to identify UPEC isolates. The ibeA gene was only identified in the phylogroup B2, suggesting that this phylogroup is associated with meningitis development. The E. coli strains belonging to phylogroups B2 and A are the most frequently isolated in pregnant women. The highest frequency of virulence genes was found in E.coli antibiotic sensitive strains of phylogroups B2 and A, indicating that the presence of virulence factors is independent of antibiotic resistance.

No clonal relation was found among the clinical isolates of UPEC suggesting that they are strains acquired in the community.

UPEC • PFGE • VIRULENCE FACTOR

POSTER | Wednesday 7th 17:40-18:40 hrs.

B60368
Basic Science
Maternal and fetal health

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Early prenatal oxidative stress, lipid profile and weight gain predict normal/small for gestational age infants in obese pregnancies: a neural network approac

Obesity during pregnancy is associated with an inflammatory and oxidant/antioxidant- unbalanced environment for the fetus, with negative consequences for its development. We hypothesized that such maternal background may be key for predetermining fetal growth, allowing to estimate normal or small for gestational age (NGA or SGA) neonates. SGA infants are not recognized before birth, present higher morbidity and may predict childhood obesity, therefore estimation of such outcome in early pregnancy is warranted. Neural networks based on learning from non-linear datasets are accurate in prediction. Thus, the aim of this study was to develop a neural network model for the estimation of SGA or NGA neonates based on maternal biochemical data in a cohort from normal, overweight and obese mothers.

Dataset was obtained from the cohort study "Epigenetic and Biochemical origin of obesity" (grant # FOSSIS-2015-3-261661), with normal, overweight and obese pregnant women and their infants. The maternal input variables were: age, pathology, pre-gestational body mass index, first trimester plasma concentration of glucose, triglycerides, total cholesterol, HDL-C, LDL-C and biomarkers for oxidation products of lipids and proteins (such as Malondialdehyde (MAD), carbonylated proteins), total anti-oxidant capacity, as well as weight gained during pregnancy and gestational age, assessed at birth. The output was the prediction of either NGA or SGA neonates. An artificial neural network was trained, tested/validated with a BPNN. A sensitivity analysis was then performed to identify which maternal variables were more important for the prediction. We obtained a prediction model for NGA or SGA neonates with a regression coefficient of R2=0.96 between the experimental and estimated data. Total anti-oxidant capacity and weight gained during pregnancy were the most important variables for the prediction followed by HDL-C, LDL-C MDA and gestational age. (Grant #2017-2-65 INPer).

A neural network approach was able to estimate NGA or SGA neonates based upon first trimester biochemical and clinical maternal biomarkers. Early pregnancy maternal anti-oxidant/oxidant balance (in particular lipid peroxidation) together with HDL-C and LDL-C are key factors for estimating fetal growth, as wells as maternal weight control at the end of pregnancy. These results allow to generate novel hypothesis into the mechanisms regulating fetal growth and neonatal outcome. They may also be used in clinical settings to estimate NGA or SGA neonates from the first trimester of pregnancy.

obese pregnancy • fetal growth • machine learning

POSTER | Thursday 8th 10:40-11:40 hrs.

B60368

B70216
Basic Science
Placental programming

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No Evidence Of Insulin Resistance In Placental Villous Explants From Pregnancies Complicated By Maternal Obesity And/Or Gestational Diabetes

Maternal obesity and/or gestational diabetes (GDM) are associated with poor pregnancy outcomes, including an increased risk of fetal overgrowth. Fetal growth and development are dependent on placental function, such as hormone secretion, protein synthesis and amino acid transport, which is stimulated by maternal insulin through the activation of the PI3K/AKT/mTOR pathway. Pregnancies complicated by obesity and GDM are associated with peripheral insulin resistance and it is widely assumed that the placenta also is insulin resistant in these conditions. However, there is little experimental evidence to support this conclusion. We tested the hypothesis that placental villous explants remain insulin responsive in pregnancies complicated by maternal obesity and/or GDM.

Methods: Term placentas were collected from women with normal body mass index (NORMAL, BMI; 18.5-24.9, n=9), obesity (OB, BMI >30-40, n=6), GDM with normal BMI (N-GDM, n=6) and obesity with GDM (OB-GDM; n=5). Placental villous explants were cultured at 37oC for 3 hours in varying concentrations of insulin (0, 0.25, 0.5, 1 nM). Activation of the insulin signaling pathway was determined by western blot for p-AKT(T308), p-Ribosomal S6(235/236) and p-4E-BP1(T35/36). One-way ANOVA testing was used to determine statistical significance at $P<0.05$. Results: Insulin treatment of 1nM, representing high physiological post-prandial concentration in pregnant women, significantly increased phosphorylation of AKT in placental villous explants when compared to untreated controls in each condition (Normal p=0.01, N-GDM p=0.008, OB p=0.05, OB-GDM p=0.04). Phosphorylation of 4E-BPI was significantly increased after insulin stimulation in normal (p=0.05) and OB (p=0.01) explants, while phosphorylation of S6 increased in Normal (p=0.01), N-GDM (p=0.03) and OB-GDM (p=0.01). We found no difference in the magnitude of insulin responsiveness between pregnancy conditions tested by two-w

We found no evidence of insulin resistance in placental villous explants from pregnancies complicated by maternal obesity and/or GDM. Skeletal muscle and adipose tissue become insulin resistant and islet insulin secretion increases as a physiological adaptation to normal pregnancy. Peripheral insulin resistance is exacerbated in pregnancies complicated by obesity and/or GDM. In contrast, our data suggest that the placenta remains fully insulin responsive in these pregnancy complications. We suggest that elevated maternal insulin levels which are associated with maternal

obesity and/or GDM promotes critical placental functions such as nutrient transport, thereby contributing to increased fetal adiposity and accelerated growth which is more common in these pregnancies.

Diabetes • Placenta • Fetal growth

ORAL | Thursday 8th 15:00-16:00 hrs.

B70272
Basic Science
Placental programming

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Protein expression of nutritional transporters in human placenta and its relationship with birth weight.

Birth weight alterations have been associated with appearance of the complications and diseases in adulthood life, such obesity, hypertension among others. The growth fetal depends mostly of the availability of maternal nutrients, as well the placental transport capacity towards the fetal circulation. The nutrients, such as glucose, amino acids and fatty acids, are transported by transporters proteins that expressed on the surface of the syncytiotrophoblasts. Glucose and amino acids transporters have been studied in human placenta of de woman with pregnancy complications. Hence, our aim of study was evaluate the relationship between birth weight and protein expression of the nutritional transporters in human placenta of the woman without without pregnancy complications with birth weight.

A total of 60 placental samples were included, from woman without pregnancy complications: 20 SGA, 20 AGA and 20 LGA. Placental homogenates were obtained. Protein was quantified by Lowry assay. Proteins were separated by 10% SDS-PAGE. Placenta proteins were electrotransfered to nitrocellulose membranes. Protein expression of GLUT-1, GLUT-3 and SNAT-4 was detected in all study groups by immunodetection with anti-GLUT-1 (1:1500), anti-GLUT-3 (1:500) and anti-SNAT-4 (1:1000) antibodies overnight at 4ºC. Antibodies anti-Rabbit (125000), anti-Mouse (1:5000) and anti-Goat (1:50000) were used for the detection of antibodies anti-GLUT-1, anti- GLUT-3 and anti SNAT-4 respectively. Expression of each nutrients transporter was normalized with ?-Tubulin protein and control group (AGA). Protein expression of GLUT-1 transporter in placenta of LGA group was 90% higher in comparison with SGA group (p=0.001) and 50% higher in comparison with AGA group (p=0.021). In addition, there was a positive correlation between GLUT-1 expression and birth weight (00.034, r=0.278). There were not differences in the expression of GLUT-3 (p=0.433) and SNAT-4 (p=0.078) between all groups.

There were no differences in the GLUT-3 expression between all groups of study. Several studies suggest that the expression of GLUT-3 is regulated by pathological conditions during pregnancy, such as IUGR and Gestational Diabetes Mellitus. This is mainly due to the role of GLUT-3 in placen-

tal tissue, which is to recapture glucose from the fetal circulation, increasing the glucose concentration gradient and therefore increasing the flux of this carbohydrate in the maternal- fetal interface. On other hand, there were not differences in SNAT-4 expression. Consistent with previous studies, in which the expression of this transporter was not affected in placentas of mice with a high- fat diet during pregnancy, as well as in placentas from obese women and neonates with IUGR. Suggesting that SNAT-4 is not involved in fetal growth. However, our results indicated an up-regulation of GLUT-1 protein expression in LGA placentas. Also, previous studies showed a positive regulation of GLUT-1 expression in placentas of women with obesity. Together these findings suggest that GLUT-1 could be involve in fetal growth.

SGA • AGA • LGA

ORAL | Thursday 8th 15:00-16:00 hrs.

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
International Society for Developmental Origins of Health and Disease
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B70284
Basic Science
Placental programming

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Changes in GHS-R1 expression induced by des-acyl ghrelin in BeWo cells of human placenta

Introduction. Ghrelin is an orexigenic hormone with two isoforms: Acyl ghrelin (AG) and Des-acyl ghrelin (DAG). AG binds to its specific receptor GHS-R1 and stimulates the secretion of growth hormone. DAG binds to the GHS-R1 receptor with an affinity 1000 times less than AG. In a previous study we showed umbilical cord blood DAG was more than 50% increased in SGA neonates (small for gestational age) compared to AGA neonates (adequate for gestational age), suggesting that DAG could be involved in fetal growth. Moreover, effects of DAG on cell proliferation and inhibition of apoptosis have been reported. However, there are not studies of DAG action on human placenta. Aim of study was assay effects of DAG on viability and proliferation of BeWo cells and protein expression of GHS-R1 receptor.

Methods and Results. BeWo cells were incubated for 24 h and treated with 3 nM DAG for 12, 24, 48 and 72 h for viability assays (Trypan Blue), and 24 h for cell proliferation (XTT). Protein expression of GHS-R1 receptor was performed in the total cell homogenates at 12, 24, 48 and 72 h by Western Blot using anti-GHS-R1 (1:1000) and anti-mouse IgG HRP (1:22,500). BeWo cells were treated with a receptor antagonist [D-Lys3]-GHRP-6 (30 nM), for 12 and 24 h, as well as with the combination of DAG (3 nM) and receptor antagonist [D-Lys3]-GHRP-6 (30 nM) during 12 and 24 h. Protein expression of GHS-R1 was detected in cellular homogenates. Results were analyzed by ANOVA, considering p ? 0.05 as significant. Cells treated with DAG showed no differences in viability or cell proliferation (p> 0.05). In cells treated with DAG, protein expression of GHS-R1 receptor increased 42% at 12 h (p = 0.029), 36% at 24 h (p = 0.025) and decreased 35% at 48 h (p = 0.005) compared to control. In addition, in the cells treated only with receptor antagonist [D-Lys3]-GHRP-6, GHS-R1 protein expression decreased 43% compared to cells treated with DAG at 12 h (p = 0.002) and 14% at 24 h (p = 0.003).

Conclusions. A previous study of our research group showed that DAG of umbilical cord blood in SGA neonates was more than 50% higher compared to AGA neonates. Also, DAG levels of newborns showed a negative correlation with birth weight and placental weight, suggesting that DAG could be an important determinant of fetal development as well as of placental physiology. In this study it was demonstrated that BeWo cells, cytotrophoblast of human placenta, exposed with DAG does not

present changes in viability or cell proliferation which is contrary to that reported in other placental cell lines such as JEG-3 cells where ghrelin induces an increase in cell proliferation, this can be explained due to cellular stage since BeWo cells are human cytotrophoblast and JEG-3 cells are human syncytiotrophoblast. However, our data showed that DAG induces changes on protein expression of GHS-R1 receptor in a positive way. Suggesting that DAG regulates the expression of GHS-R1 receptor and of downstream molecules such as those involved in nutrient transport or nutrient sensors in human placenta.

Acyl ghrelin • Des-acyl ghrelin • GHS-R1 receptor

ORAL | Thursday 8th 15:00-16:00 hrs.

B70286
Basic Science
Placental programming

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Maternal DHA supplementation in patients with pregestational obesity is associated with downregulation of genes involved in lipid metabolism in placenta.

Pregestational obesity (PGO, BMI >30 kg/m2) is one of the most common high-risk obstetric conditions, both for the mother and the offspring. Obesity during pregnancy has been related with alterations in lipid metabolism in the placenta and the newborn. There is scare knowledge whether supplementation with Docosahexaenoic Acid (DHA) during pregnancy has an effect on the offspring fatty acid profile and on the expression of lipid metabolism markers in the placenta of patients with PGO. The aim of this study was to evaluate if maternal DHA supplementation during pregnancy exerts any change in the fatty acid profile (FAP) and the expression of lipid metabolism markers in the placenta of patients with PGO.

In a cross-sectional study, double-blinded randomized controlled trial (MIGHT, Maternal obesIty control throuGh Healthy nuTrition), where women with PGO were recruited in the first prenatal visit and assigned to two groups that received 200 mg or 800 mg/day of DHA supplementation (named #12 or #13 indistinctively). For the EpiFat study, placentas were collected at the time of delivery. Approximately 50 mg of villous tissue were incubated with RNAlater for 24 h. Total RNA was isolated using Trizol (Invitrogen, USA). The mRNA expression of PPAR alpha, CPT-1, PPAR gamma, SREBP-1 (RT-qPCR). The FAP in cord blood erythrocytes at birth was determined by gas chromatography. The descriptive variables are presented as average, standard deviation. The offspring from #12 (n=11) and #13 (n=12) were all born at term (39, 1 w). Their birth weight was 3533, 593 g (30% female), and placental weight was 443, 92 g. No differences in the FAP in the cord blood erythrocytes from both groups (#12, n=25 and #13 n=15) were detected. However, the mRNA expression of PPAR alpha ($p<0.0001$), CPT-1 ($p=0.0008$), PPAR gamma ($p=0.0013$), SREBP-1 ($p<0.0001$) were lower in group #13.

Since the samples in this study belong to patients of a double-blind randomized controlled trial, we do not know which of both groups received 200 or 800 mg/day DHA (# 12 or # 13). Although maternal supplementation with DHA, had no effect on the levels of the fatty acid profile of umbilical cord blood, we could speculate that DHA could be exerting significant downregulation in the placental expression of both the beta- oxidation (PPARa and CPT-1) and lipogenesis (PPARy and SREBF-1) genes studied.

Maternal obesity • Lipid metabolism • Placenta

ORAL | Thursday 8th 15:00-16:00 hrs.

B70286

B70325
Basic Science
Placental programming

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Alterations Of Birth Weight And Its Association With Placenta Signaling Pathways

Placental triglycerides of SGA, AGA and LGA newborns and its association with fetal growth and adiposity

Birth weight alterations are an important factor for neonatal survival and postnatal health and may impact metabolic health during adult life. Therefore, the study of birth weight establishment and its modifications remains as an important issue for metabolic diseases prevention. Maternal conditions (such as pregnancy complications, obesity, malnutrition, etc.) and placental physiology play a key role in fetal growth. Several studies have reported an association between maternal triglycerides levels, in pregnant women with and without pregnancy complications, with birth weight. However, the role of placenta triglycerides (TGs) in the development of fetal has not been elucidated.

Transversal comparative study in placentas (n=60) from healthy mothers of term newborns SGA, AGA and LGA (small, adequate, and large for gestational age, respectively). Levels of triglycerides (TG) were evaluated in placental tissue samples of SGA (n=20), AGA (n=20) and LGA (n=20). Approximately 200 mg of placental tissue was homogenized with 5% NP-40 at 4°C using Polytron homogenizer. Placental TG was quantified in homogenates of tissue with a commercial spectrophotometric assay (Spinreact). As a measure of adiposity, maternal and cord blood leptin were quantified using Human Leptin immunoassay ELISA kit (Quantikine, R&D Systems). TG levels of placental were higher in group LGA (191±35 mg/dl) compared to AGA and SGA (144±33 mg/dl, $p<0.001$ and 138±58 mg/dl, $p<0.001$ respectively). TG placenta levels did not show differences between AGA and SGA groups ($p=0.6$). Placental TG correlated with birth weight ($r2=0.412$, $p=0.00108$), length at birth ($r2=0.346$, $p=0.00669$), placenta weight ($r2=0.267$, $p=0.0407$) and cord blood leptin ($r2=0.376$, $p=0.00308$). Also, data showed a correlation of pregestational weight and maternal leptin ($r2=0.358$, $p=0.00721$ and $r2=0.258$, $p=0.0485$ respective

In summary, our study showed an association of placental TG with growth and fetal adiposity, measured as leptin levels of newborn (cord blood). Also, was demonstrated a correlation of placental TG with pregestational weight and with maternal adiposity (maternal leptin). Suggesting that placental triglycerides levels are determined from early stages of pregnancy. More studies are required to elucidate the metabolism of TG in the placenta, for example evaluation of protein expression and activity of lipogenic enzymes and fatty acid transporters such as FATPs. For our understanding, it is the first report that shows an influence of maternal adiposity on placental TG, suggesting an influence on the phenotype of the offspring.

Placenta • Triglycerides •Fetal Growth

ORAL | Thursday 8th 15:00-16:00 hrs.

B70325

B80187
Basic Science
Paternal programming

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Reduced mitochondrial response capacity in rats offspring of protein restricted mothers

The fetal and neonatal environments exert a profound influence on the phenotype of individuals as a result of a process known as "fetal programming". The deficiency of protein intake during pregnancy and lactation has been associated with the development of type 2 diabetes (T2D) and cardiovascular diseases in adult life. However, the mechanisms involved are not yet clear. It is known that mitochondrial dysfunction is linked to diseases such as hypertension, fatty liver and T2D. Thus, the programming of the mitochondria could link malnutrition during fetal development and adult disease. Our objective is to evaluate the mitochondrial function in liver and kidney tissue of male offspring of rats exposed to low protein diet during the gestation and lactation.

Dams Wistar rats were fed with a control diet (CD, 20% protein) or a low protein diet (LP, 6% protein) during pregnancy and lactation. The offspring were evaluated on day P28 or postnatal day P180. On P28 and P180 a group of offspring was exposed to thermal stress (4°C/1h), to stimulate mitochondrial activity and to reveal possible functional damage resulted from the LP diet. Mitochondrial function was evaluated through the rate of oxygen consumption and the generation of membrane potential in liver and kidney mitochondria. The mRNA levels of AMPK and mTOR were quantified by qPCR-TR. Exposure to cold stress showed that the respiratory control in the liver of the LP offspring at P28 was lower than the CD offspring ($p < 0.05$). On P180, the liver mitochondria of the LP offspring had a lower ADP-induced respiration rate and their respiratory control decreased by 18% compared to the CD group. The reduction of mitochondrial respiratory control correlated with a decrease in the hepatic mRNA of AMPK and mTOR in P28 and P180. In the renal mitochondria, an increase in the oxygen consumption rate of the uncoupled state of the restricted offspring between P28 and P180 was observed

The results of this study indicate that a LP diet during pregnancy and lactation alters the respiratory capacity of the liver and kidney mitochondria that becomes evident when the animals are exposed to a thermal stress. Our findings showed that these alterations are the result of mitochondria programming under a protein restriction, also the decrease in mitochondrial function occurs before the onset of metabolic disorders such as T2D.

mitochondria • malnutrition • programming

ORAL | Friday 9th 08:20-09:20 hrs.

B80187

B80278
Basic Science
Paternal programming

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Beneficial effects of supplementation with micronutrients in the expression of AMPK and mTOR in the offspring of rats with dietary restriction

Malnutrition in the intrauterine environment causes the fetus to respond with permanent adaptations in the energy metabolism genes expression, and in the physiology of the organs to increase the probability of their postnatal survival. Under this circumstances, the fetal programming of individuals lead to a higher predisposition to develop of obesity and metabolic diseases in adulthood. The aim of this study is to analyze the effect of a supplementation (S), based on omega-3 polyunsaturated fatty acids (n-3) LC-PUFA, folic acid, zinc, iron and selenium, in the expression of energy sensor genes AMPK and mTOR in the progeny of Wistar rats in a model of chronic malnutrition.

A model of rat dams that were 50% food restricted during pregnancy and lactation was utilized. Rats were provided of standard laboratory chow or a 50% food-restricted diet determined by quantification of normal intake in the ad libitum-fed rats. The Animal Research Committee of Faculty of Chemistry (CICUAL) approved this study. The dams were randomly assigned into four groups: control (C), control and supplement (CS), restricted (R) and restricted with supplement (RS). The S was administered in the water daily. On the 28th postnatal day, the offspring were sacrificed, and the organs were weighed. Glucose, cholesterol, triglycerides, total proteins, albumin, insulin and antioxidant capacity levels were measured, and the expression of AMPK and mTOR in the liver was quantified by qPCR-TR. The dams with an RS diet had a lower concentration of insulin and a higher antioxidant capacity. In the female offspring of the RS group, there was an expression of AMPK and mTOR similar to C group, whereas in male offspring of the CS group the expression of mTOR decreased significantly ($p < 0.05$) compared to C group.

These results show that supplementation with essential micronutrients administered under conditions of dietary restriction during the gestation and lactation period programs the offspring to maintain normal levels in the expression of critical genes of energy metabolism such as AMPK and mTOR. The supplement in the offspring without dietary restriction increases the efficiency in the sensing and use of nutrients of the medium. On the other hand, supplementation also has beneficial effects on the mothers. The designed supplement represents the first approach to a possible strategy to reduce the harmful effects produced by an intrauterine environment devoid of nutrients.

AMPK • mTOR • programming

ORAL | Friday 9th 08:20-09:20 hrs.

B80278

B80360
Basic Science
Paternal programming

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Understanding transgenerational effects of parental obesity in mice

Epidemiological and experimental data indicate that maternal (mHF) and/or paternal (pHF) high-fat diet consumption leads to a metabolic imbalance in the offspring, which includes changes in metabolic phenotype and glucose metabolism. Maternal obesity can also lead to cardiovascular disease, in the adult offspring, with or without changes in body weight. Recent studies showed that paternal obesity can induce intergenerational transmission of obesity and insulin resistance through sperm epigenetic changes, but not much is known about how it can affect offspring heart function. This ongoing project aims to understand how parental HF and/or obesity impacts heart function and modulates transcriptional and proteomic profiles throughout subsequent generations.

For this study, F0 male and female C57BL/6J mice were fed control (NC; 6% fat) or high fat (HF45; 45% fat and HF60, 60% fat) ad libitum from 4-10wk of age. At 10wk, nuclear magnetic resonance (NMR) was performed. F0 NC, mHF and pHF mice were mated with NC animals to produce F1 offspring (F1). To further characterize parental diet influence, F2 generation (F2) was obtained by intercrossing F1 mice within groups. Excepting F0, all mice were kept on NC throughout the experiment. All groups are being analyzed for body composition (NMR) and glucose metabolism (GTT) during the time points of 6, 10, 15 and finally at 25wk of age, when cardiac molecular, metabolomics and proteomics will be performed. F0 HF45 males had increased body weight, comparing to NC animals, while HF45 females did not. However, both HF60 male and female displayed an increase in BW and adiposity. By 15wk, F1 mHF45 female shows decreased BW due to lean mass decrease and no changes in GTT. F1 male displayed an increase in BW in both mHF45 and pHF45 groups but only pHF45 had improved GTT assay. Both sexes F2 had no body composition changes until 15wk. Female pHF45 only showed impairment in glucose handling.

Our results indicate that male mice display increased BW while feeding with 45% of fat in their diet, while female mice are resilient to BW gain. However, both maternal and paternal HF45 offspring presented metabolic changes during adulthood, in F1 and F2 generations. We are currently analyzing parental HF60 contribution and transgenerational cardiac molecular and functional changes induced by parental obesity.

high-fat diet • metabolism • heart function

ORAL | Friday 9th 08:20-09:20 hrs.

B80360

B90031
Basic Science
Epigenetics

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Profiles of networks of circulating microRNAs between mother and newborn

Obesity and overweight have been considered as an important health worldwide problem. Obesity is characterized by an increased in body fat that is associated to metabolic alterations including insulin and leptin resistance, and the inflammatory chronic state have a role in the physiopathology. Overweight and obesity are considering an important factor of risk for metabolic syndrome, diabetes type 2 and cardiovascular diseases and other pathologies as cancer. Consequences of short and long term have a social and economic impact in life. It is known that the environment has a role in the establishment of altered metabolic and inflammatory responses, and could be modulated by microRNAs.

