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EDITORIAL

# Cardiometabolic Diseases Global Pandemic: Developmental Origin of Health and Disease Concept Helps

Diabetes, obesity and hypertension form a disease triad that represents most of the cardiometabolic syndrome (CMS), occupying a central health concern worldwide. Numbers of this pandemic scare governments, health professionals and communities. The Diabetes International Federation recently released an estimation that 20-25% of the entire adult world population suffers of CMS. Brazil has an increasing CMS prevalence. Despite the efforts to combat high fat caloric intake and physical inactivity, CMS numbers do not halt its growth. To treat and prevent CMS costs lots of money, severely compromising nations' budgets, tremendously impacting developing countries like Brazil.

A new horizon to better understand CMS was opened in the 1990's, when the Developmental Origin of Health and Disease (DOHaD) concept started to propose new causalities to CMS. The main DOHaD stream suggests that adverse conditions happening during early development induce cardiometabolic dysfunctions later in life. Insults such as nutrient restriction or abundance persistently change neuronal architecture and function, leading to disruptions in the central and peripheral control of cardiometabolic function, which is expressed up to adulthood. Although we emphasize intra-uterine life, lactation and adolescence periods can also be considered as developmental windows to metabolic programming. With respect to epigenetic mechanisms of biological heritage and transgerational transmission, we can extend these windows to even before conception, when health status of a couple might influence health/disease patterns of their offspring. Thus, DOHaD studies can effectively contribute to break the rise of CMS prevalence around the world, including in Brazil. How can we do it? It is a matter that demands a whole community involvement, especially from those responsible for making public health policies.

**Metabolic Programming searching in PubMed**

| Country | Publications | 1st Article | Population |
|---|---|---|---|
| Brazil | 79 | 2003 | 206,000,000 |
| Russia | 9 | 2000 | 143,500,000 |
| India | 32 | 2003 | 1,300,000,000 |
| China | 80 | 2006 | 1,400,000,000 |
| South Africa | 10 | 2000 | 53,000,000 |
| Argentine | 19 | 2006 | 44,000,000 |
| Australia | 100 | 1991 | 23,000,000 |
| Chile | 16 | 2001 | 18,000,000 |
| Colombia | 5 | 2009 | 47,000,000 |
| France | 130 | 1991 | 67,000,000 |
| New Zealand | 38 | 1995 | 4,500,000 |
| Portugal | 10 | 2009 | 11,000,000 |
| Spain | 86 | 1996 | 48,000,000 |
| United Kingdom | 193 | 1996 | 65,000,000 |

The table shows the scientific publications up to date regarding DOHaD studies for some countries. One can notice that Brazil, among other BRICS countries, published more papers in proportion to their populations and economies. When comparing to developed countries, Brazilian numbers are more timid, but still impressive. It must be emphasized that DOHaD concept, as known, was coined from Dr. Barker's articles in the 1990's, albeit his first articles on this theme were published in the 1980's. Striking records, scientific literature in the 1930's already showed expressive articles discussing DOHaD concept before Barker's era. In the 1980's, Brazilian scientists published reasonable number of articles that clearly show metabolic programming matters. Since the beginning of DOHaD International Society meetings, Brazil has increasingly improved its participation. In the last DOHaD meeting in Cape Town, South Africa, Brazilian researchers were responsible for 50 out of 535 presented studies. A data base search for CVs from the National Council for Scientific and Technological Development, CNPq, reveals 281 Brazilian researchers working on experimental, clinical and epidemiology DOHaD areas. These scientists and their groups are from different locations throughout Brazilian territory.

The 1st International Symposium on Metabolic Programming and Stress (ISMPS) reunited 25 Brazilian researchers to discuss the DOHaD concept in Ilha Grande, Rio de Janeiro, in 2011, under financial support of CNPq and State University of Rio de Janeiro (UERJ). The 2nd ISMPS was held in Guaraqueçaba, Paraná, with 75 researchers, supported by Fundação Araucaria, the research funding agency of Paraná State, and Coordination for the Improvement of Higher Education Personnel (CAPES). In 2013, the 3rd ISMPS was held in Morretes, Paraná, and reunited 100 researchers, once again supported by Fundação Araucaria and CAPES. The 4th ISMPS also occurred in Paraná State, receiving 150 Brazilian researchers besides 50 colleagues from Uruguay, Chile, Mexico, Colombia, Venezuela and Argentina. Brazil, for its leadership in this research field along with its important investments in science, attracted these Latin-American researchers, leading the 4th ISMPS Ponta Grossa host the 1st Meeting of the Ibero-American Chapter of the DOHaD International Society (1st I-A DOHaD Chapter Meeting), which was supported by Fundação Araucaria, CAPES, OPAS and DOHaD International Society. These symposia have strengthened DOHaD concept discussion amongst Latin-American countries, besides Portugal and Spain.

During all this time, **Endocrinologia & Diabetes Clínica e Experimental** has been an essential partner and publisher of ISMPSs programs and abstracts.

Thus, on behalf of the Scientific Committee of the 5th ISMPS and 2nd I-A DOHaD Chapter Meeting, we proudly invite **Endocrinologia & Diabetes Clínica e Experimental** readers to attend our next meeting, which is moving to the marvelous city up to northern Brazil, São Luis do Maranhão, from November 2nd to 4th, 2016. Capes, UFMA, DOHaD International Society, OPAS and FAPEMA (Maranhão State Agency) support the meeting. The 5th ISMPS is plenty of discussion of outstanding experimental, clinical and epidemiological studies on DOHaD concept and beyond, which program and abstracts you shall find within this issue. For sure our meeting brings the best and latest discoveries from DOHaD field up to date.

Chairs

**Dr. Antonio Marcus de Andrade Paes**
Federal University of Maranhão

**Dr. Paulo Cezar de Freitas Mathias**
State University of Maringá

**Join us.**

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# 5TH INTERNATIONAL SYMPOSIUM ON METABOLIC PROGRAMMING AND STRESS AND THE 2ND MEETING OF IBERO-AMERICAN DOHAD CHAPTER

# SHORT PRESENTATIONS

## SC01 - Gestational protein restriction is related to differential modulation of key developmental regulators in the CA1, CA3 and dentate gyrus of the dorsal hippocampus.

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***Background:*** Studies have demonstrated that pregnancy undernutrition results in structural hippocampus abnormalities and cognitive impairment in the offspring. We demonstrate that gestational protein restriction leads to a decreased in dendritic length in the CA3 pyramidal neurons of adult male rats. **Aims:** Evaluate the effects of gestational protein restriction on hippocampal key proteins expression in 14 day old male rats. ***Methods:*** Pregnant rats received normal (NP) or low protein (LP) diet during pregnancy. CA1, CA3 and dentate gyrus (DG) regions of the dorsal hippocampus were microdissected and genic expression of brain-derived neurotrophic factor (BDNF), doublecortin (DCX), cyclin-dependent kinase inhibitor 1C (CDKN1C), transcription factor sox2 (SRY-Box 2), early growth response protein 1 (EGR1) and of receptors for glucocorticoid (GR), mineralocorticoids (MR), 5-hydroxytryptamine type 1A (5HT1A) and 2A (5HT1A), angiotensin II type 1(AT1) and type IV (AT4) were evaluated by RT-qPCR.Results: Offspring from LP group presented enhanced expression of GR (138%), CDKN1C (158%) and AT4 (136%) associated with reduced 5HT1A (70%) expression in CA1 hippocampus region, comparatively to NP rats. In CA3 hippocampal region, LP offspring present reduced expression of DCX (70%) and MR (150%) and enhanced AT1 receptor (209%) expression. In LP group, the DCX (50%), MR (12%) and 5HT1A (42%) DG expression was reduced when compared to NP age-matched offspring. ***Conclusions:*** Gestational protein restriction promoted changes in several hippocampal receptors and protein expression that are associated with structural damage and impairment on neurotransmitter systems. These changes were not symmetric in whole hippocampal regions suggesting asymmetric neurogenesis and neurons differentiation in this neural structure.

**Keywords:**Fetal Programming, hippocampus, neurogenesis.
**Financial Support:** Fapesp: 2013/20539-1 and 2013/12486-5.

## SC02 - Early and sustained exposure to high-sucrose diet triggers hippocampal impairments related to oxidative and endoplasmic reticulum stresses in adult rats.