Methods. Pregnant women were included and grouped by pre-gestational body mass index 35 with normal weight, 23 overweight, and 12 obese women. A peripheral blood sample was obtained from mother and their newborn, then miRNAs relative expression was determined through qRT-PCR. Results. There are significant differences in the expression of four microRNAs in mothers and newborns between of three groups: pre-gestational normal weight, overweight and obese: miR-146a (p=0.035), miR-155 (p=0.016 and 0.0092), miR-221 (p=<0.0001) and miR-378a (p= 0.003). An association between maternal BMI and the newborns expression of miR-155 and miR-221 expression was also observed. The miRNAs studying be a part of network that could be implicated in programming of metabolic responses due maternal environmental mainly nutritional conditions.

Conclusions. Complex networks were drawer and shown important connections between regulatory pathways suggesting that they may be participating in the programming of metabolic altered responses in the offspring.

newborn • microRNAs • obesity

POSTER | Thursday 8th 10:40-11:40 hrs.

B90031

B90135
Basic Science
Epigenetics

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Canadá

Interaction between environmental quality and the predicted prefrontal gene expression from PRKG1 gene on childhood eating behavior

PKG is a transduction pathway enzyme known for its role in cardiac function, gene expression, and hippocampal learning. Allelic variation in the foraging gene in Drosophila which encodes a PKG is linked to differences in food-related behaviors. Variants with higher levels of PKG (forR) display lower tolerance to acute starvation, more active behaviour towards food, and improved learning in social contexts. Other allelic variants (forS) change flies exploratory behaviour after chronic food deprivation in early life.Our objective was to investigate the interaction between the quality of the early environment and variation in the genetically regulated gene expression of the PRKG1 gene in the PFC on eating behavior outcomes in our human birth cohort (MAVAN).

We used data from Dutch Eating Behavior Questionnaire (DEBQ) applied at 60 months.The genetically regulated gene expression was predicted using an algorithm called PrediXcan, that applies machine-learning solutions to estimate the component of gene expression dependent from the genotype in specific brain regions.This work was focused on PRKG1 gene expression on the prefrontal cortex (PFC).The environmental score considered different variables from both adversity and buffer dimensions of the childhood environment (e.g. fetal growth, maternal mental health, household income, breastfeeding). The score ranges from negative (more adversity) to positive values (more buffering scenarios). Analyses were adjusted by sex.Our findings show that there is a significant interaction between the environmental score and the predicted gene expression of the PRKG1 gene in the external eating domain (B= neg. 0.092, P=0.034).A high PRKG1 gene expression was associated with lower scores in the external eating as the environmental support increases (B= neg. 0.114, p=0.003),with no effect on the low gene expression group (B= neg. 0.031, p=.224).

The aim of this study was to correlate the predicted gene expression from PRKG1 with food related behaviours. Although this relationship is well established in Drosophila, it is not described in humans to date. We found an association between the predicted prefrontal gene expression of PRKG1 and the external eating domain of DEBQ at 60 months of age. Our results also indicate that children with higher PRKG1 expression in the PFC might be less susceptible to poor inhibitory control in response to food cues when the environmental support increases, and no effect seen in the group with lower PRKG1 predicted expression, suggesting a differential susceptibility effect.
susceptibility

PKG1 • genotype • food behaviour

ORAL | Friday 9th 15:30-16:30 hrs.

B90144
Basic Science
Epigenetics

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High-fat diet leads to key hepatic miRNAs modulation that may drive metabolic disturbances in male mice

Hepatic microRNAs (miRs) are highly involved in energetic metabolism. The most expressed miR in the liver, miR-122 is known to regulate lipid metabolism. Let-7 is also an important hepatic miR and recent studies have been showing that it is involved with glucose homeostasis and insulin sensitivity. High-fat diet (HFD) consumption can lead to Non-Alcoholic Fatty Liver Disease (NAFLD), which is characterized by hepatic triglycerides accumulation and is directly associated with the prevalence of obesity in worldwide. Insulin resistance underlies the genesis of both obesity and NAFLD. Therefore, the aim of the present study was to investigate a possible connection between insulin resistance, obesity, NAFLD development and alterations in miR-122 and Let-7 expression in mic

Male Swiss mice were fed with chow diet or HFD (AIN 45%) for 1, 3, 7, 15, 30 or 56 days. At each experimental day, body weight, adiposity and fasting glucose were assessed. Serum was collected to cholesterol (CHOL) and triglycerides (TAG) analysis and liver fragments were collected to access hepatic TAG content and gene expression by qPCR. Body weight, adiposity and serum CHOL were gradually increasing from day 7 to 56 (HF7 to HF56). Hepatic TAG levels were higher at HF1 and increased until HF56, showing a positive correlation with fasting glucose. Hepatic miR-122 expression was decreased from HF3 until HF56, and its predict target, Agpat, was higher than control with acute and chronic exposure to HFD, showing a negative correlation. Let-7 showed an increase at HF1, returned to normal levels at HF3 and was upregulated with a chronic exposure to the HFD, at HF56. Ampk (PRKAA2), a predicted target of Let-7, was negatively modulated at HF1 and HF56, as expected.

We showed here that HFD consumption could alter miRNA expression pattern that may drive alterations in whole body homeostasis and disrupt metabolic syndrome phenotype since the first day of exposure. Hepatic miRNAs are reported to be involved in fat deposition within the liver, high levels of TAG and cholesterol in serum and hyperglycemia. miR-122 and Let-7, for example, have been showing important role in lipid and glucose metabolism. Here, miR-122 is intrinsically related to Agpat expression and Let-7 revealed a possible interaction with Ampk, since this gene was downregulated while Let-7 was upregulated with chronical high-fat exposure. In summary, the results demonstrate a close relationship between hepatic miRNAs modulation and alterations in body composition that can lead to metabolic syndrome development, obesity and NAFLD, all of them related to insulin resistance.

high-fat diet • miRNAs • fatty liver

POSTER | Friday 9th 11:10-12:10 hrs.

B90144

B90148
Basic Science
Epigenetics

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Levels of hypoxia-inducible microRNAs miR-21 & miR-126 are associated with changes in the gene expression of NO-dependent vasodilation in FGR.

Fetal growth restriction (FGR) is associated to intrauterine chronic hypoxia and, short and long term endothelial dysfunction that would result from an altered eNOS expression mediated by epigenetic mechanisms. Studies have demonstrated the contribution of DNA methylation and histone post-translational modifications in this FGR- induced eNOS programming; however no studies have determined the role of hypoxia inducible microRNAs. (i.e. miR-21 and miR-126).

Levels of miR-21 and miR-126, as well as, eNOS, DDAH1, Nrf2 y ARG2 mRNA were determined by qPCR in primary cultures of umbilical artery (HUAEC) and vein (HUVEC) endothelial cells from FGR (n=7) and control (n=7) pregnancies. Additionally, HUAEC and HUVEC from control patients were exposed to hypoxia (1% O2, for 6 to 48 h) and the expression of the previously described miRNA and mRNA quantified. FGR EC showed higher levels of miR-126 along with lower expression of the pro-NO genes, DDAH1, and Nrf2. Additionally, FGR HUVEC showed eNOS and increase ARG2 expression. Levels of miR-21 were negatively associated to eNOS expression in FGR endothelial cells. Conversely, in vitro exposure of HUAEC to hypoxia led to a transient increase in pro-NO genes (eNOS, DDAH1) along with a decrease in miR-21. Conversely, Hypoxia decreased eNOS expression in HUVEC, paralleled by an increase in miR-21, DDAH1, Nrf2 and ARG2 at 48 h. Levels of miR-126 levels did not change under in vitro hypoxia; this suggests that this cell model does not completely resemble the effects of in utero chronic hypoxia on the genes that participate in umbilical vascular dysfunction in FGR.

Micro-RNA miR-21 and miR-126 are differentially expressed in HUAEC and HUVEC from FGR pregnancies and their expression is associated with heterogenous levels of pro-NO genes. The differential regulation of these miRNAs by in vitro hypoxia and FGR suggest that miR-21 and miR-126 participate in the early and late responses to hypoxia, respectively.

miRNA • Hypoxia • FGR

ORAL | Friday 9th 10:10-11:10 hrs.

B90148

B90255
Basic Science
Epigenetics

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Overexpressed Micrornas In Large For Gestational Age Newborns. A Bioinformatic Approach

Obesity is a chronic condition that increases the risk of developing type 2 diabetes (T2D), cardiovascular and cerebrovascular diseases, and some types of cancer. Differential expression profiles of circulating microRNAs (miRNAs) have been reported in pregnant women with pregestational or gestational obesity and in large for gestational age (LGA) newborns, two high risk conditions for developing obesity and T2D. This suggest a role of miRNAs in the development of these diseases. Previous work from our laboratory showed that hsa-miR-486-5p, hsa-miR-126-3p, hsa-mir-29a-5p and hsa-miR-221-3p are overexpressed in LGA newborns. We especulate these miRNas could be involved in metabolic pathways asssociated with high risk of obesity and its comorbidities.

We analysed the putative target genes and pathways of hsa-miR-486-5p, hsa-miR-126-3p, hsa-mir-29a-5p and hsa-miR-221-3p using DIANA-miRPath v.3.0. We included predictions from Tarbase v7.0, TargetScan y microT-CDS v5.0. We found that the predicted target genes are involved in Foxo and PI3k/Akt signaling pathways. Then, we used miRTargetLink Human and found 9 genes with strong interaction with the miRNAs found dysregulated: ZNF460, GATAD2B, AMMECR1L, NDUFB5, SAPCD2, LRP6, SIRT1, FOXO3 and ACVR2B. Using WebGestalt 2017, we perform an over-representation analyses and found these genes are involved in carbohydrate metabolism, and are associated with diabetes, obesity and cardiovascular diseases.

The dysregulation of circulating miRNas is a possible explanation of the higher risk of obesity and diabetes observed in large for gestational age newborns; and could be useful as early biomarkers of risk prediction.

microRNAs • biomarker • metabolic risk

ORAL | Friday 9th 10:10-11:10 hrs.

B90255

B90264
Basic Science
Epigenetics

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Epigenetics And Fatty Acids
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A Low Dose Of Arachidonic Acid During Early Development Leads To A Cumulative Increase In Weight Gain And Dna Methylation Across Three Generations.

The peri-conceptual period is known to be vulnerable to diet-induced alterations in epigenetic modifications that can be inherited within or across generations mammals. However, most studies have focused on transgenerational effects of high fat diets (HFDs) rather than specific fatty acids. This work represents an alternative approach; i.e. whether repeated exposures to arachidonic acid early in mouse development for three generations affect weight gain and global DNA methylation and fatty acid profiles in liver and brain of the resulting progeny.

To characterize the effects of cumulative exposure to AA, we compared whole body weight (WBW), liver weight (LW) and brain weight (BW) of 28-day old sexed F1, F2 and F3 progeny of female and male Balb/C mice supplemented with arachidonic acid (AA) dissolved in soy bean oil (AA) or SBO (SBO) only, for three consecutive generations (F0, F1 and F2). Mice that received no supplements (NS) were also included. In addition, total DNA methylation and fatty acid profiles was analyzed in liver and brain tissues. The supplements were administered as follows: AA or SBO during entire pregnancy (maternal AA and SBO; MAA and MSBO, respectively), or 10 days prior to mating in males (paternal AA and SBO; PAA and PSBO, respectively). Only AA-supplemented progeny showed a significant increase in WBW relative to NS progeny: for MAA supplementation this was evident by a 25% increase in WBW in F1 and F2 generations; for PAA by an 11% increase in WBW in the F2 generation. Across generations WBW, LW and BW correlated significantly with mgs of AA, but not SBO exposure. However, only LW showed a positive correlation between mgs AA, DNA methylation and specific fatty acids.

We show that a discrete supplement of AA administered either prior to mating in males, or during pregnancy in females for three generations – can lead to a 25% increase in WBW of the resulting progeny relative to un-supplemented progeny. That increase is directly correlated with the amount of AA supplemented during early development and is observed in both liver and brain tissues. In liver, cumulative weight gain correlates positively with global methylation and the accumulation of specific fatty acids such as palmitic acid and EPA. Interestingly, both these fatty acids are known to induce changes in DNA methylation in cell culture. Taken together, the data show that AA is a potent regulator of body weight within and across generations and suggest a possible role of AA-induced changes in fatty acid in modulating DNA methylation in liver.

arachidonic acid • cumulative • dna methylation

ORAL | Friday 9th 10:10-11:10 hrs.

B90264

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
International Society for Developmental Origins of Health and Disease
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B90302
Basic Science
Epigenetics

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Association between adult vascular dysfunction and nos3 promoter DNA methylation and its prevention with N-acetylcysteine treatment in fetal growth restriction

Fetal growth restriction (FGR) has short- and long-term consequences, such as increased mor-bi-mortality, deficient growth and vascular dysfunction. This FGR-programing is associated to increased oxidative stress which lead to epigenetic changes in important genes, such as nos3 promoter DNA methylation. Therefore, this work aims to determine the persistence of this changes in adulthood and assess its prevention with N-acetylcysteine (NAC) treatment.

Pirbright White guinea pigs were assigned to control (n = 10) or FGR (n = 16) group. At mid gestation, half of the FGR group were treated with NAC (500 mg/Kg/day) and every sow was submitted to a surgery foe progressive uterine artery occlusion (FGR). Postnatal body weight (BW), biparetial diameter (BPD), digital-tarso length (DTL) and abdominal circumference (AC) were measured once per week. At 8 months old, animals were euthanized, ex-vivo vasodilator function was assessed by Wire myography, the eNOS expression was measured by real time PCR and the methylation status of the endothelial promoter of nos3 was determined by DNA Pyrosequencing. FGR neonates showed a reduced BW adjusted by the length of gestation, along with altered BPD-to-DTL and BPD-to-AC ratios, indicating an asymmetric growth. Postnatal growth and adult weight were decreased in FGR compared to CN. Femoral vasodilation response to ACh was diminished in FGR relative to CN. Levels of eNOS mRNA were decreased, but nos3 promoter DNA methylation increased in aorta endothelial cells from FGR adults relative to CN. All of the FGR-induced changes were reverted by NAC treatment during gestation.

This work demonstrates that FGR-induced effects on growth rate and vascular endothelial dysfunction are maintained until adulthood, and are associated with eNOS promoter methylation. Fur-

ther, we showed that a NAC treatment during gestation can prevent these longlasting effects. Furthermore, the use of femoral artery as a peripheral territory to evaluate endothelial function demonstrate a maintained vascular dysfunction at adulthood. This functional impairment was associated with increased nos3 methylation and decreased eNOS expression in adulthood. Importantly, NAC treatment prevent the effects, confirming the importance of ROS balance in intrauterine life. Considering our findings, we aim to evaluate in the future the oxidative stress levels, cardiovascular function and metabolic balance and their association with other genes expression modifications. Our study shows that FGR related diseases increased risk can be prevented using an antenatal antioxidant treatment.

Fetal growth • epigenetics • antioxidants

ORAL | Friday 9th 10:10-11:10 hrs.

B90314
Basic Science
Epigenetics

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Circulating levels of miRNA-486-5p, miRNA-126-3p, miRNA-29a-5p and miRNA-221-3p from dried blood spots are differentially expressed in macrosomi

Low birth weight and macrosomia have been associated with later-in-life metabolic alterations, probably associated to the developmental origins of the disease. The aim of this study was to characterize the relative expression of microRNAs (miRNAs) participating on the adulthood development of metabolic diseases on a pediatric population with normal, low birth weight and macrosomia.

Eleven chosen miRNAs were obtained from dried blood spots of newborns with low birth weight, macrosomia and normal birth weight (controls); using a technique previously standardized by our laboratory and subsequent analysis by stem-loop RT-qPCR. The data revealed 4 miRNAs (miR-486-5p, miR-126-3p, miR-29a-5p and miR-221-3p) showed significant change in macrosomic newborns compared to controls; whereas no miRNa had significant change in low birth weight newborns compared to controls. Six miRNAs were absent on neonatal samples.

MiRNAs found to be altered in macrosomic newborns have been associated to processes such as glucose homeostasis and regulation of lipid catabolism. In this study we have confirmed newborn dried blood spots are an appropriate source of amplificable miRNAs. Our data also suggests that altered levels of miRNAs in newborn dried blood have potential to be non-invasive biomarkers of early metabolic alterations. Further research is needed to explore miRNAs expression relation to other variables, including newborn gender and clinical metabolic status of progenitors.

MicroRNA • Macrosomia • Metabolism

POSTER | Friday 9th 11:10-12:10 hrs.

B90314

B90425
Basic Science
Epigenetics

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Persistence of epigenetic alterations in adipocytes derived from obese diabetic patients

In obesity the adipose tissue (AT) shows a dysregulation which may not only induce insulin resistance locally, but it can affect the whole body contributing to the development of type 2 diabetes (T2D). Even though the deleterious effects of obesity are clear, the health impact presents individual heterogeneity, and epigenetic regulation plays a role in this variability. Altered DNA methylation has been found in subjects with T2D in tissues important for glucose homeostasis, suggesting that these epigenetic alterations may be implicated in its dysregulation. The aim of this study is to evaluate the presence of epigenetic alterations in mesenchymal cells derived from AT from obese diabetic patients and the persistence of these alterations during in vitro differentiation to adipocytes.

19 obese women were classified as non-diabetic (NDO) or as diabetic (DO). Biopsies of visceral adipose tissue (VAT) were obtained during bariatric surgery procedures. Mesenchymal stromal cells (MSC) were isolated and differentiated to mature adipocytes (MA). DNA and RNA were extracted from these samples to assess DNA methylation and gene expression. Comparing the methylation levels between the DO and the NDO of VATs showed 1573 differentially methylated CpG sites (DMCs) (Delta-Beta>=5% and $p < 0.05$) from which 10 were also differentially methylated in the MSC, none of them were altered in MA. 98 DMCs where altered as in MSC as in MA. None of the DMCs identified were shared between the 3 samples analyzed. To identify the epigenetic alterations that may affect gene expression, we compared the transcription profile in VAT from the DO and the NDO and found 331 differentially expressed genes (logFC>=|0.5| and $p < 0.05$.) from which 30 showed DMCs in VAT. Currently, we are analyzing the transcription profiles from the MSC and MA to identify those epigenetic alterations that have an effect in gene expression during differentiation, so we can functionally evaluate them in the MA cultures.

In conclusion, the current study shows that there are specific DNA methylation patterns in OD patients in VAT, and that some of these alterations are also found in the precursor cells, suggesting that some of the alterations observed in VAT may be epigenetically programmed since the MSC and that these alterations persist during the process of differentiation in vitro. We also found genes whose expression levels correlated to DNA methylation changes in VAT which suggests that epigenetic alterations have an impact on the function of these genes, and it is necessary to evaluate these epigenetic dysregulations on the function of the adipose tissue.

Dna Methylation • Adipose Tissue • Type 2 Diabetes

ORAL | Friday 9th 10:10-11:10 hrs.

B90425

C10196
Clinical Science
Breast milk and early feeding

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Complementary feeding practices and adiposity indices at 12 months of life.

The first 1000 days of life are a critical window in which nutrition influences the risk of developing chronic diseases in adulthood. Some studies show that early initiation of complementary feeding (CF) is associated with greater obesity in later stages. The starting of solids or liquids different to breast milk/formula before the 4th month of age has an apparent relationship with greater obesity risk. However, cross-sectional and cohort systematic reviews have been non-conclusive. The type of foods introduced early has not been studied, except for allergy risk. The aim of this study was to evaluate the association of CF practices with indicators of adiposity at 12 months of life in a group of healthy term infants.

Healthy term newborns (n=92, 48% girls) from a prospective cohort of pregnant women at INPer (Mexico City). Anthropometric measurements were done at 12 months (6M,12M). At 6M, a questionnaire about infant feeding practices was applied. Descriptive statistics, correlations and linear regressions were performed (SPSS). At 6M, 33.7% of them received exclusive/predominant breastfeeding, 34.8% mixed feeding and 31.5% formula. CF started at a mean age of 4.2±1.3 months; 26.4% began <4th month. Half of the infants (54.2%) started CF with added sugars. Infants who started CF<4th month had greater weight, waist circumference -WC- and length/WC –L/WC- at 12M ($p<0.05$). Inverse significant correlations were observed between the month at which added sugars were introduced and weight/length ($r= -0.497$, $p=0.007$), WC ($r= -0.272$,$p=0.03$), ICL ($r= -0.246$,$p=0.05$). The month of introduction of juices and fruits also correlated inversely with body mass index (zscore), weight/length, WC and L/WC at 12 months ($r>0.400$,$p<0.05$). The CF starting month predicted 30% of weight ($p<0.05$) and 22.7% of WC at 12M ($p<0.05$). Starting with sugars explained 24.3% of weight ($p<0.05$) and 23.3% of WC ($p<0.05$) at 12M.

Starting complementary feeding before the 4th month of age is associated with higher BMI, WC and L/WC at 12 months of age. It appears that with earlier introduction of different types of sugars (added sugars, juices and fruits) in the infant's diet some adiposity indicators are higher at 12 months of age. Type of lactation was not associated with the adiposity. It appears that the introduction of sugars (added sugars, juices and fruits) before 4 months of age should not be recommended. Parents should be educated to avoid early introduction of these foods.

Infants • sugars • anthropometry

POSTER | Wednesday 7th 17:40-18:40 hrs.

C10196

C10198
Clinical Science
Breast milk and early feeding

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Adipokines in human milk during different stages of lactation

Breast milk plays an important role in the communication between mother and child. A variety of adipokines in the milk such as leptin, insulin and resistin, influence growth and development of the infants in the neonatal life. Few studies have focused on milk composition in Mexican women. Our objective was to investigate adipokine concentrations in human milk at different stages of lactation in a Mexican population.

Milk from Mexican women was obtained by breast pump at different stages of lactation and was divided into: first week (1Â° S, n=11), months 1-3 (1-3M, n=18), months 4-5 (4-5M, n=6) and more than six months (>6M, n=4). Milk leptin, insulin, C-peptide and resistin levels were measured by magnetic beadâ€“based assays that detect diabetes and obesity biomarkers. As lactation advances, the concentration of insulin and resistin decreases, while the concentration of leptin increases. However, there were not significant differences between leptin and insulin concentrations in the different stages of lactation; the concentration of resistin during the first week was higher compared with the other stages ($p<0.05$). C- peptide was not detected in human milk.

From the nutritional perspective, human milk during the period that covers the first months of life until two years of age is very important because it has the adequate source of nutriments, and also bioactive components, that are not present in formulas, such as leptin, insulin and resistin at any stage of lactation, regardless the concentration. These adipokines are important for the central regulation of the energy balance involved in metabolism. The presence of these adipokines in human milk may play an important role in developmental programming during lactation, and be an important link to prevent obesity, insulin resistance and diabetes in later life. This work was supported by CONACyT (FOSSIS 273137).

Adipokine • Breast milk • Mexican women

POSTER | Friday 9th 11:10-12:10 hrs.

C10198

C10203
Clinical Science
Breast milk and early feeding

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Correlation between maternal human serum and milk cortisol concentrations

Cortisol during gestation and lactation is an essential hormone for fetal and newborn development. It is transferred from serum to human milk and it has an impact in the childâ€™s hypothalamicâ€“pituitaryâ€“adrenal axis, temperament, growth, weight gain and development. Although cortisol is present in human milk, it is unknown the relationship between human serum and milk cortisol concentrations. The objective of the present study was to investigate if there is a correlation between maternal serum and milk cortisol levels at different stages of lactation.

At different stages of lactation (â‰¤48 hours, first week, 1st month, 2nd-3rd month, 4th-5th month, 6th-11th month and â‰¥12 months), the cortisol levels in serum and milk were quantified by radioimmunoassay (RIA). To determine if a correlation between cortisol concentration in both maternal serum and milk exists, a Spearman correlation analysis was performed; a linear regression analysis was also performed to determine the influence of both cortisol serum levels and the lactation stage on milk cortisol concentration. Cortisol serum levels have a positive correlation with the concentration of cortisol in milk (rs= 0.770, P= 2x10-7). In addition, the linear regression analysis showed that the concentration of cortisol in milk depends on both serum cortisol concentration and the lactation stage (F1,131 = 165.3505, F6,131 = 4.0464, P = 0.001) and the interaction of both variables (F6,131 = 5.2590, P = 0.001). Milk cortisol levels were significantly higher during the first 48 hours of lactation and dropped in the first week and even more in the 1st month and remain similar in further stages of lactation.