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**Background:** The DOHaD concept describes how exposure to environmental factors during the initial phases of growing can program the long-term development of chronic diseases, such as metabolic syndrome and neurological disorders. **Aims:** We sought investigate whether early and sustained exposure to high-sucrose diet (HSD) is capable to promote metabolic disturbances and to anticipate neurological impairments and senescence. **Methods:** Weaned Wistar rats (21 days age) started to be fed a standard chow (CTR) or HSD (25 % sucrose) for 6 months. At 5th month an old animals group (20 months of life, OLD) fed with standard chow were added on experiment, to serve as age control. **Results:** HSD was capable to increase weight gain and lee index even with decrease of feed consumption. The HSD showed weight increase of liver, visceral, non-visceral and brown adipose tissue and skeletal muscle loss. The liver showed higher deposit of fat, especially, triglycerides. The levels of fasting and fed glucose and serum triglycerides and free fatty acids were elevated too. Insulin resistance was inferred from glucose tolerance, hyperinsulinemia and increase of HOMA and TyG indexes. Malondialdehyde levels and SOD activity were higher, showing an oxidative stress condition. Assessment of hippocampal gene and protein expression showed decrease of endoplasmic reticulum stress pathways (IRE1α, ATF6 and PERK), chaperones (GRP94, GRP78, PDIA2, calnexin and calreticulin), neuroplasticity factor (BDNF) and anti-apoptotic marker (BCL2). The CHOP and PARP-1 (apoptotic markers) and P21 (senescence gene) expression were increase in HSD. The HSD results were very similar to those found in OLD group (except for CHOP and PARP-1 that would not rise). Finally, HSD rats demonstrated impaired motor and cognitive functions (learning and memory), similarly of OLD group. **Conclusions:** Our data indicate that early and sustained exposure to HSD promote metabolic disturbances, which disrupt hippocampus homeostasis and affect its neurological functions.

**Keywords:** High-sucrose diet, metabolic syndrome, neurological impairment, developmental origins of health and disease (DOHaD).
**Financial Support:** Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão – FAPEMA and Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq.

## SC03 - High-Fat Diet modulates the Expression of HIF-1 in Hypothalamus: Impact on POMC Expression.

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Hypothalamic neurons play key role in the regulation of caloric intake and energy expenditure. Hypoxia- inducible factor-1 (HIF-1) is a transcription factor that activates several genes in response to hypoxia or other potentially harmful conditions. HIF regulates the expression of POMC, regulating food intake and energy metabolism. HIF-KO animals have increased food intake and energy expenditure suggesting its role in energy metabolism. Our hypothesis is that the expression of HIF-1 in the hypothalamus is modulated by high-fat diet leading to changes in the expression of pomc and, consequently, to alterations in neuronal pathways that control food intake. The main purpose of this study was to analyze the expression of HIF-1 in hypothalamus and evaluate the mechanisms involved in the regulation of its expression by dietary fats. Eight-week, male C57Bl6 mice were fed either chow or a high-fat diet for 1, 3, 7, 14 or 28 days. Expression of HIF-15 and HIF1F was determined by PCR and its hypothalamic distribution was evaluated by fluorescence immunohistochemistry. Most HIF1-5 and HIF1- F were detected in the arcuate nucleus of hypothalamus. Both proteins were colocalized with POMC and with ACTH but not with AgRP, suggesting that HIF-15 and HIF-1F are present in POMC neurons, only. As expected, HIF-15 and HIF-1F were colocalized with microglia and glial cell markers. The expression of mRNA of HIF-15 and HIF-1F was significantly decreased after 3 and 7 days of high-fat feeding, and after 14 and 28 days of high fat diet no changes were observed. In conclusion, HIF-1 is predominantly expressed in POMC neurons in the arcuate nucleus of hypothalamus. The decrease in the expression of HIF-1 induced by high-fat feeding may contribute to the anomalous control of caloric intake in obesity.

**Keywords:** HIF-15α, hypothalamus, food intake, POMC neurons, obesity.
**Financial Support:** FAPESP (2015/10078-2).

## SC04 - Early Fecal Microbiota Transplantation: Programming of Pancreatic Islet Function.

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**Background/Aims:** Changes in the intestinal microbiota composition are related with obesity onset. One of the targets of metabolic programming is the pancreatic beta-cell. The aim of this work was to access whether fecal microbiota transplantation at an early age in obese and lean animals can program impairment or protection of pancreatic beta-cell function. **Methods:** Normal Litter rats were mated and the offspring was divided in two groups, Normal litter (NL) and small litter (SL). Offspring were also mated at 90 Days Old (NL vs NL; SL vs SL; different parents and litters). Offspring of NL had their litter size adjusted to 9 pups per dam, and offspring of SL parents had their liter size adjusted to 3 pups per dam. From the 10th until the 25th day of life all animals received saline 0,9% or a solution of maternal fecal microbiota in a dose of 1g/kg/bw. Four experimental groups, NLS (normal litter saline), NLM (Normal Litter microbiota, received fecal microbiota transplantation from SL mothers), SLS (Small litter saline), SLM (Small litter microbiota, received fecal microbiota transplantation from NL mothers) were studied. At 90 days old, the animals were euthanized. Pancreatic islets were isolated and exposed to different glucose concentration to observe insulin secretion. Islets were also stimulated by muscarinic and adrenergic receptor agonists and antagonists. **Results:** All groups had an increased insulin secretion stimulated by 5.6 and 8.3 mmol/l of glucose compared with NLS. Fecal microbiota transplantation in the NLM group lead to reduced cholinergic and adrenergic response. By the other hand, the SLM group showed increased response to a muscarinic antagonist and an ameliorated adrenergic response. **Conclusion:** Fecal microbiota transplantation from obese to lean rat pups lead to pancreatic islet dysfunction and improved islet dysfunction when fecal material from lean rats where transplanted in obese pups.

**Keywords:** Fecal microbiota transplantation, obesity, metabolic programming, insulin secretion.
**Financial Support:** CNPq, CAPES.

## SC05 - Roux-en-Y Gastric Bypass improves glucose tolerance on male rats fed a cafeteria diet and their offspring.

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**Background/Aims:** Bariatric surgery improves glucose homeostasis and reduces the augmented insulin secretion in obese subjects.Here, we investigated the effects of Roux-en-Y Gastric Bypass (RYGB) on glucose homeostasis of male rats fed a Cafeteria diet and their male offspring. **Methods:** Male Wistar rats, aged 60 days, received chow-rodent (CON) or cafeteria diet (CAF) for 10 weeks Rats from CAF group were subjected to RYGB surgery (CAF-RYGB) or sham operation ( CAF-SHAM ). The ipGTT was performed 30 and 60 days of postoperative. After 10 weeks of surgery, males were mated with control females. The male offspring was fed a control diet and subjected to an ipGTT, at 30 days old. Two weeks later, we evaluated blood glucose, plasma insulin, and insulin secretion in islets isolated from the fathers at increasing glucose

concentrations. **Results:** At 30 and 60 days of postoperative, CAF-SHAM group showed glucose intolerance and increased insulinemia during the test, compared to CON group. The RYGB normalized these parameters. As expected, cafeteria diet increased body weight, glycemia, and retroperitoneal and perigonadal fat pad accumulation (1,2; 1,2; 2,2 and 2,0, respectively) compared to CON. RYGB normalized body and fat pad weights, but did not alter the glycemia. Insulin secretion stimulated with 5.6 and 22.2 mM glucose was similar between groups. However, at11.1 mM glucose, RYGB rats showed a 46% decrease in insulin secretion, compared to CAF-SHAM group. CAF-SHAM male offspring presented glucose intolerance, and the RYGB, performed on fathers, seems to have a protective effect on male offspring glucose tolerance, at 30 days of life. **Conclusions:** The RYGB reduced the adiposity of obese fathers, decreased insulin secretion, stimulated by 11.1 mM glucose, and improved the glucose tolerance at 30 and 60 days of postoperative. Additionally, father's RYGB improved glucose tolerance in male offsprings.
**Keywords:** Obesity, insulin secretion,bariatric surgery, epigenetic.
**Financial Support:** FAPESP and CAPES.

## SC06 - Maternal Obesity Leads to Negative Outcomes on Male Offspring Metabolism: Effects of Maternal Metformin Intervention.

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**Background:** Maternal metabolic disturbances associated to obesity, such as impaired glucose metabolism play an important role in offspring developmental programming. Maternal interventions may contribute to prevent the adverse metabolic programming in the offspring. Metformin treatment improves glycemic control by increasing insulin sensitivity. We hypothesized that maternal metformin intervention prevents the negative metabolic outcomes in offspring from obese mothers. **Aim:** To evaluate the effects of metformin intervention in obese mothers prior to and throughout pregnancy on male offspring metabolism. Methods: Female wistar (F0) rats were weaned whether on a control diet (C= 4 kcal/g) or a high energy obesogenic diet (MO= 5 kcal/g) (C and MO groups). At PND 120, F0 rats were mated. Previously, half of each group received metformin orally, 300 mg/kg/day, from PND 90 until the end of pregnancy (CMet and MOMet groups). All male offspring (F1) were weaned on C diet and named according to their maternal group (n=8/group). At PND 110, F1 body weight (BW), Adiposity Index (AI= Total visceral fat weight **X** 100/ body weight), serum leptin and triglycerides as well as Insulin Resistance Index (IRI) were determined. Fat cell size (FCS) was measured as cross sectional area in histological slides (H&E staining). Data were analyzed by 1-Way ANOVA ($p<0.05$, Mean±SEM). Results: In F1 at PND 110, despite of there were no differences in BW among groups, MO lead to increased AI (C=2.7±0.2a, CMet=3.1±0.3a, MO=3.6±0.3b, MOMet=3.4±0.1ab), FCS, serum leptin and triglycerides, as well as IRI (C=3.6±0.5a, CMet=3.6±0.6a, MO=6.1±0.8b, MOMet=4.2±1ab); however, maternal metformin intervention partially reduced all these variables, without any improvement in FCS.**Conclusion:** Metformin intervention in obese mothers before and during pregnancy, partially prevents male offspring negative metabolic outcomes by improving lipid and glucose metabolism.
**Key words:** Maternal obesity, metformin, adiposity, insulin, leptin.
**Financial Support:** G. Lira León received a scholarship as a Research Assistant from CONACyT, Mexico.