Cortisol concentration in maternal serum has a positive correlation with the cortisol concentration in milk and this relationship is modified throughout lactation. In addition, cortisol concentration in milk is not only affected by serum concentration, but also by the lactation stage and the relationship between these two variables. Milk acts as a link in the transmission of the glucocorticoid signal from mother to child. It is necessary to continue deepening in the aspects that help to describe in greater detail the factors that affect the transport of cortisol through the mammary gland to milk and other determinants of cortisol levels in human milk. This work was supported by CONACyT (FOSISS 273137).

Cortisol • Human milk • Lactation

POSTER | Friday 9th 11:10-12:10 hrs.

C10203

C10247
Clinical Science
Breast milk and early feeding

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Higher increment of Fat mass from 1 to 6 months in infants receiving Exclusive Breastfeeding

The early postnatal period has been identified as a sensitive period for the programming of obesity and other associated non-communicable diseases at later ages. Early feeding choices influence growth patterns and body composition. Breast milk influences multiple pathways that determine infant health and growth, probably impacting the risk for obesity. While some studies have found higher fat mass in breastfed infants, and lower fat free mass in formula fed ones, other studies have found no difference in body composition with different types of feeding. In addition, little is known about this association in early infancy. The aim of this study was to evaluate the effect of exclusive/predominant breastfeeding on the change in fat mass percentage during the first six months of life.

Healthy, term newborns (n=122) from a prospective cohort were evaluated at birth and at month 1, 3, 6, recording BMI-for-age (BMI/A) and, except at birth, fat mass percentage (%FM) (air-displacement plethysmography). Exclusive/predominant breastfed (EBF) infants were identified. Duration of breastfeeding (BF) and the timing of complementary feeding (CF) were recorded. Maternal data was documented. General mixed linear models were performed to evaluate the effect of EBF on %FM. Most infants had normal BMI/A (93.6%) at birth. No infants had obesity (BMI/A) during the first six months of life. Mean duration of BF was 4.95±1.87months, and 30.2% of infants were EBF for 6 months. Mean %FM of EBF infants was 18.00±5.56 and 29.38±5.57 at 1 and 6 months respectively; for those not EBF was 16.44±5.06 and 24.53±5.56. %FM increased during the first six months in all infants ($p<0.001$). EBF infants had a higher increment of FM from month 1 to 6 (B=4.77, CI95%: 7.50-2.03, p=0.001), compared to those who did not receive EBF (R2=0.423). This was the strongest model and was adjusted by maternal educational level, parity, maternal weight gain, gender, BMI/A at birth, months of BF, and timing of CF

For elucidating the complexity of growth and body composition, and improving prevention strategies targeting childhood obesity, it is important to identify which modifiable factors influence changes in body composition in early infancy. Fat mass increases during the first 6 months of life, and infants that received exclusive or predominant breastfeeding have a higher increment in fat mass from month 1 to 6. Differences in the growth pattern of EBF versus infants exposed to formula fe-

eding could be attributed to differences in nutrient intake, as well as other bioactive factors with metabolic influence, such as leptin. Leptin is present in human milk and could be promoting the greater increment in FM. Higher FM in the first 6 months of life could be a protective factor, not only during a precarious weaning period, but also, through leptin, by programming appetite regulation and other metabolic processes. The first 6 months of life represent a window of opportunity for targeting preventive strategies where promotion of exclusive breastfeeding continues to be essential.

Breastfeeding • Fat mass • Obesity

ORAL | Wednesday 7th 16:40-17:40 hrs.

C10293
Clinical Science
Breast milk and early feeding

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Pregnancy, Breastfeeding And Infant Gut Health
Kings College London
Reino Unido

PROMESA Study: Can exclusive breastfeeding supplemented with a probiotic promote a sustained healthy gut microbiota in babies born by caesarean section?

The composition of the initial infant intestinal microbiota influences immune function, the future microbiome and risk of childhood disease. Historically, Bifidobacterium have been abundant in the breastfed infant gut, but infants in resource rich countries show an abundance of taxa related to dysbiosis. Reduction in Bifidobacterium longum subsp. infantis (B. infantis), which has a unique capacity to transport and consume human milk oligosaccharides, leads to reduced faecal acetate and lactate and higher pH. Reduction in infant B. infantis is attributed to infant delivery mode, diet, maternal faecal load and antibiotics. We hypothesise that short term supplementation of breast milk with B. infantis will improve longer term gut colonisation and health of infants.

The PROMESA study is a randomised double-blinded placebo-controlled trial of a probiotic (B. infantis, EVC001) added to breast milk to improve the normal neonatal gut microbiome in term babies delivered by caesarean section. Recruitment of 70 women undergoing caesarean section (who intend to breastfeed exclusively) from a UK teaching hospital began in Feb 2018. Mothers provide vaginal and rectal swabs for maternal microbiome assessment, and breast milk and infant faecal samples on postnatal day 4-7. On Day 7-9, eligible infants (i.e. breastfed and not exposed to antibiotics for >3 days) are randomised to receive either a daily supplement of B. infantis or placebo in breast milk for 28 days. All women are provided with lactation support. Infant stool, faecal swabs and breast milk samples are collected regularly until 6 months, with additional samples collected at 12, 18 and 24 months of age. Infant stooling, feeding, and health data are collected. The infant gut microbiome, metabolites, other biomarkers of gut health, breast milk components and infant immune function are being analysed. To date, 34 women have consented to participate.

This is the first randomised placebo controlled trial of B. infantis (EVC001). Follow up of infants until 2 years of age will allow for longer term assessment of the impact on B. infantis supplementation on the establishment of the infant gut microbiome, faecal metabolite composition and infant health. Shorter term outcomes such as incidence of colic and nappy rash will also be

determined. Positive results will provide evidence for the potential of B. infantis supplementation to promote infant wellbeing and an intervention that could help avoid the reported negative impacts of caesarean section on childhood health.

gut microbiome • breastfeeding • infant health

ORAL | Wednesday 7th 16:40-17:40 hrs.

C110295
Clinical Science
Intervention studies

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Diabetes
UNAM
México

Lipid profile improvement in Maya children under dietary supplement

The malnutrition is the result of a poor diet, and can prevail through generations. Represents a health problem because in addition to cognitive damage have been associated with obesity, insulin resistance (IR) and type 2 diabetes in adulthood. In Mexico, this has become a national health problem affecting over 1.5 million children under five years old and over 33% of children with overweight and obesity. The most affected are indigenous and low-income populations. In Yucatan, 19.4% of the population cannot access to adequate food. In a previous study, we found a 50% prevalence of metabolic syndrome and 34.9% of IR in indigenous children. Thus, the aim of the present study is to evaluate the effect of a dietary supplement intervention in the nutritional status of Maya children.

The study includes 29 Maya children of 9 years old. The protocol has approval of the Human Research Ethics Committee of HRAEPY. The parents signed an informed consent and the children an agreement to participate in the study. We evaluated body weight, height; wrist, arm; tricipital skin fold; and femur diameter according to standardized methods. Biochemical and blood biometrics assessments were performed before and after the intervention by commercial kits. The intervention was carried out through a cookie enriched with vitamins, minerals, antioxidants, essential oils, amino acids and calcium with recommended doses of nutrients for school children. The acceptance of the supplement for the children was 88%. The data prior intervention showed that 71% of the children had linear growth problems, 25% had chronic malnutrition, and 30% deficiency of bone mass. After the intervention, the percentage of children with excess fat mass decreased from 31% to 27%, in pPAS> 90 (46% to 7%) and pPAD> 90 (21% to 0%). Biochemical parameters were also improved: glucose>100 mg/dl (18% to 11%), triglycerides>100 mg/dl (52% to 39%), cholesterol> 200 mg/dl (7% to 0%) and HDL-c<40 mg/dl (7

Our findings revealed the positive effect of a nutritional intervention on lipid metabolism in Maya

children. It is well known that impairment of lipid metabolism is a risk factor for developing hyperlipidemias, non-alcoholic fatty liver disease, type 2 diabetes and cardiovascular diseases. Therefore, timely interventions at early ages could delay the onset of metabolic diseases in adult life. Thus, the implementation of intervention programs with functional supplements in childhood is of great importance.

malnutrition • Maya • children

POSTER | Friday 9th 11:10-12:10 hrs.

C110295

C120442
Clinical Science
Others

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Effect of acute ingestion of sucralose on glucose tolerance and monocyte subpopulations in healthy young adults.

It has not been studied whether the acute consumption of sucralose is capable of triggering a state of systemic inflammation and if this is related to the onset of glucose intolerance in healthy subjects. All this has left the scientific community in a situation of uncertainty about if there is an association between the consumption of sweeteners and the development of glucose intolerance, typified by elevated insulin, glucose, C-peptide, glucagon, GIP and GLP-1, as well as an increase in systemic inflammatory factors. The purpose of this work is to demonstrate whether acute exposure to sucralose in young, healthy adults produces an increase in insulin, glucose, as well as an increase in inflammatory monocytes, being able to induce a state of glucose intolerance and insulin resista

It is a randomized, double-blind, placebo-controlled clinical trial with two groups, with 30 healthy volunteers each. One group will receive 48 mg / 30 ml of fasting sucralose in a single shot, while the control group will receive 30 ml of water as a placebo, and then a CTOG (75 g / 180 min) will be performed. Concentrations of insulin, glucose, C-peptide, glucagon and incretins will be measured every 15 minutes, as well as initial and final levels of systemic inflammatory markers and inflammatory monocytes.There was an increase in insulin concentrations but not glucose as well as differences between the concentrations of glucagon, peptide c and c- reactive protein. An increase in the concentrations of non- classical monocytes was observed, and clasics with differences in the expression of cd11c, cd206, ccr2, cx3cr1.

the augmented consumption of sucrolase influences the metabolism of carbohydrates as well as a greater pancreatic effort to level glucose concentrations, having a synergistic effect with glp1, gip. On the other hand, the inflammatory response is increased by increasing the percentage of non-classical monocytes as well as their expression of markers for migration and proinflammatory markers of surface area measured by flow cytometry.

sucralose • pro-imflamatory • insulinresistanc

POSTER | Friday 9th 11:10-12:10 hrs.

C120442

C20083
Clinical Science
Maternal nutrition and gestational disorders

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Vitamin D status in a group of Mexican healthy pregnant women.

Vitamin D deficiency has been frequently reported in pregnancy and associated with higher risk of preeclampsia, gestational diabetes, caesarean section, preterm birth, intrauterine growth restriction and risk for offspring of asthma, bone health, allergies and impaired neurodevelopment. Risk factors for low vitamin D include ethnicity, low exposure to sun, overweight and obesity, low vitamin D intake and seasonal variations. Intake recommendations for vitamin D during pregnancy range between 200-600 IU/d. It has been reported that these doses are not enough to achieve sufficiency in vitamin D deficient women. The aim of this study was to describe vitamin D status during pregnancy in healthy Mexican women, and evaluate clinical and nutrition factors that affect its concentration.

Preliminary analysis from an ongoing prospective cohort of pregnant women in Mexico City. Women were excluded if they had previous diseases or were on medications. Clinical and nutrition assessment were performed in each trimester of pregnancy. Pregestational body mass index (p-BMI) was computed. A fasting blood sample was taken for 25-OH vitamin D measurement (CMIA). Descriptive, statistics and multivariate analysis was done. A total of 70 women were included, 60% of them were overweight or obese. The majority of women received vitamin D supplementation during 2nd and 3rd trimester (76.7%), while only 51.4% did in the 1st. Most of them received <250 IU/d. Vitamin D deficiency (<20 ng/ml) was observed in 38%, 25.7% and 21.4% of women in each trimester. Vitamin D concentrations above 30 ng/mL were observed in 10% of women (1st trimester) and 32.9% and 37.1% in the 2nd and 3rd trimesters. Serum vitamin D concentrations were increased ($p<0.0001$); supplementation increased concentrations ($p<0.05$). Higher concentrations were observed in Spring/Summer vs Fall/Winter in the 3rd trimester ($p=0.004$). No associations were observed with p-BMI or other maternal factors.

In women participating in the "Epigenetic and Biochemical Origin of Obesity" cohort (FOSISS-2015-3-261661), a high prevalence of low serum vitamin D concentrations was observed. Supplementation increased vitamin D concentrations, but frequently used doses appear insufficient to achieve concentrations above 30 ng/mL. It is urgent to evaluate vitamin D status periconceptionally to identify deficiencies and implement strategies to decrease risk associated with inadequate vitamin D status.

pregnancy • vitamin D • supplementation

POSTER | Friday 9th 11:10-12:10 hrs.

C20083

C20171
Clinical Science
Maternal nutrition and gestational disorders

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Maternal malnutrition alters metabolic glucose and insulin circadian rhythms in the rat male offspring

Intrauterine and early postnatal malnutrition have been described to produce developmental and long term physiological deleterious consequences in the offspring. Prolonged maternal hipercaloric/hipoproteinic malnutrition have been reported to produce brain and metabolic adjustments. Ã¢â‚¬Å“Cafeteria dietÃ¢â‚¬Â has been linked to overweight and metabolic disruptions from childhood to adulthood. However, there is limited research regarding mainly energetic requirements along the day, its circadian expression and those related mechanisms. The aim of the present study was to analyze the glucose and insulin circadian rhythms in male juvenile offspring of dams under Ã¢â‚¬Å“cafeteria dietÃ¢â‚¬Â on gestational and lactating periods.

Sprague-Dawley adult female rats were randomly divided in 2 nutritional protocols: control (CO) given rodent lab diet (5001 purina Chow 4.15kcal) and Cafeteria diet (CD-6.32kcal) and maintained under 12/12 light-dark cycle, room temperature 22-24Ã‚Â°C with food and water ad libitum for three weeks before mating, during gestation and lactation and chow rodent diet after weaning. All tests were performed in the 40 and 90 days old male offspring. Postnatal body weight and size from birthing trough adulthood were recorded. Plasma was obtained every 4hr during a complete 24 hr day. A commercial insulin ELISA kit and colorimetric analyses for glucose were applied to measure those metabolites concentration. Results show that CD presented a decrease in weight and size. Cosinor analysis was carried out to analyze plasmatic glucose circadian parameters. Forty days old males showed hypoglycemia and lower glucose concentration on the glucose tolerance test. Insulin concentrations were similar to CO. CD adults showed hyperglycemia. but similar insulin concentration than CO. Both groups and ages circadian rhythmicity but disturbances in acrophase, mesor and amplitude.

Intrauterine and postnatal early malnutrition impact the metabolic energetic requirements as well as the daily temporal glucose and insulin distribution differentially from 40 to 90 days of age. The similar insulin concentration but hypoglycemia at 40days of age suggests an increased sensibility to insulin in the CD group. Meanwhile, at 90 days of age, the hyperglucemia but similar insulin during the day, suggest similar sensibility, where the glucose-insulin regulatory mechanism is less efficient than early ages, with basal glucose concentration appears increased. At birth both groups were similar in weight and body size, but LeeÃ¢â‚¬â„¢s Index suggest that exposure to maternal Ã¢â‚¬Å“cafeteria dietÃ¢â‚¬Â modifies the metabolic maturation and physiology throughout the lifespan. As well circadian regulation appears to be altered differently by age. Therefore it can be inferred that

the disparity presented in the CD group daily rhythm of glucose and insulin interaction, as well as the delay in the growth is due to the early in life exposure of a hypercaloric/hipoproteinic. Therefore this malnutrition influences also the neural control of insulin-glucose circadian rhytmicity.

Malnutrition • Metabolism • Circadian

POSTER | Friday 9th 11:10-12:10 hrs.

C20186
Clinical Science
Maternal nutrition and gestational disorders

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Prenatal assessment of fetal fat area with 3D Ultrasound in Children of Diabetic Mothers, with no Growth Alterations

Gestational diabetes can produce alterations in fetal growth and development. These can range from embryopathy resulting from diabetes (structural alterations) to fetopathy from this same disease (alterations in growth and development). One of the most common complications produced in children of diabetic mothers is growth alterations, such as macrosomia. Other alterations exist that are unrelated to fetal weight and could help to predict short-, medium- and long-term complications in the offspring of diabetic mothers. The aim of this study was to use 3D ultrasound to evaluate fatty tissue in the arm and leg of the fetuses of diabetic mothers, with no growth alterations.

This study was performed from January 2016 to July 2016. A total of 60 patients were included: 30 diabetics and 30 controls. A US was performed to estimate fetal weight and fetal age and gender (All fetuses included had a normal weight). US evaluation were performed to determine the area corresponding to the subcutaneous fatty tissue (SFT) in the arm and tight in three axial planes using TUI (tomographic ultrasound imaging) (1: union of the proximal third and two distals, 2: the middle, and 3: the union of the distal third and two proximals). Paired t-test and non-parametric Wilcoxon ranks were used to assess differences. Results: 30 patients diagnosed with diabetes were included (16 pregestational and 14 with GD) and 30 controls, paired for gestational age. No differences were found in estimated fetal weight. A difference was found in the SFT in the three femur planes: 1 (10.1 cm2 SD 2.0 vs 8.9 cm2 p=0.024), 2 (9.0 cm2 SD 2.0 v 7.8 cm2 SD 1.7 p=0.026) and 3 (8.8 cm2 SD 1.8 vs 7.3 cm2 SD 1.7 p=0.005). Differences in fat area were also found at the plane 1 (6.1 cm2 SD 1.4 vs 5.4 cm2 SD 1.6 p=0.045) and plane 3 (5.3 cm2 SD 1.2 vs 4.7 cm2 SD 1.2 p=0.0

Our research unit has standardized the use of 3D ultrasound to evaluate fetal fat. The differences in femoral and humeral fat in the different segments studied support the hypothesis that the fat area and body composition of fetuses of diabetic mothers are greater irrespective of fetal weight, which was within normal ranges. The evaluation of fetal fat or fetal body composition appears to be a useful tool that offers advantages over and above the only evaluation of fetal weight, enabling us to detect early changes (fat mass/lean mass) even before weight is affected. The findings from our line of investigation enable this variable to be used as a predictive factor of short-, me-

dium- and long-term adverse results. In the future, it may be possible to demonstrate that changes in fetal body composition are equally or more useful than birth weight alone to identify newborns who have a higher risk of developing metabolic syndrome, diabetes, heart disease, obesity and high blood pressure in childhood, adolescence and adulthood.

Diabetes • Pregnancy • Body composition

POSTER | Friday 9th 11:10-12:10 hrs.

C20193
Clinical Science
Maternal nutrition and gestational disorders

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Obesity and iron nutrition status in pregnancy

During pregnancy iron requirement increases significantly to meet the demand imposed by erythropoiesis and the formation and growth of the fetus and the placenta. To achieve this, there is a decrease in hepcidin concentration, which promotes the mobilization of iron reserves, and an increase in the proportion of this nutrient absorbed from food. On the other hand, the excess adipose tissue of obesity triggers an inflammatory response that induces an increase in the production of hepcidin, which inhibits iron mobilization and absorption. The objective of this study is to evaluate the impact of maternal obesity on maternal iron status during pregnancy.

93 non-anemic pregnant adult women were included, 40 had obesity (Ob) and 53 had adequate weight (AW); all took 30mg of supplementary iron. Sociodemographic variables were recorded, and in weeks 13, 20, 27 and 35 information on diet iron and a blood sample were obtained. A series of repeated measures analysis was performed using Linear Regression Models to know the effect of obesity on each iron indicator; iron intake, hepcidin (Hp) and C-reactive protein (PCR) were successively introduced as covariates. No difference was observed in ferritin concentration (25.27 ± 1.06 vs. 25.53 ± 1.05 ng/mL, p = 0.879) or hemoglobin (13.03 ± 0.08 vs. 13.16 ± 0.07 g/dL, p = 0.235) between groups. However, the Ob group showed a higher concentration of Hepcidin (8.58 ± 1.05 vs. 6.82 ± 1.05 ng/mL, p = 0.002) and soluble serum transferrin receptor (sTfr) (16.60 ± 1.03 vs. 14.73 ± 1.03 nmol/L, p = 0.005); and lower serum iron (138.98 ± 4.86 vs. 155.98 ± 4.86, ?g/dL p = 0.018) than the AW group. The differences in Hp and rTfs were maintained after including iron intake and serum Hp in the models, but the difference in FeS was lost when serum CRP was included.

In non-anemic pregnant adult women receiving iron supplementation, the presence of obesity was associated with deleterious changes in iron homeostasis and maternal nutritional status. The Ob group showed an hypoferremia profile characterized by a lower concentration of serum available iron (higher concentration of rTfs and lower concentration of FeS), while the quantity of iron storage (ferritin) and oxygen transporting protein (hemoglobin) was the same in both groups. In at risk populations these changes could increase the risk of developing real iron deficiency or even anemia, which negatively affect maternal and fetal outcomes.

hepcidin • iron • obesity

POSTER | Wednesday 7th 17:40-18:40 hrs.

C20193

C20213
Clinical Science
Maternal nutrition and gestational disorders

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Intrauterine and early malnutrition alters metabolic glucose and insulin circadian rhythms in the rat female offspring

Maternal malnutrition plays a crucial role in functional development, resulting in behavioral, cognitive and metabolic abnormalities and disturbances. As attested in the male adjacent study, â€œCafeteria dietâ€ has been linked to overweight, metabolic syndrome, diabetes and other metabolic disruptions in the animal lifespan. However, there are very few reports about the effect of intrauterine and early postnatal malnutrition in the female offspring, and even less regarding the circadian expression for metabolic parameters as glucose and insulin. The aim of the present study was to analyze the intrauterine malnutrition mid and long term consequences in the female rat.

Sprague-Dawley adult female rats were randomly divided in 2 nutritional protocols: control (CO) Lab Chow and Cafeteria diet (CD-6.32kcal) and maintained under 12/12 light-dark cycle, 22-24Â°C, food and water ad libitum for three weeks before mating-gestation-lactation. After weaning were maintained under CO diet. All tests were performed in 40 and 90 days old female offspring. Postnatal body weight and size from birthing trough adulthood were recorded. Plasma was obtained every 4hr during a complete 24 hr day. A commercial insulin ELISA kit and colorimetric analyses for glucose were applied. Results show a decrease in weight and size in CD. Cosinor analysis was carried out to analyze plasmatic glucose circadian parameters. Juvenile females showed hypoglycemia only during the scotophase and lower glucose concentration for the glucose tolerance test (GTT). Though insulin levels were similar to CO there was a tendency to increase in the CD juveniles. At adulthood, the CD group had higher levels of glucose at all temporal points. Although GTT was not altered, a tendency to higher levels was showed in CD. Circadian rhythmicity disturbances in acrophase, mesor and amplitude were foun

The similar insulin concentration but hypoglycemia at 40 days of age suggests an increased sensibility to insulin in the CD group Circadian oscillation for glucose in juveniles was similar to CO, however the acrophase (high peak) showed a 3 hr advance, suggesting the phase relationship from the central to peripheral oscillators was lost or broken. Although GTT was not altered, a tendency to higher levels was showed in CD suggesting a developing insulin resistance. The above results suggest intrauterine and early postnatal malnutrition impact those critical periods on structures that control and regulate the physiological and circadian response for metabolites related to the energetic regulation and metabolism.

Malnutrition • Metabolism • Circadian

POSTER | Friday 9th 11:10-12:10 hrs.

C20213

C20231
Clinical Science
Maternal nutrition and gestational disorders

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Adverse Perinatal Results Related To Growth In Children Of Overweight Mothers And Obesity At The National Instute Of Perinatology

The estimated prevalence of obesity in pregnant women ranges from 18.5 to 38.5% worldwide. Women who are obese and overweight during pregnancy have a higher risk of complications, such as hypertension, gestational Diabetes (GD), and preeclampsia (PE). The children of obese pregnant women have an increased risk of prematurity, stillbirth, birth defects, impaired growth; either large for gestational age or macrosomia, resulting in trauma at birth and obesity in childhood or adulthood.Objective: To determine whether is an association between the alterations of fetal growth such as small for gestational age, large for gestational age or macrosomia and maternal overweight or obesity in patients from the Instituto Nacional de Perinatologia

A comparative cohort study that included 480 patients without comorbidities was performed. Two groups were analyzed, the group of women with Body Mass Index (BMI) between 19 and 24.9 (n=160) and a group of patients with BMI > 25 (n=320). From this group 188 were classified as overweight and 132 as obese according to their BMI before pregnancy. Perinatal outcomes were compared: alterations in fetal growth (large for gestational age, normal weight and small for gestational age) of each of the groups. Results: 480 patients divided into 2 groups; First group with a BMI < 24.9 (n=160), and a second group with a BMI < 25 (n=320). We found an OR of 2.4 (95%CI 1.428 - 4.061) to have a large baby for gestational age adjusted with weight gain in pregnancy. Sub analysis was performed with the group BMI > 25, in which overweight patients (BMI > 25 and <29.9) showed an increased of births with large for gestational age babies with an OR 2.4 (CI 95% 1.355 – 4.49) p 0.036, adjusted for weight gain in pregnancy. For the group of patients with BMI greater than 30 an OR of 4.62 (95% CI 1.4848 – 14.41) for macrosomia was observed.