## SC07 - Intrauterine growth restriction persistently changes the degree of reward to the sweet food - study of dopaminergic pathway.

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**Background/Aims:** Intrauterine growth restriction (IUGR) is related to increased preference for palatable foods and enhanced adiposity. Central dopamine modulation by insulin can lead to changes in response to reward. We aimed at evaluating the release of dopamine during palatable food intake in animals submitted to an IUGR protocol. **Methods:** At gestation day 10, Sprague-Dawley dams started to receive ad *libitum* diet or 50% restricted diet (FR). At birth, pups were cross-fostered generating two groups (pregnancy/lactation): AdLib/AdLib (Controls) and FR/Adlib (IUGR). In adulthood, the dopamine release facing standard chow and palatable food was measured by chronoamperometry (a measurement in real time) recordings in NAcc, with or without previous systemic insulin treatment (5UI/kg). **Results:** There was a delayed dopamine release in the IUGR group in response to Froot Loops® (time to reach the peak DA release (Control:599.8+188; IUGR:1258+194 sec, p=0.047), but not in response to standard chow (Control:668+317; IUGR:775+246 sec, p=0.806). Insulin treatment reverted the difference observed when Froot Loops® were available (Control:1093+320; IUGR: 254+127 sec, p=0.05). Western blot analysis showed that SOCS3 was increased in the hypothalamus (OR_%controls, Control:100.0+39.68; IUGR:347.3+82.72 p=0.0168) and decreased in the VTA of IUGR (OR_%controls, Control:100+7.41; IUGR:46.72+11.78 p=0.009); pTH/TH was increased in the NAcc of IUGR as we have previously shown (ratio pTH/TH, Control:1.10+0.10; IUGR:1.40+0.06 p=0.027), but similarly to the chronoamperometry findings, this was reverted by insulin (ratio pTH/TH, Control: 1.07+0.10; IUGR:0.95+0.062 p=0.338).**Conclusion:** It was observed a delay in the dopamine release and metabolic alterations in response to palatable foods in the IUGR group when compared to the Control group. IUGR individuals might need to eat more sweet food to get the same level of pleasure, probably due to a delay in the dopamine release. These chan-

ges in the dopaminergic response to sweet food may lead to binge eating and obesity in IUGR individuals.

**Keywords:** Dopamine, reward, insulin.
**Financial Support:** FIPE-HCPA.

## SC08 - Maternal overnutrition induces sex-dependent endocannabinoid system dysfunction and oxidative stress in rat offspring liver at adulthood.

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**Background/Aims:** Maternal overnutrition programs offspring to obesity and metabolic dysfunctions in early and later life. Obesity is associated with changes in endocannabinoid system (ECS) in both humans and experimental models. Although the ECS has been studied for understanding the pathophysiology of obesity, the relationship between this system and metabolic programming is unknown. The goal of this study was to investigate the association of the ECS with liver disease in offspring from obese mothers. **Methods:** Female Wistar rats received control or high-fat diet (HFD) for 8 weeks before mating and during pregnancy and lactation. We evaluated the male and female offspring from HFD mothers at 180-day-old. **Results:** Male and female offspring had increased food intake, body weight and subcutaneous adipose tissue. In the liver from male offspring we found higher protein expression of cannabinoid receptors type 1 and 2 (+68%, p<0.05; +60%, p<0.001), enzyme fatty acid amide hydrolase (+65%, p<0.01) and enzyme monoglyceride lipase (2 fold, p<0.001). We also found decreased in Thiol content (-31%, p<0.001) and increased protein carbonyl groups (+30%, p<0.01). However, female offspring did not present these alterations. **Conclusions:** Maternal overnutrition alters the ECS and biomarkers of oxidative stress in the liver of male rats offspring only, demonstrating a different mechanism depending on sexual dimorphism.

**Keywords:** Maternal obesity, metabolic programming, endocannabinoid system, oxidative stress.
**Financial Support:** Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro- FAPERJ.

## SC09 - Soy isoflavone treatment in early postnatally overfed rats affect metabolism and autonomic nervous system.

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**Purpose.** Soy isoflavones have been identified as an important dietary factor for preventing and treating metabolic dysfunction. This study examined the effects of high doses of isoflavone on glucose and fat metabolism in a model of programmed obesity and evaluated its effects on the autonomic nervous system. **Methods:** Litters of Wistar rats were standardized at 9 pups per dam in normal litters (NL) or reduced to 3 pups per dam at the 3rd day of life (P3) in small litters (SL) to induce postnatal overfeeding. Gavage with a soy beanisoflavone mixture (1 g/day) diluted in water was started at P60 and continued for 30 days. The control animals received vehicle gavage. At P90, biometric and metabolic parameters as well as direct autonomic nerve activity were measured. **Results:** Increases in glycaemia and insulinaemia observed in SL rats were reduced by isoflavone treatment, which also caused lower glucose-induced insulin secretion by pancreatic islets. Sympathetic activity in the major splanchnic nerve was increased, while vagus nerve activity was reduced by isoflavone treatment. The dyslipidaemia induced by overfeeding in SL rats was restored by isoflavone treatment. **Conclusion:** The present study shows that treatment with isoflavone reduces adiposity and improves glucose and lipid metabolism. Collectively, these effects may depend on autonomic changes.

**Keywords:** Isoflavone, small litters, glucose metabolism, autonomic nervous system, metabolic dysfunction.
**Financial Support:** This work was supported by the Brazilian Federal Foundation, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), andthe Paraná Science Foundation (Fundação Araucária).

## SC10 - Unbalanced M1 and M2 responses in neonatal monocyte-derived macrophages from women with pre-gestational obesity.

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**Background/aim:** Worldwide prevalence of obesity is increasing affecting ~30% of women in fertile age. Evidence suggests that obese women´s offspring have a higher risk of developing chronic diseases associated with an altered immune function. We aim to determine whether maternal obesity is associated with increased expression of pro-inflammatory as well as decreased anti-inflammatory mediators, along with a higher pro-inflammatory response in neonatal monocyte-derived macrophages. **Methods:** Cord blood samples from 26 newborns of obese (OM) and 25 newborns of lean (control) women were obtained at delivery. Fetal monocytes were isolated by adhesion, cultivated and differentiated into macrophages, in which M1 (LPS 100 ng/ml e IFNγ 20 ng/ml) and M2 (IL-4 20 ng/ml) polarization were assayed. M1 and M2 responses were analyzed in terms of mRNA levels for cytokines TNFα, IL-1β, IL-12A, IL-12B, IL-10 e IL-4R, which were quantified by qPCR. DNA methylation of candidate genes was determined by pyrosequencing.

**Results:** Monocytes from children of OM had decreased levels of mRNA for pro-inflammatory cytokines IL-1β and IL-12B and no significant changes in the other transcripts assayed. OM monocyte-derived macrophages showed increased levels of mRNA for TNFα, IL-4R and IL-10. Response to LPS/IFNγ was comparable between both groups, characterized by an important induction of TNFα and IL-1β. Control macrophages stimulated with IL-4 showed a decreased expression of inflammatory mediators while OM macrophages had an additional suppression of the anti-inflammatory mediator IL-10. Changes in IL-1β (monocytes) and IL-10 (macrophages) in OM were paralleled by changes in their promoter DNA methylation in fetal monocytes. **Conclusion:** These results suggest that monocyte-derived macrophages from OM-newborns show a basal anti-inflammatory phenotype with an unbalanced response to M1 and M2 polarization stimuli. Changes in DNA methylation of key inflammatory genes in neonatal monocytes need a further analysis to determine a potential programming of immune function by maternal obesity.

**Keywords:** Monocyte, macrophage, offspring, maternal obesity, inflammation.

**Financial Support:** Funded by grants nº 1130801 and 1141195 from the National Fund for Scientific and Technological Development (FONDECYT-Chile).

## SC11 - Eating Behavior in Fetal Growth Restricted Adolescents: Programming Goes Beyond Food Preferences. Eating Behavior in Fetal Growth Restricted Adolescents: Programming Goes Beyond Food Preferences.