Women with a pregestational body mass index > 25 have an increased risk of having a large for gestational age newborn, this is now more important due to the increase in the rate of overweight and obesity in women at reproductive age in our country, which will have implications in the fetal programming of the newborn, according to Barkers hypothesis, with which we will be having adults with metabolic syndrome and cardiovascular alterations, those prolonging the circle of the mother with overweight or obesity, large newborn for gestational age, sick and obese children and adults. Health policies should be focused on the preventive aspects through campaigns that promote healthier lifestyles, which can be implemented from the first level care center.

Obesity • large for gestat • macrosomia

POSTER | Friday 9th 11:10-12:10 hrs.

C20231

C20348
Clinical Science
Maternal nutrition and gestational disorders

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Association Between Dietary Factors During Pregnancy And Perinatal Outcomes In A Group Of Women With Chronic Kidney Disease At The National Institute Of Perin

Nutrition during pregnancy is a determinant factor for maternal health and her offspring. Growing evidence suggests that some dietary factors have the potential to produce adaptations in the fetal growth and development. According Baker's postulate, the intrauterine growth is a key factor for health in short and long term. Nutrition recommendations for chronic kidney disease (CKD) without dialysis tend to be restrictive; situation opposite regarding nutritional requirements for pregnancy. As a matter of fact, it is well known that protein restriction during pregnancy leads to lower fetal growth. The aim of this study was to evaluate the association between dietary factors during pregnancy with perinatal outcomes in a group of women with CKD.

Since March 2016, we have followed-up 34 pregnant women with CKD According to CDK-stage, 50% (n=17) were stage 1-2, 38% (n=13) stage 3 and 12% (n=4) stage 4. None of them needed dialysis. The main etiology for CKD was diabetes (29.4%) and hypertension and nephrotic syndrome (23.5%). Dietetic assessment was done during 2nd and 3rd trimester by the use of 24-hour recall method. We developed an index to evaluate nutrients' intake adequacy (energy, protein, saturated fat, vitamin D, folic acid, calcium, phosphorus, potassium, zinc and omega-3 and -6 fatty acids). The index total score ranked from 0 to 14 (0 worst score; 14 the best). We observed a positive association between total calories (r= 0.385, p=0.024) and total protein intake (r= 0.351, p=0.042) with birthweight. When consumption score was categorize as "adequate" or "not adequate", the frequency of preeclampsia (57% vs 33%), C-section (100% vs 70%), prematurity (57% vs 41%) and intrauterine growth restriction (14% vs 7%) was higher in women with "not adequate" consumption, none of these was statistically significant.

Dietetic assessment in pregnant women with CKD should include energy, protein, saturated fat, vitamin D, folic acid, calcium, iron, phosphorus, potassium, zinc and omega-3 and -6 fatty acids. According to literature, total energy and protein consumption during pregnancy has an impact in birthweight, phenomenon also observed in CKD. Our results show that a worst perinatal outcome is associated with: 1) an energy consumption <85%, 2) vitamin D, folic acid, calcium and iron consumption <95%, 3) protein consumption >115% and 4) a total caloric value of saturated fat >10%. Energy, protein and other micronutrients intake are associated with birthweight and perinatal outcomes. An adequate and opportune nutrition counseling in pregnant women with chronic kidney disease could has a positive impact in the maternal and fetal health outcomes in short and long term.

pregnancy • kidney disease •intake

ORAL | Wednesday 7th 15:20-16:20 hrs.

C20348

C20356
Clinical Science
Maternal nutrition and gestational disorders

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Maternal Obesity And Gestational Diabetes Mellitus
Mum´S Equilibrium
México

Mum´S Equilibrium For The Prevention And Management Of Maternal Obesity And Gestational Diabetes Mellitus (Gdm) In Mexico.

THE PROBLEM According to the World Obesity Federation, 35.5% of Mexican women are overweight and 37.5% are obese. Obesity is greater in females than in males. GDM is defined as any degree of carbohydrate intolerance with first recognition during pregnancy and develops in one of every 25 pregnancies worldwide. The incidence of GDM among women of reproductive age will further increase as the prevalence of obesity continues to rise among this age group. Approximately half of the women with a history of GDM develop type 2 diabetes within the first ten years after delivery. Also, infants of women with GDM have higher risk of obesity at early stages of life and therefore an increased risk of developing type 2 diabetes. These two facts contribute to the escalating diabetes epidemic.

THE OPPORTUNITY What we do: Mum´s Equilibrium aims to provide a series of interventions such as education in nutrition and diabetes along with fitness classes (pre-natal & post-natal yoga and fitness) for the prevention and management of maternal obesity and GDM, with follow up after delivery in order to tackle the rising prevalence of type 2 diabetes in Mexico. Mission: Healthy Moms for Healthy Babies. Mum´s Equilibrium will focus its work on the following three stages to address this approach; preconception, pregnancy and post-pregnancy. The clinic will be allied to a multidisciplinary health team to ensure healthy outcomes, and will be allied to researchers to measure the impact of the interventions.

GROWTH PLAN • Start running the project in 2019 with local people from Irapuato, Guanajuato, with the vision of further expansion. The pilot test is immense and could provide a replicable and scalable model for the Mexican Health System. • Use three transfer mechanisms to run the project and create national impact: Private and Public Hospitals and National Health Centers. In summary, Mum´s Equilibrium will provide a framework that can stop the vicious circle of sick mom=sick baby. This project represents an effective solution that could contribute to support the decrease of obesity and diabetes epidemics in Mexico.

GDM • Maternal obesity • Nutrition

POSTER | Friday 9th 11:10-12:10 hrs.

C20356

C20407
Clinical Science
Maternal nutrition and gestational disorders

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Increased serum levels of miR-29a-3p and potential exposure to endocrine disruptors are associated with gestational diabetes mellitus.

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that starts or is first recognized during pregnancy. Although GDM etiology remains unknown, it is clear that environmental factors are involved in GDM onset. Bisphenol A (BPA) and phthalates are two of the most widely studied endocrine disruptors (EDs). Notwithstanding some studies have associated higher levels of BPA and phthalates with GDM, their role in GDM etiology is still unclear. It has been demonstrated that either GDM or EDs exposure is associated with changes in the content of serum microRNAs. The aim of the present study was to analyze the content of miR-29a-3p, miR-137 and miR-200a-3p in the serum of patients diagnosed with GDM, and to evaluate their potential exposure to BPA and phthalates.

Peripheral blood was collected from 16 patients diagnosed with GDM and 15 normoglycemic pregnant women (control group) after obtaining informed consent. Patients and control group answered a test about potential consumption of EDs sources during the last two days before peripheral blood sampling. Total RNA was isolated from serum samples using miRNeasy serum/plasma kit (QIAGEN). RT-PCR was performed using Taqman Advanced miRNA cDNA Synthesis kit (Applied Biosystem) to determine the relative expression of miR-29a-3p, miR-137 and miR-200a-3p. RT-qPCR was done in a Step One Plus thermal cycler (Applied Biosystems). miR-454-5p was used as an endogenous internal control. Statistical analysis was performed using Mann-Whitney U test and Yates's chi-squared test. The results showed that miR-29a-3p serum levels were significantly higher in patients with GDM as compared to control group ($p<0.05$). On the other hand, miR-137 and miR-200a-3p serum levels did not show significant differences between GDM and normoglycemic women. In relation to EDs exposure test, soap usage was greater in women with GDM ($p<0.05$). There were no statistical differences regarding exposure to other potential EDs sour

The present study demonstrates that higher serum levels of miR-29a-3p are associated with GDM. Interestingly, an increase in miR-29a-3p levels has been associated with BPA and phthalates exposure. Furthermore, this microRNA regulates the expression of several genes associated with EDs metabolism such as AHR, UGT1A1 and UGT1A9, which suggests that AhR, UGT1A1 and UGT1A9 le-

vels may be decreased and therefore BPA and phthalates may accumulate in the systemic circulation. Our results suggest that soap usage, a broadly proven phthalates source, is greater among GDM patients, which suggest a higher phthalates ingestion that may have a role in GDM development and progression. Further studies are required to support these findings.

GDM •Bisphenol A •Phthalates

POSTER | Friday 9th 11:10-12:10 hrs.

C30172
Clinical Science
Environmental health and neurodevelopment

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Neurodevelopment comparison in selective intrauterine growth restriction type 3 twins at 24 months

The RSCI type III is a condition that affects 15% of twin pregnancies and is manifested by a lower growth of one of the twins, theoretically affecting the development of one of the twins and putting the risk of pregnancy viability (at least the 20% of survivors will develop neurological damage). Obstetric management is controversial. When the diagnosis is integrated in the early stages of pregnancy, the intervention is offered to the parents through the selective occlusion of one of the cords. There is also an expectant management option in which follow-up is carried out and only the interruption of pregnancy is decided when there is alteration in the placental venous flow. There is no information on the outcome of the neurodevelopment of the surviving twins treated conservatively

The Bayley III Scale (BSDI-3) was applied at 20 Â± 8 months of corrected gestational age to 26 surviving twins of RSCI type III in a case-control model (the twin of lower birth weight was considered a case) nested in a cohort. All were born by elective cesarean section at 30.9 Â± 2.20 weeks of gestation after receiving steroids for lung maturation. The socio-emotional scale showed average values (105/104 points in cases and controls respectively), the motor scales (85/87) and cognitive (85/83) low averages and the language scale (76/78) values below of the average. The results are similar for both cases and controls. No significant differences were found when comparing values between cases and controls (motor scale F = 1.39, p-0.24, cognitive F = 1.39, p-0.53, Language F = 0.010, p = -0.24, Socio-emotional F = 0.024, p-0.08).

The pathophysiological changes associated with the selective restriction of type 3 intrauterine growth, such as the disproportionate distribution of the territory and the placental circulation between both fetuses, would theoretically lead us to suppose that the neurological prognosis of the surviving twins of lower weight would be worse than that of their brother; this study shows that the neurodevelopment of both twins is impacted equally even when the weight difference between both is greater than 30%. Conservative treatment is a viable alternative since the neurodevelopmental disorders found are confined to the domain of expressive language and the delay found is considered “mild”.

neurodevelopment •twins •restriction

ORAL | Friday 9th 15:30-16:30 hrs.

C30172

C30 386
Clinical Science
Environmental health and neurodevelopment

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Birth hypoxic-ischemic conditions interact with the dopamine transporter gene network influencing attentional flexibility and gray matter density in children

Perinatal complications associated with poor oxygenation affect the developing dopamine (DA) system and consequently the risk for attention-deficit hyperactivity disorder (ADHD). Different genetic variants associated with the dopamine transporter gene (DAT1) were also identified as risk factors for ADHD. In this work, we aimed to evaluate the interaction effect between a score reflecting the birth hypoxic-ischemic-associated conditions to the newborn (HICs score) and a novel genetic metric reflecting variations in the function of the DAT1 gene network (ePRS-DAT1) in the prefrontal cortex (PFC) on ADHD-related outcomes - attentional flexibility and gray matter (GM) density in children.

We used data from two birth cohorts: MAVAN (n=139) and GUSTO (n=305). The HICs score summarized features associated with variation in oxygenation levels to the fetus at birth and the polygenic score (ePRS-DAT1) was built based on genes co-expressed with DAT1 in the PFC. Attentional flexibility was measured via the Intra-Extra/dimensional task (IED) at 6 years (MAVAN) and Dimensional Change Card Sort (DCCS) at 4.5 years (GUSTO). Parallel-independent component analysis (P-ICA) was conducted to analyze the SNPs' weighted ePRS and GM relationships (MAVAN, 9-11 years). We observed ePRS x HICs interaction for latency to respond (p=0.001) on the extra-dimensional shift of the IED and accuracy (p=0.049) in the post-switch phase of the DCCS. Higher HICs was associated with longer latency to respond (?=16636, p<0.001) and lower accuracy (?=-0.33, p=0.002) only in the high ePRS group. In the P-ICA, two highly correlated components between SNPs and GM were observed in frontal, parietal and cingulate cortices (r=0.84) and bilateral thalamus (r=0.76) areas; and these relationships were moderated by the birth environment (low and high HICs had different loading coefficients for all comp

We observed an interaction between birth HICs and the genetic background reflecting DAT1 gene network, influencing attentional flexibility performance and GM density in children. The birth environment (HICs score) modifies the relationship between the genetic component and GM density

in areas involved in executive (frontal, parietal and cingulate cortices) and integrative (bilateral thalamus) functions. The high ePRS group likely reflects higher expression of genes involved in DA reuptake in the PFC and consequently lower DA signaling. For this group only, higher HICs were associated with attentional inflexibility in two ethnically distinct birth cohorts. Previously, we had demonstrated in an animal model that perinatal HICs damaged PFC DA signaling, as well as impaired attentional set-shifting (Miguel PM et al 2017). The current study translates these experimental findings to a human sample, generating an environmental and genetic score with potential relevance as markers of vulnerability. These factors can disrupt DA pathways' development, affecting the risk for disturbances such as ADHD. Prefrontal DAT1 gene network seems to be an important player in modulating these e

hypoxia-ischemia • dopamine system • flexibility

POSTER | Thursday 8th 10:40-11:40 hrs.

C30393
Clinical Science
Environmental health and neurodevelopment

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Use of antidepressant, anxiolytic and illegal psychotropic drugs during pregnancy and its effect on the neurodevelopment of Mexican children

The psychotropic drugs used in the treatment of depression and anxiety or some illegal drugs have the ability to affect the central nervous system. Most psychoactive substances cross the placental barrier by passive diffusion and can exert toxicity on the fetus. The use of antidepressants / anxiolytics during the first trimester of pregnancy increases the risk of presenting functional and structural alterations in the brain, interrupts the normal maturation of the serotonergic system and alters serotonin-dependent neuronal processes. The long-term effect of psychoactive exposure during pregnancy involves a delay in psychomotor development, and alterations in language, memory, attention and behavior. However, in Mexican population, the impact of these drugs in neurodevelopment of exposed childre

Methods A descriptive cross-sectional study was conducted in 10 children of women who presented depression and / or anxiety during pregnancy and who used psychoactive substances. For the evaluation of the presence of traits of depression and / or anxiety in these mothers, the following psychological battery was used: Beck Depression Inventory, Anxiety and Hospital Depression Scale and Trait-State Anxiety Inventory. As part of the protocol, a blood sample was taken from the mothers to identify those who used psychotropic drugs and / or illegal drugs. The Bayley 3 child development assessment scale was applied to all children at 2 ± 1 months of age. Results 60% of pregnant patients used antidepressants, and 40% illegal drugs. 100% of children of depressed women who used illegal drugs presented cognitive delay, while 50% of children of depressed women who used psychotropic drugs exhibited it.

The consumption of illegal and antidepressant drugs during pregnancy delayed the cognitive development of Mexican children. This work was financially supported by grant: 272458, Consejo Nacional de Ciencia y Tecnología (Conacyt)/FOSISS.

pregnacy • drugs of abuse •neurodevelopment

POSTER | Friday 9th 11:10-12:10 hrs.

C30393

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
International Society for Developmental Origins of Health and Disease
CANCÚN, MÉXICO 2018

C40125
Clinical Science
Life style and perinatal nutrition

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Prenatal evaluation fat in the fetus with 3D ultrasound technique, can predict the percentage of fat in the new-born at month of age measured by PEA-Pod.

Alterations in growth and body composition in the fetus increase perinatal morbidity and mortality, some authors have found a direct relationship between these alterations and fetal programming. In 1997, Bernstein described a 2D US technique to measure subcutaneous fatty tissue in the arm and thigh, by manually selecting the axial planes of the bone. In 2017, Borboa, GuzmÃƒÂ¡n and cols standardized the technique for measuring the subcutaneous area of fat mass in the arm and thigh in the fetus by 3D ultrasound and an offline analysis with TUI. The aim of this study was to evaluate whether fetal subcutaneous fat mass area (SFMA) measured in the prenatal period can predict infant fat grass mass measured at 1 month of age

This is a preliminary analysis of a prospective cohort of pregnant women and their infants (2017-2018). In this cut-ff were included 47 newborn, an US assessment was performed between 32.0-36.6 weeks of gestation using a Voluson E8 (GE) with a volumetric transducer. The volumes acquired were evaluated in an offline analysis using the GE 4D view, using the tool Tomographic Ultrasound Imaging (TUI). SFMA was obtained by taking the total area obtained in this image and subtracting the center area (lean mass). Body composition of the newborn was measured at 1 month of age by air displacement plethysmography. Data analisys was made with random forrest models using the Python software, to evaluate prediction. Results: A total of 47 pregnant women and their infants were included. Mean maternal age was 30.3 years old. 25% of women were overweight/obese before pregnancy. 55% of newborns were malea. Mean birthweight was 2.8 kgs SD 0.42. Mean body fat percentage at 1 month was 15.98 SD 4.8. The random forrest model predicts 67.25 +/- 3.23% of the variability of fat mass percentage and 75.033 +/- 4.28% of fat mass (kg) at one month of age, adjusted for fetal g

Alterations in growth and body composition in the fetus increase perinatal morbidity and mortality as well as the pathological processes that continue well beyond the neonatal period. Some authors have even found a direct relationship between these alterations and the presentation of certain degenerative chronic illnesses in adulthood, such as hypertension, diabetes, metabolic syndrome and cardiovascular disease, among others. In this study, we showed that measurements of the

fetal subcutaneous fat mass area measured in the arm and thighusing 3D ultrasound techniques can predict body fat masspercentage and fat mass at one month of age. This finding is important because it shows that the adiposity in the prenatal period predicts the body composition in the infant. This study is part of a large cohort, so the next step will be to develop a prediction equation that calculates the percentage of fat mass at birth and in the first months of life, using fetal fat mass measurments. Finally, reference values may be estabilished that could be used for interventions in high-risk patients such as fetuses with IUGR, children of diabetic mothers, children of ob

fetal programmin • Body composition • Ultrasound

POSTER | Friday 9th 11:10-12:10 hrs.

C40177
Clinical Science
Life style and perinatal nutrition

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Ovarian function and metabolic profile at the time of birth in female offspring of pregnancies complicated with diabetes

Diabetes is associated with hyperandrogenism in non-pregnant women. However, the effect of maternal diabetes on placental steroidogenesis and ovarian function of the female offspring is unclear. The aim of the present study is to analyze the effect of maternal diabetes on placental steroidogenesis during pregnancy, and over ovarian function and metabolic profile of female newborns at the time of birth (TOB).

A prospective study of pregnant women with Type 2 diabetes (MT2D, n=24), gestational diabetes (MGD, n=26), and control (MC, n=25) during the second half of gestation was performed. Clinical assessment and a blood sample were drawn at V1 (24-28 weeks), V2 (32-34) and TOB (37-40). A clinical evaluation of their daughter (DT2D, DGD, and DC) and venous blood cord sample were drawn at TOB. Sex steroids, insulin, glucose, IGF- 1, adiponectin and antimullerian hormone (AMH) were measured. T levels were higher in the T2D than in the C group at V1[1.7 (0.4- 4.2); 1.4 (3.5 - 4.5)], V2 [3.1 (0.7 - 5.9); 2.1 (0.4 - 5.2)] and TOB [3.5 (1.0 - 6.2); 2.4 (1.0- 4.2) nmol/l, P <0.05, respectively]. HOMA- IR was higher in the T2D than in the GD and C groups at V1, V2 and TOB (P < 0.0001). Higher macrosomia prevalence was found in D2TD.Higher HOMA and IGF1 levels were observed in DT2D compared to DGD and DC (1,3 Â± 0.7; 0,8 Â± 0.3; 0.5 Â± 0.3 ng/ml P= 0.042, respectively / 145.0 Â± 26.1; 88.0 Â± 13.9; 84.2 Â± 9.8 ng/ml P= 0.036. Higher AMH levels were found in DT2D compared to DC. Lower Adiponectin levels were observed in D2T2D compared to GD and DC (34.6 Â± 3.3; 45.8 Â±

Hyperandrogenemia and higher insulin resistance are observed in T2D during pregnancy. Daughters of T2D pregnant women are more insulin resistant, have higher IGF-1 and AMH levels and lower adiponectin levels at birth. Maternal insulin resistance is associated with elevated AMH and insulin levels in the newborn. These data suggest that maternal T2D may impair ovarian function and metabolic profile of their female offspring. FONDECYT No 11.12146.

Diabetes •androgens • fetal ovary

ORAL | Thursday 8th 09:40-10:40 hrs.

C40177

C50436
Clinical Science
Perinatal infection and programming

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Lipids Profile Of Newborns Children Of Pregnant Women Seropositive To Hiv.

HIV-positive pregnant women have various factors that condition changes in their metabolic status, these changes can influence the metabolic condition of their newborns. The objectives of the study were to identify factors associated with an elevation of serum cholesterol and triglyceride levels in newborns (NB) children of HIV positive mothers, and to identify the neonatal morbidity associated with the hyperlipidemia condition.

A case-control study was carried out in which 84 newborns (RN) were included, 51 with altered lipid profile corresponded to cases and 33 with normal serum lipid values conformed the controls. Cholesterol reference serum values were taken: 50 to 120 mg/dL, triglycerides: 35 to 85 mg/dL. It was evaluated the association of various maternal and perinatal variables with the development of neonatal hyperlipidemia, and the association of serum lipid elevation in the neonate with an increase in neonatal morbidity. Chi square was used to evaluate the hypotheses and were calculated odd ratios with a confidence interval of 95%. The 60.7% of HIV-positive pregnant women newborns had hyperlipidemia. The finding of maternal alterations in glucose metabolism was the variable mainly related to neonatal hyperlipidemia (OR 6.5, 95% CI 1.2-34). The neonates with hyperlipidemia had a mayor number of complications (OR 2.7, CI 95% 1.1-7.1), being the most frequent prematurity and low weight for their gestational age.

In HIV-positive women children metabolic alterations should be evaluated early.

Hyperlipidemia • HIV pregnant • Newborn

POSTER | Friday 9th 11:10-12:10 hrs

C50436

C60047
Clinical Science
Maternal and fetal health
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Risk factors for adolescent pregnancy

Adolescent pregnancy has a higher risk of low birth weight and several other health and nutrition morbidities than adult pregnancy. We aimed to determine possible independent influences that may predict a higher risk of pregnancy during adolescence.

Girls having 12-19 years old were surveyed in 10 secondary schools located in the city of Loja during year 2017. Those 10 secondary schools were randomly selected from 52. Among them, 4 were public, 3 private and 3 belonged to the local Catholic Church. A proportional sample of adolescents younger (12-14 years old) and older (15 to 19 years old) was made within a universe of 30,252 students with a confidence level of 95%. Logistic regression assessed the relative influence of each risk factor was calculated, 632 girls were selected. A prevalence of adolescent pregnancy of 5.7% was found in the public and religious schools; while there were not those cases in the private schools. Intrafamily violence was found in 27% of the public schools and 28% of the religious schools while there were not those cases in the private schools. Being the daughter of a teenage mother was present in 46% of public schools, 39.5% in religious schools and 44% in private schools. The factor Ã¢â‚¬Å“start of sexual lifeÃ¢â‚¬Â was present in 67% of private schools, 54% of religious schools and 63% of private ones. In 61% of the girls, the age range of initiation of sexual life was 15-16 years.

Logistic regression selected three independent risk factors of adolescent pregnancy. They were: the fact of being the daughter of a teenage mother, the presence of intrafamily violence, and the history of having started sexual life. We propose discussion sessions of those risk factors with adolescents, using a qualitative methodology, in order to develop adolescent pregnancy prevention strategies.

risk factor • Adolescent • pregnancy

POSTER | Friday 9th 11:10-12:10 hrs.

C60047

C60069
Clinical Science
Maternal and fetal health

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Adverse Perinatal Results Associated With Obesity And Overweight In Obstetric Patients Of The National Institute Of Perinatology Isidro Espinosa De Los R

Introduction. Obesity is a risk factor to develop an adverse perinatal outcomes. Mexico is located in the 5 countries with the highest obesity and overweight poblation. The prevalence has increased up to 70% of the population of reproductive age. In obstetrics dominates this problem, increasing the likelihood for patients to present adverse outcomes. Objective To determine the association between adverse perinatal outcomes in obese and non- obese patients with single pregnancy in the National institute of perinatology, in Mexico city.

Materials and methods. A study of historical cohort of 1145 patients with singleton pregnancy and follow-up from the first trimester of pregnancy was performed, three groups were divided according to their BMI (normal, overweight and obese). Its association with macrosomia, large for gestational age and other perinatal outcomes was determined. Results. 1128 patients were included in total. The normal BMI groups were formed 310 patients (27%). overweight 443 patients (39.9%) and 375 obese patients (33.8%). In the group of obese womwn we observed 51 cases of macrosomia (48%) OR 2.1 (95% CI 1.3-2.9 p 0.001). 76 cases (42%) of large for gestational age, odds ratio of 1.7 (95% CI 1.1-2.1 p 0.006). 42 cases of gestational diabetes (64%) Odds Ratio 4.1 (95% 2.2.-6.4 p <0.0001). Obese patients with greater weight gain than recommended had an OR of 2.1 (95% CI 1.2-4.0 p <0.01). We observed a protective effect of metabolic control for most outcomes.

Conclusions. Obesity is a condition that increases the likelihood of developing an adverse perinatal outcome. The results show a higher incidence in the obesity group. However adequate control weight gain and interventions from the start or before prenatal care seem to be the tool to reduce the impact of this problem.

obesity • pregnancy • perinatal outcom

ORAL | Thursday 8th 12:00-13:00 hrs.

C60091
Clinical Science
Maternal and fetal health

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Correlation Of The Levels Of Vitamin D In The Mother With Obesity And In The Neonate

The origin of vitamin D goes back approximately until 500 to 750 million years ago, was identified accidentally by E. Mellanby in 1918 as a fat-soluble nutrient, its main function is the regulation of bone metabolism. Vitamin D influences the integrity of the immune system, Its deficiency is a common clinical problem in premature from developed and developing countries that may allow poor linear growth. The level of this vitamin in the fetus and newborn is determined by the maternal state of vitamin D. A subclinical deficiency of vitamin D in preterm infants is associated with severe lower respiratory tract infections, requiring hospitalization and intensive care. In the first 6-8 weeks of postnatal life, serious vitamin D levels depend on vitamin D acquired by the

Transverse analytical study in the Neonatal Intensive Care Unit of a Hospital in Mexico. All those who were born in the hospital with diagnosis of SGA were included, between 30 and 40 weeks of gestation, that their breasts were overweight or obese according to the BMI at hospital admission, with informed consent and authorization for bioethics. We excluded those major congenital malformations, an Apgar low to the minute. We used the Rcmdr 2.3-1 package of R software version 3.2-5 with 95% confidence level, descriptive analysis of the variables and Spearman correlation coefficient. We took 130 samples 62 breasts and 68 RN at 6 hours before the resolution of pregnancy and in the first 6 hours of life respectively. The maternal age range was 18-38 years, 98% had prenatal control, folic acid and iron intake but not vitamin D during pregnancy, the maternal weight range at admission 49-120 and the BMI 23.7-45.7 Mothers with overweight and obesity show greater deficiency and insufficiency of vitamin D. Of the 68 RNs, all were small for gestational age with no difference in gender. Samples taken in the first 6 hours of life were centrifuged and froz

Vitamin D deficiency is a global public health problem as evidenced by Mara RÃºbia et al. There are few articles that evaluate vitamin D deficiency in the mom and her newborns but there are no articles that evaluate moms with morbid obesity and the correlation of vitamin D levels in their neonates We have data that support the correlation of maternal deficiency and their RN as well as the repercussion of it during its development, Although we already have knowledge of this correlation, we have found vitamin D insufficiency and insufficiency. 95% of pregnant mothers of the Central Hospital Dr. “Ignacio Morones Prieto” present some degree of obesity, however, it is

not statistically significant to present vitamin deficiency In pregnant women Potosinas, vitamin D levels are below what is necessary for fetal development. In our study, all newborns included were below the 10th percentile, which classified them as small for gestational age and with intrauterine growth restriction and 89.7% found some degree of insufficiency. All this leads to an impact on the morbidity and mortality of preterm infants (<37 SDG) since they have low mineral reserves

vitamin D defici • Maternal obesity • SGA

POSTER |Friday 9th 11:10-12:10 hrs.

C60120
Clinical Science
Maternal and fetal health

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Prediction of adverse perinatal outcomes in patients with gestational diabetes whithin biochemical control limits.

Alterations in the glucose tolerance curve, such as gestational diabetes or carbohydrate intolerance, are very important in relation to maternal obesity and overweight. They are risk factors for adverse perinatal outcomes. Traditionally it is considered that the gestational diabetic patient in glycemic control is unlikely to develop an adverse perinatal outcome. However, there does not appear to be a direct correlation between glycemic control and a good perinatal outcome. The objective of this work is to explore additional maternal and fetal variables that can provide tools to classify the risk in patients with impaired glucose metabolism who are considered to be within biochemical control standards.

Records of women who underwent an oral glucose tolerance curve (CTGO) during pregnancy were included in this study. They were classified into three groups: Patients with CTGO with normal values, Patients with one abnormal value and Patients with two or more abnormal values. A retrolective cohort was then performed and maternal factors such as BMI at the beginning of pregnancy, the presence of overweight at the beginning and at the end of pregnancy, fasting CTGO values, at 1 hour and 2 hours were analyzed. Fetal factors such as the presence of polyhydramnios or a fetal abdominal circumference â‰¥ 75th percentile were also included in the assessments. Univariate analyses was performed to evaluate differences between the three groups, binary logistic regression for the proposed predictor variables for adverse perinatal outcome within each group and decision trees were also executed. 755 patients were included. 326 normal CTGO, 122 with an altered value and 308 with two or more. In the group of gestational diabetes, the BMI at the beginning of pregnancy had an OR of 2.93(IC 1.19 a 7.20). The fetal abdominal circumference had an OR of 4.65 (IC 2.68 - 8.06) for adverse

In those patients with altered values in the glycemic curve, and glycemic control within normal limits, additional variables must be considered in order to evaluate whether they behave as low or high risk patients for developing an adverse perinatal outcome, among them are: BMI at the beginning of pregnancy, polyhydramnios and fetal abdominal circumference equal to or greater than the 75th percentile in the third trimester of pregnancy. This study shows evidence that support a

different way of dealing with gestational diabetes, and a different approach for the surveillance of the mother and the fetus. It looks like it is not enough to take into account the glycemic control but, the characteristics of both of them to determine the group of risk they belong to and to define the best strategy to diminish the prevalence of adverse perinatal outcomes at short and long time in the fetuses and in the newborns. Considering as adverse perinatal outcome: macrosomia, larger for gestational age, neonatal hypoglycemia, number of days at the hospital, etc. Once the patients are classified in a group of risk according to their characteristics, the management can be individualize

diabetes • glycemic control • pregnancy

ORAL | Thursday 8th 12:00-13:00 hrs.

C60149
Clinical Science
Maternal and fetal health

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Association Of Maternal Factors With Fetal Ultrasonographic Measures Predictors Of Endothelial Damage.

Several adult diseases originate through adaptations of the fetus in the intrauterine environment. Early endothelial dysfunction has been proposed origining in fetal life, however, to date it is not known which are the factors that could intervene in the development of this pathology. The fetal aortic intima media thickness (aIMT) and the aortic diameter (AD) have been suggested as biomarkers for predicting metabolic disorders and cardiovascular disease (CVD) risk in children. The aim of the study is to evaluate the association of maternal factors and the estimated fetal weight (EFW) with the measurement of aIMT and AD in fetus.

Fetal biometry were performed at 20-24 gestation weeks in 60 women between 18 and 43 years old, with a single pregnancy. The measurement of fetal aIMT and AD, which were obtained from the portion of the fetal abdominal aorta located between the renal and the iliac arteries, by high-resolution ultrasound. A venous blood samples were obtained from the mother after an overnight fasting for the measurement of plasma glucose and lipid profile. Multiple regression analysis was performed to show the correlation between aIMT and AD with maternal factors. The P value â‰¤0.05 was considered as statistically significant. Within the maternal metabolic measurements, the mean of glucose was 86.7 Â± 10.4 mg/dl, total- cholesterol 241.4 Â± 50.6 mg/dl, HDL-cholesterol 65.9 Â± 16.2 mg/dl, LDL-cholesterol 132.9 Â± 41.2 mg/dl, triglycerides 197.4 Â± 67.1 mg/dl. The mean of EFW was 807.2 Â± 319.6 gr. The analysis of the association between the maternal factors and the EFW with the fetal aIMT and AD, showed a positive association between the fetal AD and EFW (R2= 0.168, p< 0.012). On the other hand,a positive association was observed between the fetal aIMT with the maternal se

Maternal hyperglycaemia is associated with fetal endothelial damage. The molecular mechanism could be through the increase of ROS levels associated with reduction of nitric oxide. These findings show the clinical importance for the control of glucose in pregnant women, and in addition, the implementation of the measurement of aIMT during prenatal control to detect endothelial damage in early stages. More studies are needed to obtain more information on the subject.

cardiovascular • fetuses • maternal factors

POSTER | Wednesday 7th 17:40-18:40 hrs.

C60149

C60251
Clinical Science
Maternal and fetal health

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Correlation Of Maternal Metabolic Factors With Presence Of Placental Histopathological Lesions

The placental lesions, as the presence of multiple infarctions, acute atherosis, distal villous hypoplasia, and increased syncytial knots, are associated with major pregnancy disorders like preeclampsia, preterm labor and intrauterine growth restriction. Maternal hypercholesterolemia has been associated with alteration of placental microvascular endothelial function. However, no previous reports has analyzed clinical or metabolic maternal factors that could predispose to specific type of placental lesion. The aim of this study was to investigate the relationship of maternal factors and placental histopathological lesions.

Prospective longitudinal clinical study was performed in 17 pregnant patients. The patients were ranged from 18 to 40 years old, with 24 to 28 weeks of gestation, without evidence of metabolic diseases. Anthropometric and metabolic measurements were realized during these weeks, and at the end of pregnancy the histopathological study of placenta was performed. Our results shows that multiple placental infarcts correlates positively with LDL-cholesterol levels (r=0.629, p=0.011). The presence of acute atherosis correlates negatively with HDL-cholesterol levels (r=-0.522, p=0.045). Finally, villus hypoplasia correlates with a higher maternal BMI before pregnancy (r=0.503, p=0.039) and during each trimester; first (r=0.608, p=0.012), second (r=0.607, p=0.012) and third (r=0.585, p=0.045).

In conclusion this study shows a correlation between placental alterations with lipid profile and maternal body mass index. Due to these results, is important to maintain close monitoring of BMI and lipid profile before and during pregnancy with the purpose to avoiding maternal-fetal complications.

placenta • metabolic factor • pregnancy

POSTER | Wednesday 7th 17:40-18:40 hrs.

C60251

C60262
Clinical Science
Maternal and fetal health

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Hair Cortisol in Women exposed to Domestic Violence during Gestation and its effects on the Newborn

Animal literature has many papers demonstrating that the association between maternal psychosocial stress and low birth weight is mediated by changes in the HHA axis. In humans the HPA axis seems to be overloaded in pregnant women under psychosocial stress. Cortisol crosses the placental barrier, which inhibits intrauterine growth when at high levels. Despite the great changes associated with gestation in maternal endocrine physiology, the neuroendocrine system is responsive to maternal psychosocial stress states.

This is a population-based birth cohort with 183 pregnant women who were followed up from the 25th week of gestation up to the puerperium. Interviews with trained psychologists were performed to assess the exposure to domestic violence and other explanatory variables. Birth weight was extracted from medical charts. Hair samples were collected from the posterior vertex of the mothers. Tufts of approximately 7 cm of hair were cut, close to the scalp, using scissors. They were analysed with ELISA, according to standard methodology. Logarithmized means were compared between exposed and non exposed groups, according to the gestational period. The slope of the cortisol curve was calculated and correlated with birth weight. Exposed mothers had a significantly lower mean than those not exposed to violence in all months prior to delivery (25th-28th; 29th-32nd; 33rd-36th; 37th-40th gestational week periods). The slope of the cortisol curve was negatively correlated with birth weight (the higher the first, the lower the second).

The decrease in cortisol that we found would be explained by a deregulation of the HPA axis, with reduced feedback sensitivity. In our study, women exposed to violence, therefore, behaved like subjects exposed to anxiety disorders and to chronic stressors behave, according to the literature. If the concentrations among exposed women were lower, the speed with which they increased during the final gestational period was greater, probably aiming to approach more physiological levels at the end of gestation.

violence • cortisol • pregnancy

POSTER | Thursday 8th 10:40-11:40 hrs.

C60262

C60265
Clinical Science
Maternal and fetal health

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Oxidative Stress And Total Antioxidant Capacity Throughout Pregnancy Among Normal Weight, Overweight And Obese Mexican Women

Obesity during pregnancy is associated with adverse maternal and neonatal outcomes, and with a higher risk of developing cardiovascular and metabolic diseases in childhood and adult stages. Obesity is an inflammatory state, that is frequently characterized by increased free fatty acids, reactive oxygen species and inflammatory cells. Some evidence has shown increased levels of lipid peroxidation products in the plasma of obese (OB) women during pregnancy. The aim of this study was to evaluate the differences in lipid and protein oxidation and in the total antioxidant capacity (TAC) throughout pregnancy between normal weight (NW), overweight (OW) and OB women.

Methods: A prospective cohort study included Mexican women followed during pregnancy in trimester T1:10–14 weeks of gestation (WG), T2:14–27 WG, and T3:?27– 36 WG. Women were excluded if they have previous diseases. MDA, PC and TAC were quantified in plasma, using a spectrophotometer Beckman DU800. Descriptive statistics, one-way ANOVA, and repeated measures ANOVA test were performed. Results: A total of 82 women were included (NW n=30, OW n=31 and OB n=21). Maternal weight gain (MWG) was insufficient in 28.4% and excessive in 24.7% of women. In T3, higher concentrations of MDA and PC were observed in OB women (0.520±21 pmolMDA/mg dry weight and 13.42±4.8 nmolPC/mg protein) compared to OW women (0.338±0.14 pmolMDA/mg dry weight and 8.61±5.6 nmolPC/mg protein) and NW women (0.306 ±0.12 pmolMDA/mg dry weight and 6.17±2.2 nmolPC/mg protein), p<0.0.001. MDA and PC concentrations correlated positively with p-BMI in T3 r=0.33 and r=0.45, respectively (p<0.001). TAC did not correlate with p-BMI. Repeated measures ANOVA showed a significant increase in MDA and PC during pregnancy with higher concentrations given by p-BMI classification (p intragroup <0.001 and p

Protein damage and lipid oxidation increase throughout pregnancy. Oxidative stress markers are higher in OB women compared to OW and NW women. However, TAC is not modified significantly during pregnancy. MWG did not correlated with oxidative damage.

obesity • malondialdehyde • protein carbonyl

POSTER | Thursday 8th 10:40-11:40 hrs.

C60265

C60270
Clinical Science
Maternal and fetal health

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Maternal Cortisol during Pregnancy and Newborn and Infant Outcoumes: a Sex-related Association

Violence against women is very prevalent, even during pregnancy. Some physiological changes of the woman during gestation depend on the sex of the fetus, among them the adaptations of the HHA axis. It was shown that cortisol levels during the second gestational trimester were lower in women generating female fetuses compared to women generating male fetuses; and these levels reversed in the third quarter. It has also been demonstrated that the daily patterns of maternal cortisol curves and the amount of secreted cortisol differ according to the sex of the fetus. The response to violence during gestation, therefore, may be sex- depended.

This is a population-based birth cohort with 183 pregnant women who were followed up from the 25th week of gestation up to the puerperium. Interviews with trained psychologists were performed to assess the exposure to domestic violence and other explanatory variables. Birth weight was extracted from medical charts. Hair samples were collected from the posterior vertex of the mothers. Tufts of approximately 7 cm of hair were cut, close to the scalp, using scissors. They were analysed with ELISA, according to standard methodology. Logarithmized means were compared between exposed and non exposed groups, according to the gestational period. The slope of the cortisol curve was calculated. Its association with being born small for gestational age (SGA), hospitalization, weight gain and development in the 1st semester of life was assessed, according to the sex of the infant. We found that stress caused by violence and signaled by cortisol was associated with SGA more in females and with cognitive delay more in males. No association was found with hospitalization and weight gain in the first months of life.

These findings are supported by the literature that studies stress. Some authors state that mental disorders and cardiovascular diseases have common biological substrates at the anatomical, molecular and / or genetic level. According to these authors, these ails have their origin in fetal stress exposure and present a sex- dependent response.

violence • fetus sex • infant outcomes

POSTER | Friday 9th 11:10-12:10 hrs.

C60270

C60315
Clinical Science
Maternal and fetal health

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Differences in fetal cardiac function, evaluated by ultrasound in M-mode in fetuses of diabetic mothers versus fetuses of non diabetic mothers

The fetal myocardium undergoes pathological changes in maternal diabetes mellitus reported as hypertrophic cardiomyopathy with disproportionate thickening of the interventricular septum attributed to fetal hyperinsulinism secondary to maternal hyperglycemia. In children born of diabetic mothers an 2D US echocardiography hypertrophy with decreased ventricular dimensions and low cardiac output due to diastolic dysfunction was determined, with a prevalence between 10 and 35%. The aim of this study is to evaluate the displacement of valves in the atrioventricular plane using ultrasound (TAPSE / f-MAPSE), which is a simple, rapid and non-invasive tool that can be used in routine echocardiography

The study was carried out in the Translational Medicine Unit of the National Institute of Perinatology "Isidro Espinosa de los Reyes" from March 2016 to April 2018. US evaluation was performed in Voluson E8 GE (Health Care). 43 pregestational diabetic patients and 43 non diabetic(controls) with single pregnancies, between 25 to 38 of gestation were included. Echocardiography was performed to evaluate myocadiac motility at the level of the fetal mitral annulus (f-MAPSE) and fetal tricuspid (f-TAPSE) with M mode, in a 4 chambers view. The longitudinal displacement at the end of diastole to the maximum extension in systole was measured. The difference in measures was evaluated with wilcoxon signed Ranks to paired data in SPSS software. In the group of pregestational diabetes the TAPSE mean was 8.1 mm SD of 1.6 (4.20 - 11.80) and MAPSE 6.50 mm SD 1.43 (3.70-10). In non- diabetic mother TAPSE mean was 7.7 mm SD 1.6 (5.3-12.40), and MAPSE mean was 6.08 mm SD 1.2 (4.10-9.50). No statistically significant difference was found between the TAPSE measurements (p = 0.218). In MAPSE if a significant difference was observed (p = 0.038).

In our study, no difference was observed in the measurement of TAPSE between fetuses of diabetic mothers and controls, on the other hand, an evident difference was observed in the MAPSE between the fetuses children of diabetic mothers compared to the non-diabetic mothers, perhaps as a consequence to the pathological change previously in the fetal myocardium (hypertrophy of the interventricular septum) that produces secondary decrease in ventricular dimensions and low cardiac output due to ventricular dysfunction. The systolic displacement of the plane of the tricus-

pid and mitral fetal rings are simple , rapid quantitative, non-invasive and accessible ultrasonographic tool modality to evaluate systolic ventricular function and the results obtained suggest that they can detect changes in cardiac function in early pathophysiological process.

diabetic mothers • cardiac function • M-mode

POSTER | Friday 9th 11:10-12:10 hrs.

C60353
Clinical Science
Maternal and fetal health

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Maternal Obesity in pregnancy and Determinants of Neonatal Cardiovascular Dysfunction at Birth

The prevalence of obesity among pregnant women has risen in line with the general population, with implications not just for maternal pregnancy outcome but also for the developing fetus exposed to an obesogenic environment in utero. There is now widespread concern about the long-term effects of maternal obesity on offspring health, particularly in terms of the developmental programming of cardio- metabolic disease in later life. Here we investigated the influence of maternal obesity in pregnancy on neonatal heart rate variability (HRV) within 48 hours of birth.

This trial was a nested case control study performed at Guy's and St Thomas' NHS foundation trust hospitals. We recruited pregnant women who were either obese (n=45, BMI?30kgm2) or lean (n=60, BMI 20-25 kgm2). HRV (ECG, 20 mins), routine clinic blood pressure measurements, and anthropometric measurements were made within 48 hours of birth. The primary outcome of the study was the cardiovascular function of the neonates. The mean BMI of women in the obese cohort was 35.9 and the mean BMI of women in the lean category was 22.4. HRV analysis during sleep state revealed significant increases in the minimum HR (Mean difference: -13.74, 95% CI -26.79 to 0.69; p=0.012) and mean heart rate (Mean difference -10.55, 95% CI -20.57 to -0.53; p=0.015) of the neonates born to obese mothers in comparison to those born to lean mothers. Furthermore, the obese cohort also had significantly reduced power in the high frequency (HF) band (54.89, 2.74 to 107.04; p=0.0016) and total power (637.84, 31.89 to 1243.79; p=0.039) compared to their lean counterparts. Adiposity, as measured by skinfold thickness, and blood pressure did not differ between maternal BMI

Exposure to maternal obesity in utero significantly alters basal parameters of cardiovascular function in neonates independent of neonatal birthweight, neonatal gender, maternal education level and mode of delivery. HRV analysis was consistent with a decline in the global activity of the autonomic nervous system, reduced efferent parasympathetic activity and an increase in basal heart rate and which may present a risk for susceptibility to cardiovascular disease in later life.

prenatal • obesity • HRV

POSTER | Thursday 8th 10:40-11:40 hrs.

C60353

C60367
Clinical Science
Maternal and fetal health

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Maternal Obesity and Determinants of Childhood Cardiovascular Dysfunction at 3-4 years.

Several mother-child cohort studies have reported associations between obesity in pregnancy and adverse offspring cardio-metabolic outcomes. However, a causal relationship has yet to be established. To provide further insight, we explored associations of maternal obesity in pregnancy with cardiovascular parameters and adiposity in 3-4-year-old children. 60 mothers who were obese (BMI ?30 kg/m2) in early pregnancy and their 3-4-year-old children were recruited from the UPBEAT cohort, a randomised controlled trial that examined the effects of a complex lifestyle intervention on the incidence of gestational diabetes and macrosomia. 48 lean controls (BMI 18.5-24.9 kg/m2) and their 3-4-year-old children were recruited for comparison and matched for maternal age and ethnicity.

Measurements taken for each child included BMI and skin fold thicknesses, systolic and diastolic blood pressure (routine clinic BP measurements), heart rate variability (HRV, time and frequency domains) by electrocardiography and cardiac dimensions were obtained by echocardiography. Children's cardiovascular parameters for each maternal BMI category were compared first by a simple t-test and then by linear regression, adjusting for maternal smoking, maternal education, household income, mode of delivery, child's gender and current BMI. Obesity in pregnancy was significantly associated with a higher minimum and mean heart rate, lower SDNN (HRV), reduced low frequency power, and lower total power, shorter ejection duration (ED) and increased left atrial volume (LAV, $p<0.05$). Positive associations were also observed between obesity in pregnancy and child BMI and abdominal skin fold thickness ($p<0.05$). The association between obesity in pregnancy and minimum heart rate remained significant after adjustment for confounders. There were no associations between obesity in pregnancy and offspring systolic or diastolic blood pressure.

Children of obese mothers exhibit several markers of cardiovascular dysfunction, including altered autonomic function, indicating reduced parasympathetic tone, and alterations in cardiac structure, when compared with children of lean control mothers. Children of obese mothers also showed increased adiposity. Maternal obesity, therefore, appears to influence cardiac remodelling in the offspring, with no apparent change in blood pressure at age 3-4 years, but which may have cardiovascular consequences in later life. This work was funded by the British Heart Foundation.

Maternal • Obesity • Cardiovascular

ORAL | Thursday 8th 12:00-13:00 hrs.

C60367

C60421
Clinical Science
Maternal and fetal health

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Advanced glycation end products levels in preeclampsia and their implications in insulin resistance.

Advanced glycation end products (AGEs) are glycated biomolecules from both exogenous and endogenous sources. The accumulation of these compounds in the body contributes to cellular damage at the vascular system, and especially alters the metabolic responses mediated by insulin. An increase in the concentration of AGEs in placental tissue from normoglycemic pregnant women has been reported; however there are few studies about AGEs levels during inflammatory obstetric disorders unrelated to hyperglycemia, such as in preeclampsia (PE). Therefore, the aim of the present study was to determine the circulating levels of maternal AGEs in preeclampsia and to evaluate their possible correlation with clinical parameters of glucose metabolism.