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**Background/Aims:** Intrauterine growth restriction (IUGR) is associated with altered food preferences (usually increased preference for palatable foods) from the beginning of life to adulthood. This altered behavior can contribute to enhance body fat mass and increase the risk of developin g chronic diseases. The aim was to investigate if IUGR adolescents have an altered eating behavior in a food choice task, as well as verify if they have changes in brain resting state connectivity between the orbitofrontal cortex (OFC) and the dorsolateral prefrontal cortex (DL-P FC), brain regions related to value determination. **Methods:** Seventy-five participants, classified in IUGR or controls according to the b irth weight ratio (IUGR= BWR<0.85), had anthropometric d ata assessed and performed a real food choice task, in which they received a monetary value to purchase a snack. Resting state fMRI was perf ormed, and connectivity between the OFC and DL-PFC was analyzed in 40 subjects. **Results:** There were no differences between IUGR and controls in anthropometric m easurements. However, healthy IUGR adolescents had a different behavior when buying the snack. They spent less money than the control group (SGA: 7.29±0.53, control: 8.54±0.28, p=0.043) for buying the same amount of calories. An interaction between BWR and sex was observed in the resting state connectivity be tween the left OFC and right DL-PFC (B=0.952, p=0.02), showing that the connectivity was positively correla ted to BWR in boys and negatively correlated in girls. **Conclusions:** We confirmed that I UGR adolescents have altered feeding behavior and introduced the idea that IUGR is associated with changes in brain resting state connectivity for a net work of areas related to decision-making, which seems to be sex-specific in adolescence. The absence of anthropometric differences between IUGR and controls suggests that the neurobehavioral changes precede the development of obesity and its metabolic consequences in IUGR individuals.

**Keywords:** Intrauterine growth restriction, feeding behavior, functional connectivity, resting state fMRI.

**Financial Support:** Universal National Counsel of Technological and Scientific Development (CNPq) (Silveira PP, 478820/2010 0); Foundation for the Coordination of Higher Education and Graduate Training (PNPD/CAPES, 3024/2010); Fundo de Incentivo à Pesquisa e Eventos do Hospital de Clínicas de Porto Alegre (FIPE/HCPA).

## SC12 - Birth Weight is Associated with Lean Mass Compartment in Young Healthy Adults from Nutritionists' Health Study.

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**Background:** Studies have been evaluating the role of early life events for body adiposity and chronic diseases in adulthood. However, there is a lack of knowledge about their relevance for the lean mass compartment. The loss of muscle mass and strength (sarcopenia) has been interpreted as a continuous process in the life course, related with morbi-mortality in elderly. **Aims:** To evaluate the association between birth weight and lean mass compartment in young adults from the Nutritionists' Health Study (NutriHS). **Methods:** The NutriHS is a cohort study enrolling undergraduates and graduates from Nutrition courses in São Paulo, Brazil. The current cross-sectional analysis assessed 121 young healthy adults (90%women, 20-40yrs). They were invited to answer online questionnaires about their early life events, and to collect anthropometric measurements, muscle strength (handgrip-Jamar®), muscle performance (chair-stand test)

and lean mass assessment (dual-energy X-ray absorptiometry-DXA-LunarGE®). Appendicular skeletal muscle mass index (ASMI) was calculated. Associations between birth weight quartiles (exposure) and calf circumference, handgrip, chair-stand test and ASMI (outcomes) were tested using multiple linear regression. **Results:** Mean values of age, BMI and birth weight were 24.4±5.2yr, 23.5±4.3kg/m2 and 3227.9±440.0g, respectively; 70% Caucasians. The mean of maternal prepregnancy BMI was 22.1±3.5kg/m2. In linear regression models, after adjustments for confounders direct associations of birth weight quartiles with calf circumference(cm) [β:0.83; 95%CI 0.27-1.40; r2=0.09; p=0.006], handgrip(kg) [β:1.24; 95%CI 0.23-2.26; r2=0.48; p<0.001] and ASMI(kg/m2) [β:0.19; 95%CI: 0.00-0.38; r2=0.35; p<0.001], but not with chair-stand test, were observed. **Conclusions:** The finding of the association of birth weight with muscle mass and strength in young health adults suggest that low birth weight could be deleterious not only to adult body adiposity but also to muscle tissue amount and function and chronic non communicable disease. The NutriHS promising data should contribute to clarify the role of early life events for body composition-related diseases in adulthood.