The study was conducted and approved as a research protocol at the Instituto Nacional de Perinatología (Mexico City, Mexico). All samples were obtained from women with 36-40 weeks of gestation after obtaining informed consent. Plasma levels of total AGEs were determined by competitive enzyme- linked immunosorbent assay (ELISA; Lamider,México) and plasma levels of intact albumin-AGE complexes were measured by radioimmunoassay (RIA) in women with normoevolutive pregnancy (control group, n=28) and in patients diagnosed with PE (n=15). We also evaluated the correlation between levels of AGEs and metabolic profiles for the preeclamptic patients. Plasma levels of total AGEs in patients with PE (29.66±2.99 ?g/mL) were significantly higher ($p<0.05$) than those observed in the control group (19.68±2.41 ?g/mL), while the levels of intact albumin-AGEs complex did not show significant differences between control and PE group (0.011±0.003 and 0.010±0.004 ?g/mL respectively). A positive correlation between the circulating levels of total AGEs and insulin ($r=0.61$), glucose ($r=0.62$), and HOMA ($r=0.74$) levels was observed.

In the present study, we have demonstrated that plasmatic total AGEs are increased in PE normoglycemic patients. In contrast, we did not find statistical differences in the content of intact albumin-AGEs complexes between PE patients and control group, which suggests a probable increase in the activation of AGEs degradation system. Interestingly, we also found a positive correlation of insulin resistance with AGEs levels even in normoglycemia, suggesting that glycation-promoting mechanisms may affect signaling pathway of insulin. Due to PE is an obstetric disorder of high

worldwide incidence, it is necessary to study any factor that potentially contributes to PE onset. The association between glycation and PE can help us to understand the factors that promote this disorder, and it can explain the evolution of organ damage before maternal symptoms appear. This would contribute to the development of subsequent studies that allow the design of strategies for early non-invasive detection and/or therapeutic management of systemic complications.

glycation • preeclampsia • insulin

POSTER | Wednesday 7th 17:40-18:40 hrs.

C60426
Clinical Science
Maternal and fetal health

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1st trimester LDL in women with pregestational obesity and anthropometry at birth correlate with adiposity at 4 months, independent of DHA-supplementation

Maternal obesity is an important risk factor for childhood obesity. Nutritional interventions during pregnancy, such as LC- PUFAs, have been appointed to safeguard the metabolic effect of maternal obesity on the offspring. The MIGHT study is a double- blinded, randomized, placebo-controlled clinical trial where women with pregestational obesity were allocated to receive 200 or 800 mg/day of DHA. Since the MIGHT study is blind, the groups are identified as #12 or #13. Epifat is a nested cohort of the offspring of the MIGHT study, looking at early markers of adiposity. Our aim was to evaluate the effect of maternal DHA supplementation in women with pregestational obesity on body fat (BF%) in the offspring at birth and at 4 months, identifying perinatal risk factors.

A sample of 57 children from the EpiFat cohort were included in this analysis. Neonatal anthropometry was performed 24-48 h after birth including weight, height, circumferences and skinfold thickness at 5 body sites. At 4 months of age (4m) BF% was evaluated by PeaPod. Maternal variables analyzed were age, parity, pregestational weight, gestational weight gain (GWG), glycaemia, insulin and lipid profile. T-test and Chi-square for continuous or categorical variables respectively, were used to assess differences between groups. The relation between BF% at 4m and BC at birth, maternal and neonatal factors were investigated using Pearson correlation coefficient. At birth, children length was higher in #12 (n=28) compared to #13 (n=29) (mean ± SD; 50.27 ± 1.56 vs 49.31 ± 1.55 cm; p=0.025). There were no differences in maternal, neonatal and BF% at 4m between DHA supplemented groups. BF% at 4m showed a positive correlation with 1st trimester LDL levels (r=0.344; p<0.018) and an important effect of GWG was observed (r=0.64; p=0.645). Several anthropometric measurements at birth correlated positively with BF% at 4m: weight/height ratio (r=0.281; p=0.038), subscapular (r=0.

High LDL in the first trimester in patients with maternal obesity correlate significantly with infant adiposity at 4m. Several anthropometric measures in the newborn, including skinfolds in the first 24 to 48 hours of birth, could be good early indicators of adiposity at 4 months. Of particular relevance is the weight/height ratio, which could be clinically useful for early intervention programs to prevent childhood obesity.

maternal obesity • body composition • DHA

POSTER | Friday 9th 11:10-12:10 hrs.

C60426

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
International Society for Developmental Origins of Health and Disease
CANCÚN, MÉXICO 2018

C70392
Clinical Science
Placental programming

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A multi-level transcriptomic analysis of human placenta in abnormal parturition

The multifaceted and multifactorial nature of pregnancy has rendered it difficult to decipher the underlying molecular machinery and has limited the ability of clinicians to predict and prevent associated life-threatening complications. A comprehensive analysis of the underlying organization of the placenta, a key organ of pregnancy, can provide a keener insight into the local and systemic physiological changes that promote cervical dilation and timely and coordinated uterine contractions during the parturition.

We perform an exhaustive investigation of transcriptomic profiles of decidual samples from 16 normal spontaneous vaginal delivery, 18 C- section, and 16 preterm labor human placentas to investigate the pathophysiology of abnormal parturition. We use high-throughput next generation sequencing (NGS) to characterize the gene expression signature of abnormal parturition and provide a comprehensive depiction of involved biological processes. We identify significant differences in the expression of genes involved in extracellular matrix (ECM) remodeling, neovascularization, fetomaternal immunologic crosstalk, inflammatory and stress response, and lipid metabolism. We also portray the co-expression architecture of human placenta during parturition and correlate it with a wide range of phenomic and clinical features to identify potential key players.

This study provides the first multi-level survey of transcriptional regulatory mechanisms of abnormal parturition in human pregnancy. Through a systems integration of RNA sequencing and clinical data, it expands on previous findings by highlighting the orchestrated and synergistic interplay of humoral, adhesion, vascular, cytoskeletal, endocrine, and metabolic factors involved in the maintenance of pregnancy – from early stages of gestation to birth.

placenta • preterm labor • RNA sequencing

ORAL | Thursday 8th 15:00-16:00 hrs.

C70392

E100123
Epidemiology
Microbioma

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Microbiota Composition And Body Adiposity According To The Type Of Delivery In Young Adults Of The Nutritionists Health Study - Nutrihs

Evidences relate caesarian delivery with obesity in adult life, considering that infant early gut colonization has a role in mechanism that favors body adiposity. Association of type of delivery and gut microbiota in childhood has been shown, but publications in young adults, who developed or not obesity, are scarce. Studies enrolling young adults, as the Nutritionists Health Study - NutriHS, a cohort of college students in nutrition, are an opportunity to identify early stages of cardiometabolic risk. Our hypothesis:microbiome, defined early in life, might persist until adulthood influencing body adiposity. We examined the association of gut microbiota composition in young adults and their type of delivery, according to BMI (normal as <25kg/m2 or excessive body weight â‰¥25kg/m2).

Data from 151 young healthy adults (90%women,18-40yrs) were obtained by on-line self-administered questionnaires and physical and lab exams (fecal microbiota by sequencing V4 region of 16SrRNAgene (IlluminaÂ®MiSeq)). Cardiometabolic variables and abundance of gut bacteria were compared according to the type of delivery using student t-test or Mann-WhitneyU test and Statiscal Package for the Social SciencesÂ®22.0 (SPSSIncorporation,2000). Cesarean delivery was reported in 48.1% of the normal weight and in 48.8% of the excessive weight groups. Individuals with BMIâ‰¥25kg/m2 (28.5%participants) had greater mean values of abdominal circumference, blood pressure and fasting plasma glucose than normal weight group, but not of HOMA-IR, C-reactive protein and lipopolysaccharides (LPS) levels. All these variables did not show any difference according to the type of delivery in both BMI gourps. In normal BMI group, there was also no difference in the microbiota composition according to the type of delivery. Among those with BMIâ‰¥25kg/m2, we observed lower abundance of L.Blautia (p=0.016) and higher of B.Bacteroides (p=0.024) in the cesarean delivery compared to the natural delivery group.

Our results show that young adults with weight excess had differences in their microbiota composition according to the type of delivery. Those who reported cesarian delivery presented higher frequencies of B. Bacteroides - a gram-negative bacteria that can influence inflammatory responses -; and lower abundance of L.Blautia - a gram positive bacteria that is found in human intestinal microbioma and has been related to infant early gut colonization after vaginal delivery. These results favor the hypothesis that microbiome, defined early in the cycle of life, can persist until adulthood and might influence body adiposity.

Microbiota • Delivery type • Obesity

ORAL | Friday 9th 12:30-13:30 hrs.

E100123

E10116
Epidemiology
Breast milk and early feeding

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Stool pattern and feeding tolerance in infants less than 1000 grams.

The elimination of meconium in the extremely low birth weight (ELBW) neonates is 32% in the first 48 hours of life, compared with 90% that is completed in term infants. The intestinal motility in neonates with 25 to 35 weeks of gestational age is not well organized and the delay of meconium elimination is associated with low grade of intestinal obstruction and altered feeding tolerance. With the advances of neonatal therapies, the survival of ELBW (less 1000 g) is increasing and information about the pattern of meconium transition in these babies has not been reported in Mexico. The objective of this study is to describe, in ELBW infants, the elimination pattern of meconium, the transition to green and yellow evacuations, and the relationship with feeding tolerance.

Cross sectional study. It was included neonates less than 1000 g, and excluded those with mortality in the first 14 days or with gastrointestinal malformations. We studied the stool patterns (first and last day of: meconium, green and yellow), day of life with feeding at 100 ml/kg/day and 150 ml/kg/day. There were 54 neonates, the mean birth weight was 826.7 g SD 116.4 g, with 28.1 SD 1.6 weeks of gestational age. The mean of first evacuation of meconium was 1.5 days, fot the green stools were 9.2 days and for the yellow one was 13.5 days. The beginning of enteral feeding was in the first 48 hours of life (95%) with human milk (96.3%). The feeding for 100 ml/kg/day was in 16.3 days SD 9 days and for 150 ml/kg/day was at 22.2 days SD 3.7 days. At 14 days of life, 32 (52%) patients were feeding with less than 100 ml/kg/day, and when compared with the rest of the group, they had lower birth weight (p=0.007), first meconium elimination after 96 hours of life OR 1.9 (95%CI 1.45, 2.52) p=0.011, last meconium elimination after 10 days of life, OR 18.3 (95%CI 4.61, 73) p=0.00 and more than 10 days of elimination of meconium OR 16 (95%CI 3.83, 68.3) p=0.00

This study describes the stool pattern of neonates less than 1000 g, and reflects the gastrointestinal inmaturity and poor intestinal motility. This report is the first in Mexico, and gives to the clinicians a useful clinical tool, without cost, and must be part of the intensive neonatal care, understanding the low intestinal motility of its patients, knowing when was the first meconium elimination, how many days a neonate had a meconium evacuations and, when they have been completed the transition to yellow color, and not only asking the presence or not of evacuations. The bias of this report is that the color of the evacuations was obtained from the nurses daily report, with

no more evaluations from anyone of the different investigators. In future investigations, the grams of each evacuation should be included, and investigate the association of this stool pattern with neonatal morbidity like necrotizing enterocolitis.

meconium • stool pattern • < 1000 g infants

POSTER | Wednesday 7th 17:40-18:40 hrs.

E10185
Epidemiology
Breast milk and early feeding

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Brazil

Early introduction of cow milk or infant formulas, but not delivery mode, is associated to children depressive symptoms at 7-8 years in a Brazilian cohort.

Depression is a major public health problem and occurs in all life- cycle groups, inclusive children. For the vast majority of the studies, the rates of depression in children and adolescents ranged between 5.9 and 12.5%. Child depression is a complex disorder and has multiple determinants such as the mode of delivery and early feeding practices. These factors have shown to influence the gut microbiota and the child cognitive development, which in turn have been associated with mental disorders, such as depression. Thus, the aim of this study was to evaluate the association between delivery mode and early introduction of cow milk or infant formulas and depressive symptoms (DS) in children at 7-8 years old

A birth cohort from São Luís, Northeast of Brazil, started in 1997-98 and a follow-up survey was conducted in 2005-06 (n=673). The Children s Depression Inventory was used to screen DS using a cutoff greater than or equal to 17. The introduction of cow milk or infant formulas was classified as early (before 4th months of life) and not early (after 4th months of life) and the mode of delivery as cesarean or vaginal. Logistic regression models were performed having DS as outcome and delivery mode (Model 1) and early introduction of cow milk or infant formulas (Model 2) as main exposures. The following confounders were selected based on the biological plausibility: number of siblings, maternal age and education and delivery mode. The prevalence of children with DS was 21.3%. A total of 31.7% children were delivered by cesarean section and the prevalence of early introduction of cow milk or infant formulas was 29.3%. We found no association between delivery mode and DS (OR: 0.72, CI95%: 0.47-1.12). However, the early introduction of cow milk or infant formulas increased the odds for DS in 59% (OR: 1.59, CI95%: 1.05-2.39), even after adjustment for conf

The delivery mode was not associated with the occurrence of DS in this sample of children aged 7-8 years, while the early introduction of cow or milk infant formulas increased the odds of developing DS at 7-8 years old. Our findings add to the evidence that exclusive breastfeeding up to six months of life should be encouraged. Due to the lack of studies evaluating that relationship and to the importance of the issue, determining the association between mode of delivery and the early introduction of cow milk or infant formulas and child DS is critical to help in the establishment of delivery and feeding decisions or interventions to improve the health of children.

delivery mode •infant formulas • depression

ORAL | Wednesday 7th 16:40-17:40 hrs.

E10185

E10309
Epidemiology
Breast milk and early feeding

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Determinants associated with breastfeeding Exclusive in Cartagena de indias - Colombia 2016

In Colombia, the practice of breastfeeding has declined significantly in recent decades, the establishment of comprehensive policies such as the Zero a Forever program and strategies such as the implementation of hospitals that are friends with women and children, seek to improve the nutrition of children from the gestation until the first two years of life. The food indicators in 2010 report that 96% of Colombian women began breastfeeding their child at birth, 4%, never breastfed, reporting as main causes: not lower milk (23%), the child died (21%)), the child refused breast milk (18%), the child was sick (11%), sick or weak mother (8%). 58% of the reasons for not breastfeeding were related to the child and 42% to the mother, the abandonment was progressive 63% in

Methods :Cross-sectional study, the population consisted of 48,929 children under two years old, sample 445, sampling by cluster randomly selected by neighborhoods and localities. The instrument used was a structured survey for knowledge and practices validated by pilot test (Conbrach alpha of 0.68). Descriptive statistics were used, using measures of central tendency as mean, median frequencies were estimated and percentages for each factor as well as prevalence for breastfeeding. To establish the association between the variables; Social factors, cultural factors and knowledge with the practice of exclusive breastfeeding were calculated Odds ratio (OR) were considered significant with a p-value less than 0.05. RESULTS: The prevalence of exclusive breastfeeding for children under 2 years of age is 70.78% and total of 96.62%, the mean 2.62 and 8.06 months respectively. As for practices is the early start of complementary feeding, only 59.78% took breast milk the previous day, although they have 82.92% knowledge that the baby should be given food whenever he wants, although do not know in 52.58% about the benefits of breastfeeding.

The mean of breastfeeding is below that established by the WHO. Lactation practices are not complemented by the knowledge that mothers possess. Food indicators show risk for children under 2 years of age. Complementary feeding starts early. The supply of water and the use of the bottle interfere with breastfeeding. The benefits of breastfeeding are not clearly identified and the scenarios and policies to support breastfeeding are unknown. There is little promotion of breastfeeding in prenatal controls.

Breastfeeding • knowledge • supplementary fe

ORAL | Wednesday 7th 16:40-17:40 hrs.

E10309

E10319
Epidemiology
Breast milk and early feeding

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Breastfeeding during the first month improve appetite regulation and satiety responsiveness during the early childhood

Epidemiologic studies have documented the association between breastfeeding and lower adiposity in children. Potential pathways though which breastfeeding can protect against obesity later in life are: I) Breastfed children eat when they are hungry, since sucking is a demanding activity; therefore breastfeeding helps preserve the appetite-satiety mechanism which leads to better energy intake regulation. II) During the early postnatal stage, leptin and adiponectin, which are present in human milk, promote the connections into the hypothalamus which promote nutritional homeostasis through the regulation of food intake and energy metabolism.Objective. Examine the association between status of breastfeeding at 1 month and 3 month and early child appetite responsiveness in a birth cohort

Methology. We studied 200 mexican children for which the Baby Eating Behaviour Questionnaire (BEBQ) and breastfeeding information at 1mo and 3 mo of age were available. The satiety responsiveness and the food responsiveness scales from BEBQ were computed. Associations between status of breastfeeding and appetite responsiveness were analyzed using multiple linear models. Results. 59.5% and 57.6% of children received exclusive or predominant breastfeeding at 1 and 3 mo, respectively. Infants who received exclusive or predominant breastfeeding during 3mo (from 0 to 3 mo) had higher satiety responsiveness score (8.8 + 0.2) than infants who received partial breastfeeding (4.6 + 0.46) or no breastfeeding (4.2 + 0.3), also slowness in eating higher in breastfed compared to non-breastfed infants. Similar patterns of association were found between status of breastfeeding and BBEQ scores at 1mo and 3 mo. Moreover, exclusive and predominant breastfeeding were associated with higher scores for food enjoyment and food responsiveness than those observed in infants who received partial breastfeeding or no breastfeeding.

Exclusive and predominant breastfeeding during 3 mo were associated with higher scores for food enjoyment, food responsiveness, slowness in eating and satiety response. Studies in children > 6 mo have documented that food enjoyment and food responsiveness were associated with higher risk of obesity later in life. However, in these studies BBEQ scale was applicate in children >6 mo with complementary feeding. In our study, the infant (1 to 3 mo) did not receive complementary feeding; and the score for slowness eating and satiety responsive were higher in infant with breastfeeding that the other status of breastfeeding.

breastfeeding • satiety • appetite

POSTER | Friday 9th 11:10-12:10 hrs.

E10319

E10372
Epidemiology
Breast milk and early feeding

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Early breastfeeding within half-hour of birth, exclusive breastfeeding and infant development at 1 month: Preliminary results from a Brazilian birth

The World Health Organization recommends to exclusive breastfed (EBF) up to six months of the newborn life. According to UNICEF/WHO the initiation of breastfeeding within 30 minutes (IB) is recommended and this practice is directly associated with longer EBF duration. It also protects from neonatal mortality. Studies have shown that longer duration of EBF provide a low risk of sepsis, diarrhea and infection-related deaths, development of immunity and adequate nutrition for infant development (ID). Besides, on the long-term, prevents child growth backwardness and improves cognition from infancy to adolescence when compared to formula fed child. That way the aim of this study was to evaluate the association between EBF and IB and ID at 28 to 45 days po

A cohort of 67 mothers/infant dyads followed in a public health center in Rio de Janeiro were recruited on the third gestational trimester and were followed at 1-7 and 28–45 days postpartum. Sociodemographic data were collected. The EBF was classified according to WHO definition and IB was defined when breastfeeding initiation occurred within 30 minutes of birth. The ID was measured with Ages and Stages Questionnaire (ASQ- 3). Statistical analyses included logistic regression models adjusted for maternal age, schooling and alcohol consumption. The median participants' age was 26 years (IQ: 22- 31); 51.5% (n=35) had IB; 54.6% (n=36) were EBF; adequate ID was 60.5% and 39.5% for communication, 55.1% and 44.9% for broad motor coordination, 52.5% and 47.5% for fine motor coordination, 63.4% and 36.6% for problem solving and 60.0% and 40.0% for personal/social, respectively for children with and without IB. IB infants presented 4 times more chances of adequate score for the personal/social ID domain (OR: 4.57; 95% CI: 1.48- 14.06; p=0.008). There was no significant association between IB/EBF among the other domains of ID

The results showed IB and EBF low rates until 45 days postpartum. Low prevalence of adequate ID was observed for all domains. The findings showyet those children who received IB were more likely to present adequate ID for the personal/social domain according to the ASQ-3 at 28– 45 days postpartum, compared to those who did not received IB. This data reinforces the

importance of promoting, supporting and guiding breastfeeding during prenatal care and right after delivery to improve infant health and reach adequate ID. Therefore, the positive effects of IB on infant health and ID should be an important topic of discussion during prenatal care and encouraged in the immediate postpartum period. Even though in these preliminary results the association between EBF and ID presented no significant findings, EBF is very important and should be promoted and stimulated. The results presented here reinforce the relevance of breastfeeding in early life. However, more longitudinal studies are needed to show greater impacts of EBF in the long term.

breastfeeding • infant • development

ORAL | Wednesday 7th 16:40-17:40 hrs.

E10377
Epidemiology
Breast milk and early feeding

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Dietary Patterns Among Children 15 To 35 Months Of Age And Association With Maternal Characteristics In A City In Northeast Of Brazil

The analysis of identification of dietary patterns emerged as an alternative and complementary approach to evaluate the food consumption, since they better express the diet consumed by a given population. Knowledge of the food consumption in children, as well as the understanding of the various factors that influence them, can provide a greater uptake of the complex relationship between diet and health in childhood. In children under two years, in addition to biological and nutritional factors, the behavior and characteristics of the mother deserve special mention, since this is the main reference of child care.

We studied 1186 children 15-32 months of age, participants following the BRISA cohort in São Luís Maranhao. Food consumption was investigated using the 24-hour recall. Dietary patterns were identified by factor analysis of principal components, followed by varimax orthogonal rotation. We used hierarchical modeling through Poisson Regression with robust variance estimation to estimate the prevalence ratios of variables related to maternal characteristics. Four dietary patterns were identified: traditional, milk/porridge, healthy and unhealthy.It highlights the negative factor load of breast milk in milk and porridge pattern. Children of mothers aged 35 or older (RP 0.30, 95% CI 0.15 to 0.58) had lower adherence to the traditional pattern, whereas mothers who had low education (RP 2.71; 95% CI 1.47 to 4.98) and with a higher number of children (RP 1.52; 95% CI 1.05 to 2.21) showed greater adherence. For the healthy pattern, we found a lower adherence between mothers who had low education (PR 0.17; 95% CI 0,04 to 0,80). The unhealthy pattern was associated with children of mothers over 35 years old (RP 0.40, 95% CI 0.23 - 0.70) and only children (RP 0.80, 95% CI 0.64 - 1.00).

Four dietary pattern were identified, three of which were starchy foods (breads, farinaceous, biscuits and plain cakes), saturated fat (margarine, butter, whole cow's milk and snacks), sugar (honey, soft drinks, artificial juices and snacks) and poor in nutrients important for the proper development of children, such as vitamins, minerals and fibers. Attention was drawn to the appearance of breast milk with a negative charge in the milk / porridge pattern, pointing to its substitution by cow's milk and modified. Multiparity, lower maternal schooling and maternal age under 20 years were asso-

ciated with lower consumption of foods considered healthy and important for child development. These results point to the need to stimulate the improvement of children's eating behavior, which requires public policies to encourage greater consumption of healthy foods, maintenance of breastfeeding up to two years of age or more, and nutritional education activities for mothers of infants in early childhood. In addition, intersectoral policies, such as greater access to education and family planning, should be priorities for reflection in several areas.

FoodConsumption • Child Nutrition • Factor Analysis

POSTER | Thursday 8th 10:40-11:40 hrs.

E120001
Epidemiology
Others

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Diagnoses of cardiovascular risk factors using anthropometry in Chilean school age children.

The World Health Organization (WHO) strategy for preventing and managing the global obesity epidemic includes the collection of population-specific data on obesity and associated morbidity. Recently, a study carried out in an adult Chilean population has shown that central obesity measurements better identified risk factors for coronary heart disease. However, similar data for children and adolescents are lacking. We aimed to compare in children the discrimination capacity (the ability to separate the instances of presence from the instances of absence of a specific event) of an increased cardiovascular risk using four anthropometry estimators of fatness - BMI, fat mass (FM), waist circumference (WC), and waist to height ratio (WHtR).

Four cardiovascular risk factors (CRF) were studied in a sample of 3325 Chilean children. Prevalence odds ratios (PORs) of CRF were calculated using anthropometry indicators of fatness. Receiver operator characteristic (ROC) curves were used to compare discrimination and estimate new optimal cutoffs, as defined by the highest area under the ROC curve, of BMI, FM, WC, and WHtR; those cutoffs were compared with literature recommendations using Net Classification Improvement (NRI) values. Overall NRI expresses the net percentages of persons with or without events correctly reclassified, which values have theoretical range -2 to 2. Results: Anthropometry measures of fatness had similar PORs for each CRF and also areas under the ROC curve had no significant differences for each CRF. New optimal cutoffs were lower than the literature ones; the higher differences with the literature values were for FM and zBMI. NRIs for the proposed cutoffs showed that FM, followed by zBMI, had the highest NRI values.

Results indicate that all anthropometry measures of adiposity were significantly associated with increased PORs of CRFs. ROC areas under the curve had no differences in favor of any of the anthropometry indicators confirming the need to apply other methods to compare the predictive ability of those indicators of fatness. NRIs showed that FM had the highest values and consistently reached the best predictive ability. In conclusion, FM had the best discrimination ability of all CRF, with the highest and significant NRIs among the four anthropometry indicator of adiposity in this study. However, new cutoff points for FM were much lower than those used in the literature reference which estimated mean FM for all 90th percentile values 10-15 years old of males and

females was about 40.5%. The new proposed cutoffs fluctuated around 28% for the four CRFs, which roughly corresponds to an estimated mean 65th percentile value for males and an estimated mean 35th percentile value for females in the 10-15 years age span of the US percentage body fat percentiles studied in 1999-2004, showing that Chilean children in this sample are heavier that US children studied in

Children • anthropometry • cardiovascular

POSTER | Thursday 8th 10:40-11:40 hrs.

E120124
Epidemiology
Others

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Maternal plasma adiponectin at 30-45 days postpartum and cognitive development of breastfed child at 6 months of age: indication of direct association

The role of plasma adiponectin in stimulation of hippocampal neurogenesis has already been demonstrated by in vitro experiments. However, little is known about the role of maternal plasma adiponectin in cognitive development of breastfeeding infants. Therefore, the aim of the present study is to evaluate if maternal plasma levels of adiponectin at 30-45 days postpartum are associated with the cognitive development of their breastfed infants at 6 months of age.

Nine pairs of mothers and children were followed in a prospective cohort in Rio de Janeiro, Brazil. Maternal plasma adiponectin concentrations (Ã‚Âµg/mL) were measured using commercial ELISA kits. Cognitive development of children at 6 months of age was assessed using Bayley Scale of Infant Development, Third Edition (BSID III). Statistical analyses included Pearson correlation test and linear regression. The confidence intervals were calculated using bootstrapping (n=10,000). As results, we observed a strong correlation between maternal adiponectin concentrations and the children weighted score of cognitive development (r=0.66; p=0.050). The linear regression model showed a significant association between adiponectin and child cognitive development (ÃŽÂ²=0.25, 95%CI: 0.01 Ã¢â‚¬â€œ 0.49; p=0.044), with a limitrophe p-value when adjusted for per capita income (ÃŽÂ²=0.30, 95%CI:-0.01 Ã¢â‚¬â€œ 0.62; p=0.061).

Our results suggest that there is a direct association between maternal adiponectin and child cognitive development. Although we need to be careful when generalizing results from small samples, we tried to minimize bias choosing a reliable approach to lead with small samples. With these results we hope to encourage other researchers to better investigate this issue in larger datasets.

adiponectin • neurodevelopment • breastfed infant

POSTER | Thursday 8th 10:40-11:40 hrs.

E120124

E120188
Epidemiology
Others

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Interaction between a polygenic risk score (PRS) for plasma polyunsatured fatty acids (PUFAs) and body composition on eating behavior in childhood

The peripheral availability of polyunsaturated fatty acids (PUFAs), affects body composition, although little is known about their relationship with eating behavior. The genetic contribution to a certain condition is derived from a combination of small effects from many genetic variants, and polygenic risk scores (PRS) summarize these genetic associations. A PRS based on a genome wide association study for plasma DHA has been created, based on Single Nucleotide Polymorphism (SNPs) from 9 genes (ELOVL2, FADS1, FADS2, SYCP2L, HERV-FRD, C15orf27, TRPA1, ME3, LRRC4C). Our objective was to analyze the interaction between the PRS associated with plasma DHA concentration and body composition with eating behavior (measured using the Children Eating Behavior Questionnaire–CEBQ) in childhood.

We analyzed a subsample of Canadian children from MAVAN cohort with measurements performed at 6 years of age (y) (n 136) and 8y (n 52): eating behavior at 6y, body fat by BIA at 6y and by BodPod at 8y. PRS was based on the GWAS from Lemaitre et al 2011(p threshold, p less than 5x10-6), and a median split created low and high PRS groups (high PRS is higher DHA concentration). High PRS children had longer breastfeeding and higher maternal age, so these variables were adjusted for in the main analysis, as were sex and ethnicity. There were no differences in other confounders. Low PRS children showed a trend to higher z score BMI (p equal to 0.07) and body fat percentage (p equal to 0.08) at 6y, with no differences on eating behavior variables by PRS groups. There were interactions between PRS and body fat percentage at 6y on Food Responsiveness and Emotional Over-Eating, in which low PRS and higher body fat were linked to altered behavior; there were also isolated effects of PRS and body fat on these outcomes. No effects were seen in children with high PRS. High emotional eating at 6y predicted higher body weight and body fat at 8y in the low PRS group, but not in the high

The polygenic risk score might be useful to estimate plasma PUFAs availability in the absence of the fatty acid profile. A lower PRS (reflecting lower plasma PUFAs) can be a risk factor for developing higher body fat associated to non-adaptive eating behavior in childhood; it is possible that the higher PRS (reflecting higher plasma PUFAs) is a protective feature

PUFAs • body fat • eating behavior

POSTER | Friday 9th 11:10-12:10 hrs.

E120220

Epidemiology
Others
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Early Determinants Of Overweight And Obesity In Schoolchildren In Palpalãƒâ, Jujuy-Argentina

Early determinants of overweight and obesity in school children, principally, when the obesity is a public health problem that affects not only adults but also children and adolescents. David BarkerÃ‚Â´s studies showed the importance of prevention in pregnancy and childhood. The purpose of this work was to detect the early determinants of obesity in children attending public schools in PalpalÃƒÂ¡, Jujuy (Argentina).

Early determinants of overweight and obesity in school children, principally, when the obesity is a public health problem that affects not only adults but also children and adolescents. David BarkerÃ‚Â´s studies showed the importance of prevention in pregnancy and childhood. The purpose of this work was to detect the early determinants of obesity in children attending public schools in PalpalÃƒÂ¡, Jujuy (Argentina).

To develop effective prevention strategies it is necessary to identify the individuals or populations at risk. Therefore, primary prevention for childhood obesity will require early detection of conditioning and predisposing factors. The first level of care, with the strategy of Primary Health Care, it is presented as the best scenario to implement prevention interventions for overweight and obesity in the stages early life. Allows early capture, timely detection of situations of risk and continuity of care in pregnancy, birth and childhood, so the policies aimed at this will achieve impact on public health at the future. To make a positive intervention it is necessary to promote a change in the knowledge and attitudes of the health personnel, which allows the translation of scientific evidence current, in standardized and humanized care practices, with the vision of acting for future health, decreasing chronic diseases

obesity •pregnancy • childhood

POSTER | Thursday 8th 10:40-11:40 hrs.

E120233
Epidemiology
Others

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Birth weight is associated with DXA-determined lean and bone mass in healthy young adults from the Nutritionistsâ€™ Health Study â€“ NutriHS

BACKGROUND: In the last decades, studies have been evaluating the role of early life events in body adiposity and obesity-related diseases in adulthood. However, there is little knowledge about its relevance in the lean and bone mass compartments. Osteosarcopenia has been associated with accelerated functional decline and disability in elderly. Its determinants have been more commonly investigated at advanced age, although early-life factors may be already influencing bone and muscle mass peaks and rates of decline. It is important to note that dual-energy X-ray absorptiometry (DXA) is currently the gold standard for estimating bone and muscle mass. Thus, this study examined whether birth weight (BW) was associated with parameters of muscle and bone compartments in he

METHODS: This cross-sectional analysis was performed in 212 healthy participants, aged 20-45yrs, who answered a questionnaire about early- life events, and had anthropometric data, muscle performance parameters, body composition and bone densitometry (iDXA-Lunar GEÂ®) and blood sample collected. Appendicular skeletal muscle mass index (ASMI) was calculated. Associations between BW quartiles (exposure) and calf circumference (CC), handgrip (HG), ASMI, bone mineral density and content (BMD and BMC) and concentrations of 25-hydroxyvitamin D (vitD), lipids, glucose and inflammatory biomarkers (outcomes) were tested using multiple linear regression. RESULTS: 90% women; mean values of age, BMI and BW were 25.4Â±5.4yrs, 24.0Â±6.6kg/m2 and 3230.4Â±437.1g, respectively. Pre-pregnancy BMI of their mothers was 21.9Â±3.0kg/m2. Comparing means values among BW quartiles (ANOVA), differences in CC (p=0.008), HG (p=0.006), ASMI (p=0.041) and BMC of total body (p=0.003) and total femoral (p = 0.034) were observed. In linear regression models, after adjustments for confounders, direct associations of BW quartiles with CC [r2=0.13; p=0.005], HG [r2=0.27; p<0.001], ASMI

CONCLUSIONS: The associations of BW with structural and functional parameters suggest that may be a predictor of muscle and skeletal health in young adults. Since BW is considered a marker of quality of the intrauterine environment, our findings reinforce to the importance of nutrition in the early stages of development also for the prevention of skeletal muscle loss. Our findings suggests that low BW could be deleterious not only to the body adiposity, but also to bone and

muscle compartments, predisposing to chronic non communicable diseases relevants in public health like osteoporosis and sarcopenia. Therefore, changes in muscle and bone compartments should not be seen as a condition that begins in old age, but as a continuous process of life. NutriHS data are promising and may contribute to clarify the role of early life events for body composition-related diseases in adulthood.

birth weight • body composition • DXA

POSTER | Friday 9th 11:10-12:10 hrs.

E120431
Epidemiology
Others

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Childhood adversities and comorbidity in adults with alcohol use disorders: Preliminary results from the largest city in Brazil.

Childhood adversities (CA) have been associated with adverse outcomes in early adulthood, including early onset of smoking, obesity, depression and alcohol use disorders (AUD). It is known that AUD often co-occur (i.e. are comorbid) with numerous mental disorders. This comorbidity leads to a worsen physical, social and occupational functioning, has a negative impact on treatment outcomes and is also associated with higher risk of nonfatal suicidal behaviors and suicide. Although numerous studies have shown that CA may lead to AUD, those turned to evaluate its role in AUD gravity are scarce. The objective of this study is to evaluate the association between CA and psychiatric comorbidities in an AUD population.

A population-based cross-sectional study of psychiatric morbidity among adults in the São Paulo Metropolitan Area (N=5037). This is part of a worldwide consortium called World Mental Health Survey, an initiative proposed by the World Health Organization (WHO). DSM-IV diagnostic criteria were applied for anxiety, mood and substance use disorders. CA included interpersonal loss, parental maladjustment, maltreatment, physical illness and economic adversity. The prevalence of psychiatric comorbidities among respondents with AUD was in general higher between those who suffered some type of CA when compared to those who did not: economic adversity (93.8 vs. 50.3%; IRR=2.1, $p<0.01$), physical illness (83.9 vs. 49.5%; IRR=1.8, $p<0.01$), parental mental illness (76.5 vs. 45.5%; IRR=1.7, $p<0.01$) and physical abuse (64.6 vs. 45.1%; IRR=1.4, $p<0.01$) for alcohol abuse; family violence (88.7 vs. 72.8%; IRR=1.2, $p=0.04$) and parental mental illness (88.1 vs. 72.3%; IRR=1.2, $p=0.04$) for alcohol dependence. Analysis were adjusted by sex and considered the complex sample design.

We found a higher prevalence of psychiatric comorbidities among respondents with AUD who suffered some type of CA when compared to those who did not. Not only CA may lead to AUD, but also might be in part responsible for its gravity. These findings raise awareness of the impact of childhood adversity and highlight the importance of the development of public health policies focusing on protection and care of children with early adversities.

Childhood • Alcohol • Comorbidity

POSTER | Wednesday 7th 17:40-18:40 hrs.

E120431

E20049
Epidemiology
Maternal nutrition and gestational disorders

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Dietary patterns in pre-gestational period and their association with neonatal outcomes: A prospective cohort

Pregnancy is a period of high nutritional requirements due to the maternal and fetal needs. An adequate intrauterine environment reduces the risk of undesired maternal-fetal outcomes, and it is known that fetal growth and development is dependent on the woman lifestyle and health condition in early pregnancy. Birth weight, birth length, and gestational age are indicators of the fetal environment and diet is one of the main factors influencing pregnancy outcomes. An unhealthy diet can impair the metabolic profile, increasing oxidative stress and insulin resistance. The aim of this study is to evaluate the association between pre-pregnancy dietary patterns and premature birth, type of delivery, birth weight, birth length and Apgar score at first minute.

A prospective cohort with 224 pregnant women was followed during 5-13th, 20-26th and 30-36th gestational weeks and 30 days postpartum. Infants birth weight (BW), birth length (BL), Apgar score at the 1st minute [<7 (health risk) vs. higher/equal 7 (normal)], and preterm birth (< 37 completed gestational week) were the outcomes. The reduced rank regression procedure was used to identify dietary patterns that explain the following response variables: fiber density, dietary energy density, and % energy from saturated fat. Statistical analyses included multiple logistic regression models. Confounders were established based on a Direct Acyclic Graph. The mean (SD) BW was 3277 g (530) and BL 49.6 cm (3.1). Large-for-gestational-age (LGA) occurred in 16% and Apgar <7 at the 1st minute in 14.2%. Three dietary patterns were identified: fast food and candies was associated with higher chance of LGA (OR=4.38, 95%CI: 1.32-14.48) and BL >90th centile (OR=4.81, 95%CI: 1.77-13.07); beans, bread and fat was inversely associated with Apgar <7 at the 1st minute (OR=0.14, 95%CI: 0.03-0.70); and vegetables and dairy was inversely associated with premature birth (OR=0.26, 95%CI: 0.06;

This is the first study to estimate the association between pre-pregnancy dietary patterns and premature birth, type of delivery, birth weight, birth length and Apgar score at first minute. Our results suggest that a higher adherence to a fast food and candies pre- pregnancy dietary patterns increases the odds of LGA births and infants in the highest birth length category. We also found

weak evidence that women in the highest tertile of adherence to vegetables and dairy dietary patterns have a lower chance of having a premature birth, compared with those in the lowest tertile. This is an important step towards a better understanding of the pre-pregnancy dietary intake and adverse perinatal outcomes.

dietary patterns • birth weight • prematurity

POSTER | Wednesday 7th 17:40-18:40 hrs.

E20160
Epidemiology
Maternal nutrition and gestational disorders

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Association of pre-gestational body mass index and gestational weight gain with adverse metabolic conditions for fetal growth and development

Hyperlipidemia, insulin resistance and changes in blood pressure (BP) are metabolic and physiologic adjustments that occur in pregnancy to support maternal and fetal metabolic demands. Presence of maternal obesity imposes an overload to these metabolic adaptations and in addition to increase cardiometabolic risk for the mother, may affect fetal growth and development. Scarce evidence of the gradient in metabolic conditions in pregnant women with different adiposity is available. Therefore, the objective of this study is to describe the trajectories of lipids, glucose and BP and to analyze the association of these metabolic markers during pregnancy with pre-gestational BMI (pgBMI) and monthly gestational weight gain (GWG) in Mexican population.

A prospective cohort study was conducted in a public hospital in Mexico City. For this analysis, pregnant women in any month of pregnancy with completed anthropometric, biochemical and BP data were included (n=721 women). Linear mixed effect regression models were estimated to describe the trajectories of total cholesterol (TC), triglycerides (TAG), glucose, systolic BP, diastolic BP, and mean arterial pressure (MAP) and its association with pgBMI and GWG. Models were adjusted by maternal age, education, marital status, preterm birth, parity and intake of energy and macronutrients. The interaction between pgBMI and GWG was tested. TC trajectory had a quadratic pattern, TAG had a lineal pattern, and SBP, DBP and MAP showed a cubic pattern through pregnancy. Women with pre-gestational obesity had less TC increase during pregnancy and high increase in glucose and BP levels than women with normal pgBMI. GWG had a positive association with BP. There was an interaction between of pgBMI with GWG to predict changes in TC, DBP and MAP: among women with higher levels of pgBMI the increase of GWG was associated with lower increments of in TC, DBP and MAP.

As we expected a positive association of pgBMI with glucose, TAG and SBP was found; whereas, GWG had a positive association with SBP. However, a negative association of pgBMI with TC during

pregnancy was found. Therefore, lipid, glucose and BP trajectories were different between pgBMI groups and in some cases GWG modified the effect of pgBMI. Our results suggest that is more important the pgBMI to predict adverse metabolic trajectories than GWG. Now we are analyzing the effects of these conditions on fetal growth and development.

Maternal obesity • Pregnancy • Metabolism

POSTER | Friday 9th 11:10-12:10 hrs.

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
DOHaD
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E30094
Epidemiology
Environmental health and neurodevelopment

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Pregnancy lead exposure and its association with altered cord blood mitochondrial DNA abundance in the PROGRESS cohort

Lead (Pb) crosses the placenta and has been related with oxidative stress, reduced fetal growth and neurological problems. Mitochondria are the power plants of human cells and the cells' principal source of oxidative stress. Therefore, disruption of mitochondria during pregnancy may represent a primary mechanism behind the adverse effects of lead. Mitochondrial DNA abundance (mtDNA abundance) is a sensitive marker of mitochondrial dysfunction. However, the association of Pb exposure during pregnancy on mtDNA abundance has not yet been evaluated. Our objective was to assess the association of Pb exposure during pregnancy with mtDNA abundance in cord blood

Methods: This study was made in mother-infant pairs from the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) study, a prospective cohort that enrolled 1050 pregnant women from Mexico City who were receiving prenatal care between December 2007 to July 2011. MtDNA abundance in cord blood and lead concentrations in both maternal blood and in cord blood were measured. Multivariable models adjusted for multiple confounders were fitted with a total 410 mother-infant pairs with full data of mtDNA abundance, lead levels and covariates. Results: Maternal blood Pb during third trimester was associated with increased cord blood mtDNA abundance (B=0.103, 95% CI 0.041, 0.164). Preterm birth, C-section and premature rupture of membranes (PROM) had significant associations with mtDNA abundance ($p<0.05$). Maternal blood Pb in cord blood Pb interacted with gestational age and premature rupture of membranes leading to a significant increase in mtDNA abundance.

This study shows mtDNA abundance can be disturbed by lead exposure in late pregnancy; therefore, alteration of mtDNA abundance might be one of the mechanisms behind the neurodevelopmental toxicity of lead.

mtDNA abundance • lead exposure • pregnancy

POSTER | Wednesday 7th 17:40-18:40 hrs.

E30094

E30288
Epidemiology
Environmental health and neurodevelopment

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Maternal mood during pregnancy interacts with genetic risk for ADHD to predict internalizing symptoms in childhood: a refined GxE approach

Maternal antenatal depression predicts offspring socio-emotional problems. Its impact varies across the population, as some individuals are resilient. Multiple attention deficit/hyperactivity disorder (ADHD)-associated genes moderate the susceptibility to perinatal influences. However, the networks in which these genes implicate their moderating effect are unclear. The polygenic risk score (PRS) assesses the genomic risk for a disorder but does not account for GxE effects. We refined the PRS methodology for GxE interactions (rPRS), examining the polygenic contribution of ADHD in the relationship between maternal antenatal depressive symptoms (MADS) and child socio-emotional outcomes. We further sought to identify gene networks that are involved in this relationship.

MADS and child socio-emotional outcomes were assessed by the Center for Epidemiologic Studies -- Depression Scale, and the Child Behavior Checklist, respectively, for 187 children in a Canadian birth cohort (MAVAN). We constructed PRS for ADHD from the child genotype data and applied them in the GxE model, creating a novel, refined score (rPRS). We replicated the analysis in validation cohorts from the Netherlands (BIBO, n=132) and Singapore (GUSTO, n=590). We used Gene Ontology enrichment analysis in MetaCore to identify overrepresented pathways in the set of SNPs that constituted the best-fit rPRS in the GxE model. rPRS moderated the relationship between MADS and child internalizing problems (p=5.50e-9). A positive association between MADS and internalizing problems was found only in children with high rPRS. Significant association was replicated in BIBO (p=0.02) but not GUSTO. The rPRS gene set is enriched in dendrite (p=8.966e-10) and postsynapse (p=5.844e-10) components, generation of neurons (p=9.735e-12) and regulation of cell projection organization (p=1.210e-9) processes, and metal ion binding (p=1.409e-9) and gated channel activity (p=1.686e-5) functions.

We found that MADS interacts with the genetic risk for ADHD to predict internalizing outcomes. The association between MADS and internalizing problems in children with high genetic risk for ADHD is further amplified using the novel rPRS. The rPRS optimizes the investigation of mechanisms important for the relationship. These findings suggest that gene networks implicated in neuronal development and synaptic functions can confer susceptibility to the influences of MADS on mental health.

GxE interaction • Mental health • Development

ORAL | Friday 9th 15:30-16:30 hrs.

E30312
Epidemiology
Environmental health and neurodevelopment

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Anthropometric indicators in children between 0-2 years residing in households of disadvantaged sectors of Venezuela

Scientific evidence increasingly confirms that the first stages of human development, particularly the first 2 years of life; are key for the programming of risk factors for future diseases such as DM, CVD, CA and other. The environmental exposure influences the nutrition of an infant and its impact on the development and growth during its initial life. These must occur during the critical period of growth (the first thousand days) and could have irreversible long-term consequences on adult health. Considering the current complex humanitarian crisis in Venezuela, this study aimed the evaluation of the nutritional impact that this phenomenon has caused in the pediatric population of less than 2 years old, to predict probable health risks for the Venezuelan population in the futur

Study was performed nationwide of the households class C, D and EF in major cities, medium, small and hamlets of 6 Venezuelan geographic regions. The Social Welfare 2017 questionnaire was used, to determine the conditions of the household, food security and anthropometric pattern of children under 2 years.The anthropometric data of weight (kg) and height (cm) of the infants were collected and analyzed following the guidelines of the WHO. Food security was evaluated according to the short module of the USDA. Of the 449 children studied; 49.7% were male and 50.3% female. The average weight was 8.85 Kg and the height was 71 cm for both sexes. It was reported that there was no sexual dimorphism in the weight for height (W/H) indicator (p=0.412) but there was for the height for age (H/A) indicator (p=0.055). The nutritional status association between W/H and H/A showed a significant association (p=0.000), showing that when W/H increases (48%), children with adequate H/A descend significantly (21.4%). The most frequent cause in households of food insecurity is lack of income for purchasing foods. In consequence food insecurity was present in the majority of households

This study shows the anthropometric profile reported by a representative sample of unprotected children under 2 years old in Venezuela during the complex humanitarian crisis. The W/H indica-

tor showed a trend toward OW in children with growth retardation determined by H/A. Currently the diet of the Venezuelan is rich is carbohydrates, but poor in proteins of high biological value and micronutrients, the latter being essential for the first peak of growth of the life course that occurs during the first 2 years of life; significantly impairing the height in children with a trend to present overweight. This is confirmed by the fact that in most households the family income is not enough to purchase food, with differences between households in the strategies used to cope with the crisis. It is important to carry out epidemiological surveillance to avoid epidemics of chronic degenerative noncommunicable diseases in future generations of Venezuelans.

Venezuela • Childrens • Anthropometric

POSTER | Thursday 8th 10:40-11:40 hrs.

E40151
Epidemiology
Life style and perinatal nutrition

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Maternal pre-pregnancy BMI is associated with increased offspring visceral adiposity in adult women from the Nutritionists Health Study-NutriHS, Brazil

Evidences suggest that maternal adiposity could contribute to explain the intergenerational cycle of obesity. However, few studies have examined particularities in women, right after adolescence, when several changes in body composition occur. Additionally, little is known about the association between the maternal adiposity and the offsprings distribution of body fat, especially DXA-determined visceral adipose tissue (VAT) accumulation which is known to trigger metabolic abnormalities. We evaluated if maternal pre- pregnancy body mass index (BMI) [<25 or >=25 kg/m2] was associated with fat mass index (FMI) [total fat (kg)/ height (m2)], android-to-gynoid fat (AG) ratio and VAT (cm3) in participants of the NutriHS which includes undergraduates and graduates from nutrition.

Historical cohort included 137 non-pregnant women (17-45 yrs), without cancer or diabetes, and excluded those whose mothers were <=19 yrs, smoker or had diabetes during pregnancy. Pre-pregnancy BMI and early life information were self-reported using online questionnaires with mothers consultation. Measures of adiposity were assessed by dual energy X-ray absorptiometry. VAT and FMI were log-transformed and linear regression employed. Maternal schooling was considered as minimal sufficient adjustment suggested by Directed Acyclic Graph. Height was also included for AG ratio and VAT. Median (IQ range) age was 22 yrs (20-28), 75% were Caucasians, 89% were undergraduates and 8% were obese. Mean (SD) values of blood pressure [106 (11)/71 (8) mmHg] and non-HDL cholesterol [116 (29) mg/dL] were within the normal ranges. Mean AG ratio was 0.78 (0.2) and median VAT and FMI were 92 cm3 (39-258) and 7.5 kg/m2 (6.1-9.5), respectively. Overall mean birthweight was 3161 g (421) and did not differ according to pre-pregnancy BMI categories. Pre-pregnancy BMI >=25 kg/m2 was independently associated with FMI (B=0.21;p=0.018), AG ratio (B=0.13;p=0.004) and VAT(B=0.80;p=0.021).

Being daughter of mothers with excessive weight at conception resulted in increments in adiposity in adult life, compared to those born from normal-weight mothers. Our findings in healthy women in reproductive age reinforce the role of inter-generation transmission of obesity predisposition -particularly of central distribution- which increases risk for cardiometabolic diseases in later life. Without disregarding genetic component, we suggest that environmental factors should be contributing to explain the associations found, highlighting the importance of obesity prevention/treatment even before conception in attempt to minimize a vicious cycle of body weight accumulation and its comorbidities.

Adipose tissue • Visceral fat • Pre-pregnancy BM

POSTER | Thursday 8th 10:40-11:40 hrs.

E40151

6th International Symposium on Metabolic Programming and Microbiome
3rd Meeting of Ibero-American DOHaD Chapter
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CANCÚN, MÉXICO 2018

E40235
Epidemiology
Life style and perinatal nutrition

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Intra uterus socioeconomics exposures and child obesity in Sao Paulo: evidence from the Western Region Cohort Study

Childhood obesity is a global burden and represents a challenge for public health interventions and policies. Overweight children are more likely to stay obese into adulthood and more likely to develop noncommunicable diseases. Perinatal exposures such as pre-pregnancy BMI, diet, and poverty have been associated with adverse child developmental and consequent risk of disease later in life. Evidence has shown that this phenomenon is modulated through epigenetic pathways. Epigenetics involves independent mechanisms of DNA sequences modification resulting in changes in gene expression allowing the cell to assume different phenotypes according to the environment. In our study, we investigated the association between intra uterus socioeconomic exposures and child overweight at 3.

In a Brazilian birth cohort (Coorte Regiao Oeste - ROC), we explored the association between gestational exposures in 1,486 children born at term and with appropriate weight at birth and its relation to overweight at age 3. Overweight was characterized as weight-for-length Z- score above 2 SD (using the WHO Child Growth Standards median). During a home visit mothers were interviewed about environmental factors (gestational exposure) that could interfere with the epigenomic profile of the newborns. Children were evaluated at birth, 1 and 3 years of age. At 3 years 11% of the sample were overweight, girls being more affected than boys (11.2% and 10.3% respectively). After adjustment for confounders, overweight and obesity at 3 years were associated with pre- pregnancy maternal obesity (OR=1.72, 95%CI 1.06, 2.79, p= 0.029), lower income (equal or less than the minimum wage) (OR = 0.34, 95%CI 0.12, 0.98, p= 0.045), and abdominal perimeter (OR= 1.23, 95%CI 0.88, 1.29, p< 0.002). No other anthropometrical or socioeconomic indicators were significantly associated with overweight or obesity at 3 years.

Our finds suggest an association between lower income, maternal obesity and overweight and obesity at 3 years old. These results indicate that poverty is associated with overweight and obesity in both, mother and child, suggesting that poverty can be an environmental factor that alters epigenetics mechanisms leading to higher BMI. The low income as a proxy for socioeconomics and a higher BMI deserves further investigations to better understand the mechanism and improve public health programs.

Child obesity • Risk Factors • Cohort studies

POSTER| Thursday 8th 10:40-11:40 hrs.

E40235

E40435

Epidemiology
Life style and perinatal nutrition
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Dietary intakes among women across lifecycle stages; from pre-conception to adolescence: A Multi-centric cross sectional analysis

The deprived nutrition of women from pre-conception to adolescence is a cause of concern and needs more focus in public health research in low-middle income countries (LMIC). Nutritional deficiencies among women of reproductive ages (WRA) have transgenerational consequences, as inadequate maternal nutrition is associated with adverse birth outcomes, poor perinatal survival and altered developmental programming in the off springs. In the present study, we aimed to describe nutrient intakes, and characterize dietary patterns among adolescent girls, newly married women (currently non-pregnant and non-lactating), pregnant and lactating mothers in four districts of India. This study was a part of the project funded by Nestlé India.

This study adopted a cross-sectional community based design employing multistage random sampling. A total of 249 adolescent girls, 615 newly married women, 528 pregnant women (PW), and 535 lactating mothers were interviewed. Data regarding socio-demographic factors, such as age, literacy status etc. and cooking practices were collected. The 24-hour recall method of diet survey was carried out to assess the food intake of women. The mean (±SD) age of girls was 15 (±4) and all others was 23 (±3.6) years. Use of solid fuel, open space cooking and open defecation was widely present. There was a significant difference in mean energy intake among 4 groups (Annova, $p=0.002$) which increased gradually from adolescence to lactation. However, there was no significant difference in the mean intake of proteins, iron and calcium ($p>0.05$). The recommended intake (RDA) of calories was <50 percent among 20-30 percent of the participants. A large number of PW (83%) were consuming <50 percent RDA of iron compared to 40-60 percent among rest of the groups. The prevalence of protein deficits (<50 % RDA) was highest (48 %) among pregnant women compared to 20-30 percent in rest of the groups.

There has not been significant change in the intake of proteins, iron and calcium from adolescence to lactation despite increased requirements. Pregnant women are at greater nutrition deficits compared to other women, which might result in poor fetal outcomes. WRA are exposed to grossly poor consumption of iron in the diet. The poor socio-demographic and household factors such as unhealthy cooking practices, lack of sanitation are additive to maternal malnutrition in LMIC. We should develop more holistic and nutrition focused health implementation projects targeting women across different phases of life cycle. Multifactorial aetiology of maternal malnutrition calls for

a comprehensive intervention plan encompassing socio-ecological model of care. Adolescence and preconception phase are two windows of opportunities for delivering proven cost effective health promotion interventions before in seeding of next generation. Given the limited coverage and longer periodicity of national nutrition surveillance in the country, ad-hoc surveys offer a swift dietary evaluation of targeted populations. This will help us monitoring the implementations effectiveness of intervention actions.

Nutritional stat • Recommended diet • pregnancy

ORAL | Thursday 8th 09:40-10:40 hrs.

E60099
Epidemiology
Maternal and fetal health

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Tobacco Exposure, Leukocyte Telomere Length and mitochondrial DNA content in Children from Six European Countries.

Background. Telomere length and mitochondrial DNA content are considered biomarkers of cellular aging, oxidative stress, and inflammation, but there is almost no information on their association with tobacco smoke exposure in fetal and early life.

Methods. As part of a multi-centre European birth cohort study HELIX (Human Early-Life Exposome) (n=1396) we assessed maternal smoking status during pregnancy through questionnaires, and through urinary cotinine levels that were then used to classify women as not exposed to smoking (<18.5 Ãƒâ€šÃ‚µg/L), second- hand smoke (SHS) exposure (18.5-50 Ãƒâ€šÃ‚µg/L) and active smokers (>50 Ãƒâ€šÃ‚µg/L). When the children were around 8 years of age (range: 5.4-12.0), leukocyte mtDNA content and LTL were measured employing real-time polymerase chain reaction (qPCR). Results. Maternal cotinine levels indicative of SHS exposure during pregnancy were associated with a decrease of 3.8% in LTL in children (95% CI: -7.07, -0.39) and active smoking measured by maternal cotinine levels was non-statistically significantly associated with a decrease of 2.8% (95%CI: -5.70, 0.30), compared to non-smoking. LTL also decreased in children with one smoking parent compared to children with no smoking parents (2.3% reduction; 95% CI: -4.79, 0.01,), although it did not reach statistical significance. Other smoking variables were not clearly associated with LTL. MtDNA content was

Conclusions. Our findings suggest that prenatal tobacco smoke exposure during pregnancy, even at SHS levels, may accelerate telomere shortening in children and thus induce biological aging from an early age.

passive smoking • telomere length •pregnancy

POSTER | Friday 9th 11:10-12:10 hrs.

E60099

E60137
Epidemiology
Maternal and fetal health

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Fatty acid profile and body composition in newborns from docosahexaenoic acid (DHA) supplemented women with pregestational obesity

Maternal pregestational obesity has been associated with higher body weight and higher body fat in the offspring at birth and higher obesity risk in their postnatal life. Studies in animal models show that DHA supplementation in mothers decrease fat mass in offspring. It is possible that DHA in early life could be a valuable nutritional intervention decreasing obesity risk in subjects from early life. This study compared the body composition and fatty acids (FA) profile (arachidonic acid 20:4n6 AA, eicosapentaenoic acid 20:5n3 EPA, docosahexaenoic acid 22:6n3 DHA, n6 long chain polyunsatured fatty acids (LCPUFAs), n3 LCPUFAs and the n6/n3 LCPUFA ratio) in umbilical cord-derived red blood cells (RBC) of newborns from pregestational obese mothers (POM) supplemented with DHA during gestation.

This is a cross-sectional analysis of a subsample of 44 newborn from Epifat cohort. Newborns from POM supplemented with DHA (200 or 800 mg per day) from 14th gestation week until to delivery (MIGHT, NTC02574767) were recruited in the maternity ward previous signature of an informed consent. At delivery, a cord blood simple was obtained, RBC separated and FA profile determined by chromatography. Newborns were separated in two groups by DHA median split (31,1 ug per mL) (low or high DHA). An anthropometric evaluation was realized between 24 and 72 hours of life. Subscapular-triceps and trunk- total skinfolds ratios describe the peripheral or central fat and estimate body fat percentage. There were no differences between groups in mother or newborn obstetric variables. The newborns with high DHA showed a trend to lower body fat and lower central fat (p less than 0.10) while having a significantly higher n3 LCPUFAs and a lower n6-n3 LCPUFA ratio than the group with low DHA (p less than 0.05). Whole group of newborns from POM had 1.2 times higher DHA, 2.3 times higher EPA and 3.7 times higher n6-n3 LCPUFA ratio (p less than 0.05) than newborns from non-supplemented mothers (c

The DHA supplementation in women with pregestacional obesity increased the DHA concentration, EPA concentration and decreased the n6-n3 LCPUFA ratio in their newborns. A higher DHA

concentration in umbilical cord red blood cells could be associated with lower body central and total fat at birth and later in life, and therefore a protective factor for later adiposity.

Maternal obesity • DHA • newborn body fat

POSTER | Thursday 8th 10:40-11:40 hrs.

E60228
Epidemiology
Maternal and fetal health

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Project SAELCI- Guanajuato. Periconceptional alcohol exposure and newborn health

Alcohol is a teratogen, whose exposure during pregnancy has effects on the morphological, biochemical and functional levels with outcomes of prematurity, low birthweight and Fetal Alcohol Syndrome (FAS).The aim of the study was to identify the periconceptional consumption of alcohol in the parents and its relationship with the state of health of the newborn.

We conducted a cross-sectional study, in pregnant women aged 15 to 45 years, attended at the Hospital Materno Infantil Irapuato, in Guanajuato, Mexico.The data for Alcohol consumption was obtained through the “Green Leaf of Reproductive Environmental Health”.Two hundred and ten pregnant women were studied, the average age was 22.5 years (95% CI, 21-24). In the preconception period, 26.7% of pregnant women consumed alcohol, with an average of 2.6 grams of alcohol / day (95% CI 1.4 - 3.9). During pregnancy, 6.2% continued consuming alcohol, with an average intake of 1.7 grams of alcohol / day (95% CI 0.8 - 4.6). There was no association between preconceptional alcohol consumption and the frequency of prematurity, 3.6% vs 3.9% (X2 = 0.12 p = 0.91), nor was there an association between low birth weight and preconceptional alcohol consumption 3.2% vs 3.6% (X2 = 0.13 p = 0.90). No cases of fetal alcholic syndrome were detected.

One in four pregnant women did not plan to suspend their alcohol use as a preventative for the possibility of pregnancy. In the knowledge of pregnancy, they do not eliminate the consumption; they simply decreased it. In our series, there wasnâ€™t any association observed between the consumption of alcohol during gestation and the frequency of prematurity or low birthweight.

Pregnant • alcohol • newborn

POSTER | Thursday 8th 10:40-11:40 hrs.

E60228

E60287
Epidemiology
Maternal and fetal health

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Testing causal pathways between domestic violence in pregnancy and offspring outcomes

Violence against women is highly prevalent. It has been associated with offspring outcomes. The mechanisms through this association occurs are not clear. One hypothesis is that it is through mother health conditions. Violence in pregnancy is associated with more hospitalization and infection. Low self-esteem, depression, anxious disorders are found more frequently these women, and those affected by mental health problems have worse self-care. Some risk behaviors are more frequent as well: smoking; use of alcohol and psychoactive substances; inadequate nutrition; inadequate prenatal care. Violence exacerbates chronic health problems, such as hypertension, Finally, pregnancy in a violent relationship is often unplanned.

A population-based birth cohort of 894 pregnant women, recruited in Primary Health facilities, was followed up from the beginning of the 3rd gestational trimester gestation till the age of 6 months of the infant. Information regarding violence perpetuated by intimate partner during gestation was collected, together with other covariates and possible mediator variables. After birth, neonate and infant variables were collected. Multivariate regression models tested the associations. Mediation analysis was through counterfactual models. The prevalence of violence was 24%. After adjustments for confounders violence increased the risk of being born small for gestational age, RR= 2.26 (1.06-3.65); of severe intrauterine growth restriction, RR=1.96 (IC95% 1.04-3.70); of low weight gain in the first semester of life, RR=1.98 (IC95% 1.06-3.68); hospitalization in the same period, RR=1.98 (IC95% 1.06-3.68); and cognitive impairment RR=3.88 (1.60-9.43). Exposed mothers had more depression and anxiety during gestation and postpartum. They used more tobacco, alcohol and had more infectious disease. No mediator alone was causal pathway between violence and offspring's outco

Violence perpetuated by intimate partner is highly prevalent, with great consequences on mother and offspring. Behavior and morbidity pathways were not enough to explain the association. The hypothesis we made is that phenotype changes occur as predictive adaptive responses programmed during evolution to enhance the evolutionary fitness of the species in front of stressful environments.

violence • infant outcomes • causal pathway

POSTER | Wednesday 7th 17:40-18:40 hrs.

E60287

E60336
Epidemiology
Maternal and fetal health

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Comparison of two pregnancy nutritional evaluation standards using national data from Uruguay

The USA Institute of Medicine (IOM) and the Rosso-Mardones (RM)maternal weight gain guidelines are widely used in Latin America. We compared those two maternal nutritional assessment proposals in their diagnostic ability of some indicators of fetal growth.

23,832 women and newborns were studied using national information from Uruguay. The nutritional status at the beginning of pregnancy was classified by means of specific body mass index (BMI) cut-offs according to both proposals. Fetal growth was classified as inadequate in certain categories of birth weight and birth length. Sensitivity, specificity and predictive values of the fetal growth indicators were calculated for each maternal nutritional assessment proposal. Proportions of BL < 50 cm and both BW < 3000 g and > 4000 g were similar at each nutritional category of both charts; absolute figures for at risk newborns were much higher in the RM underweight and obese women. The RM chart showed higher sensitivity values than the IOM. Predictive values of the two charts were similar.

It is suggested to evaluate the nutritional status at the beginning of pregnancy with the RM curve in Uruguay.

Pregnant woman • body mass index • fetal growth

POSTER | Friday 9th 11:10-12:10 hrs.

E60336

E60438
Epidemiology
Maternal and fetal health

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Prenatal exposure to endocrine disruptors chemicals and metabolic risk in Mexican preschoolers.

The hypothesis of environmental obesogens suggests that prenatal exposure to endocrine disruptors chemicals (EDCs) such as phthalates and bisphenol A (BPA) may promote weight gain and increase the risk of metabolic disease on future due to possible alterations in fetal programming. Human exposure to these compounds may come from many sources: plastic bottles, food containers, medical products, cosmetics and so on. Adults metabolize and eliminate these compounds rapidly from the body. However, fetuses and young children are more susceptible to its effects due to immaturity of their detoxifying enzymes. We investigated the association between prenatal urinary phthalates and BPA concentrations and the presence of metabolic risk markers in preschool children from Morelos, Mexico.

Methods.This study included 204 mother-child binomials. Maternal urine samples were collected in the third pregnancy trimester and analyses were conducted for BPA levels and nine phthalate metabolites: MCPP, MEP, MECPP, MEHHP, MBP, MiBP, MEOHP, MBzP and MEHP. Children´s weight, height, waist circumference (WC) and blood pressure at 4 years were measured by standardized procedures. Glucose, insulin and lipid profile were quantified in serum obtained from nonfasting blood samples. Results. At 4 years old, the prevalence of overweight was 12.7%. and almost 12% of the children had WC greater than 85th percentile. The prevalence of normal high systolic and diastolic blood pressure was 8.5% and 5.5%, respectively. For MCPP, MEHHP and MEOHP, we observed a consistently high levels of total, Non-HDL and LDL cholesterol in tertile 2 compared with tertile 1. In WC models, there was evidence of possible effect modification by sex between prenatal exposure to phthalates and BPA with a positive association observed in girls and negative in boys, except for MCPP.

The results of the present study strengthen the evidence that prenatal exposure to EDCs are associated with the presence of early metabolic markers in preschool age, a situation that may mediate/modify the risk of chronic disease in future.

Prenatal • EDC • Metabolic risk

POSTER | Wednesday 7th 17:40-18:40 hrs.

E60438

E90161
Epidemiology
Epigenetics

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Poverty and gender disparities associated with leptin cord blood DNA methylation in overweight children

Childhood obesity is a global burden representing a challenge for policymakers. Overweight and obese children are more likely to remain obese in adulthood and have more chances of developing non communicable diseases in later life. Overweight is characterized as weight- for-length Z-score more than 2 SD above WHO Child Growth Standards median. Intra uterus exposures such as pre-pregnancy BMI and diet have been associated with adverse child development Is believed that this is modulated through epigenetic pathways. Leptin gene (LEP) is involved in the regulation of energy homeostasis and fat metabolism and may be have an important rolen obesity pathogenesis. In our study, we investigated the association between cord blood DNA methylation of LEP and child overweight at 3 years old.

In a subsample of a Brazilian birth cohort (Coorte RegiÃ£o Oeste - ROC), we explored the DNA methylation of LEP in the cord blood of 31 females and 29 males, born at term and with appropriate weight at birth, and analyzed its relation to overweight at age 3. Bisulphite converted DNA was hybridized to Illumina HumanMethylation450 BeadChips. During the hospital stay after delivery, mothers were interviewed to gather information about environmental factors (gestational exposure) that could interfere with the methylation profiles of the newborns. At 3 years old 8.3% of children were overweight, girls being more affected than boys, 9.7% and 6.9% respectively. After adjustment for confounders and sex, DNA methylation was positively associated in girls with overweight at 3 years (Î²=0.01, 95%CI 0.00, 0.02, p=0.05) and negatively associated with cephalic perimeter at birth (Î²=-0.01, 95%CI 0.02, -0.00, p=0.03) we didnâ€™t find a significant association in boys. Lowest income was also associated with LEP methylation (Î²=-0.06, 95%CI -0.11, 0.00, p=0.05) in both genders. No other anthropometrical or socioeconomic indicators were significantly associated with cord blood DNA me

Our findings indicate a small association between leptin methylation in cord blood, lower income and overweight at 3 years old girls. These results suggest that girls are more likely to become overweight when early exposed to poverty and other social determinants of health than boys. The association between maternal low income as a proxy for low socioeconomic status and a higher methylation of LEP deserves further investigations to better understand the mechanism involved in poverty and obesity.

DNA methylation • Child obesity • Leptin

ORAL | Friday 9th 10:10-11:10 hrs.

E90161

B40159
Basic Science
Life style and perinatal nutrition

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Postnatal early overnutrition and high-salt intake during puberty induces cardiometabolic diseases in adult rats

Postnatal early overfeeding, by small litter (SL), is a risk factor for metabolic disorders. SL rats develop overweight, hyperphagia and hypertension when adults. Besides, high-salt diets are associated with obesity, oxidative stress and cardiac diseases. We aimed to investigate the effects of postnatal early overnutrition and high-salt intake during puberty on cardiometabolic parameters in adult rats.

Methods: At delivery, Wistar rats were divided in two groups: normal litter (NL, 9 pups) and small litter (SL, 3 pups) throughout lactation period. At 30-day-old, the pups were subdivided in two more groups: normal litter + high-salt intake (NL+HS) and small litter + high-salt intake (SL+HS). High-salt intake was from 30 until 60-days-old. Body weight and food intake were monitored to 30 a 120-days-old. Plethysmography was performed at 60, 90 and 120-days-old. At 120-day-old, glucose and insulin tolerance tests was performed, as well as the cannulation of the femoral artery, allowing the recording of cardiovascular parameters in conscious rats. Later, the offspring were euthanized for sample collection.Results: SL and SL+HS offspring developing obese phenotype, showing insulin resistance and glucose intolerance during insulin and glucose tolerance tests in relation to NL and NL+HS offspring ($p<0.05$). In addition, SL and SL+HS offspring showed hypertension during the plethysmography ($p<0.05$). The groups SL, NL+HS, SL+HS presented cardiovascular changes recorded in cannulation.

Postnatal early overfeeding causes obesity, hypertension and impairments in glucose homeostasis. Moreover, high-salt intake during the puberty can nchange cardiometabolic parameters such as systolic blood pressure, diastolic blood pressure and mean arterial pressure.

Small litter • Obesity • High-salt intake

CARTEL | Friday 9th 11:10-12:10 hrs.

B40159

E110080
Epidemiology

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Preventing postpartum weight retention: Lifestyle interventions in pregnancy, postpartum or both. A systematic review of the literature.

Obesity is a global epidemic, with 40% of adults categorised as overweight (OW) or obese (OB). The development of obesity is multifactorial, with energy intake and physical activity as two of the contributing factors. Pregnancy could also play a role, as excessive gestational weight gain (GWG) & postpartum weight retention (PPWR) may trigger development of obesity. Observational data suggests that OW/OB pregnancy women are at greater risk of excessive GWG and are less likely to return to their pre-pregnancy weight compared to normal weight women. At present, there is a lack of data to support an approach to prevent pregnancy associated obesity. The aim of this research was to evaluate the effectiveness of lifestyle interventions in OW/OB pregnant and/or postpartum women at managing PPWR.

A systematic review of the literature was completed Jan 2000-Jan 2018 in MEDLINE, Embase and CENTRAL for randomised controlled trials within the antenatal and/or postnatal period reporting the effect of lifestyle interventions on PPWR up to 2 years after delivery. Searches identified 2753 titles; 14 studies(n=2252) were included and divided into three categories, pregnancy only(n=2), postpartum only(n=9), and pregnancy and postpartum(n=3). Recruitment ranged from first trimester to 18 months postpartum. Intervention duration varied from 10 weeks to 12 months and included either diet only(n=4) or diet and exercise(n=10). Reported weight outcomes included percentage of women below pre-pregnancy weight, change in weight from baseline and PPWR. Of the 14 trials, six (postpartum only, n=363) based on short, intensive intervention designs of 10-12 weeks reported significant improvements in PPWR at the end of the interventions and subsequent follow-up(4?24 months postpartum). The remaining eight trials did not show an effect on PPWR. However, four trials (pregnancy only n=2; pregnancy and postpartum n=2) reported significant associations between appropriate GWG and reduced PPW

The antenatal and postnatal periods are a window of opportunity to prevent obesity in women due to increased contact with healthcare professionals. Previously, there is nadequate data to support the implementation of a specific approach to prevent excessive GWG and to reduce PPWR. Evidence from this review suggests that to reduce PPWR intensive interventions including diet or diet and exercise, commencing in the postpartum period, are effective. However, due to the heterogeneity of study design, recruitment strategies and small sample sizes, larger trials with similar methodology are required to provide a clear conclusion informing the development of targeted strategies to prevent PPWR.

maternal obesity • postpartum • intervention

CARTEL | Friday 9th 11:10-12:10 hrs.

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