**Key words:** Birth weight, muscle mass, DXA, body composition.

## SC13 - Birth weight and blood pressure in two cohorts 15 years apart in Valparaiso Region, Chile

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The association between birth (BW) weight and blood pressure has been barely explored in Latin America. We estimated this relationship in two cohorts born and residing in two municipalities of the Valparaiso Region (Chile). **Method:** Two retrospective random samples of men and women born between 1974-1978 (cohort 1) and between 1988-1992 (cohort 2), were respectively assessed in 2000-2002 and 2014-2016, i.e: at 24-28 years. Birth weight was obtained from newborn records while blood pressure and BMI were ascertained concurrently. Statistical analysis used multiple linear regression with sex and BMI as confounders and cohort as an effect modifier through a multiplicative interaction term.The median age at adult measurements was 25 years (IQR 23.9; 26.0). Median systolic blood pressure (SBP) in Cohort 1 was 113.5 mm-Hg (IQR:105.0; 123.0) while cohort 2 reached 119.2 mm of-Hg (109.5; 129.0). Differences between cohorts were negligible for diastolic blood pressure (DBP). Median birth weight was 3,200 g (cohort 1) and 3,350 g (cohort 2) (p <0.05). Adjusting for sex and BMI, for every kilo increase in birth weight 2.2 mmHg decreased SBP was observed (Beta coefficient -2.199 (95% CI -3.281;-1.117; p=0.0001). A significant association was also shown for DBP (Beta coefficient -1.077 95% CI -1.887; -0,268 p=0,009).No interaction cohort effect was detected suggesting that BW effect on BP does not change over time. **Conclusion:** Systolic but not diastolic blood pressure tends to increase in the newer generation. The inverse association between birth weight and both, systolic and diastolic blood pressure was verifiedin both cohorts with a gap of 15 years despite BW increases in the most recent cohort.

**Keywords:** Blood pressure, birth weight, young adults, cohort study.
**Financial Support:** Chilean National Research Fund of Chile (Fondecyt); grants 1140453.

## SC14 - Prepregnancy Nutritional Status, Gestational Weight Gain and Birth Weight in the BRISA Cohort

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**Background/Aims:** An inadequate maternal nutritional status plays a determinant role in the health of the newborn. The objective of the present study was to analyze the effects of prepregnancy nutritional status and gestational weight gain on birth weight. **Methods:** A cross-sectional study conducted on 5,024 mothers and their newborns participating in the BRISA study of São Luís - MA. A theoretical model was proposed to estimate total, direct and indirect effects using structural equation modeling in the analysis, with adjustment for sociodemographic variables, life habits, comorbidities and type of delivery, with birth weight as the outcome. **Results:** An increase in prepregnancy BMI of one standard deviation (4 kg/m2) corresponded to a significant increase in birth weight of 68 grams (p<0.001), while an increase in gestational weight gain of one standard deviation (6 kg) represented a significant increase in newborn weight of 151.2 grams (p<0.001). Socioeconomic situation, maternal age, more stable marital situation, gestational diabetes and cesarean delivery had positive total effects, whereas hypertension and smoking habit had negative effects on the outcome. Alcohol consumption during pregnancy had no total effect. **Conclusions:** Mothers with a higher prepregnancy BMI and with elevated gestational weight gain can give birth to babies of greater weight. Thus, we emphasize the need for greater health care for women of reproductive age and for the maintenance of an adequate weight during pregnancy, which may contribute to the reduction of risks of maternal and newborn intercurrences.

**Key words:** Prepregnancy BMI, pregnancy, gestational weight gain, birth weight, models statistical.
**Financial Support:** The presentinvestigationispartof a studyentitled "Etiologicalfactorsofpretermbirthandconsequencesof perinatal factors for infanthealth: birthcohortsfromtwoBraziliancities", with financial supportfrom Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa do Estado do Maranhão (FAPEMA) and Programa de Apoio aos Núcleos de Excelência (PRONEX).

# 5TH INTERNATIONAL SYMPOSIUM ON METABOLIC PROGRAMMING AND STRESS AND THE 2ND MEETING OF IBERO-AMERICAN DOHAD CHAPTER

# CLINICAL SESSION

## CLI01 - Sex-specific differences in feeding preferences in school-aged children born with low birth weight.

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**Background/Aims:** Recent evidence suggests that individuals with intrauterine growth restriction (IUGR) have altered feeding behavior and food preferences, favoring the intake of foods rich in sugar or fat. Parental food rules may influence in this process. We aimed at verifying if IUGR was associated with increased intake of sugar and/or fat at 6-12 years of age, and if parental food rules were different between IUGR and normal birth weight children at this age. **Methods:** 616 families were recruited from Montreal Metropolitan Area for a 50-minute telephone interview regarding to household demographic information, children's anthropometrics (height and weight) and physical activities. A subsample of 254 families also answered additional questions on a two-hour online follow-up, including family food rules and a complete food frequency questionnaire. Birth weight ratio (BWR) was calculated (observed birth weight/ mean population birth weight, sex and gestational age specific), and considered IUGR those having a BWR lower than 0.85. **Results:** There were 130 boys (25 IUGR) and 124 girls (13 IUGR), and no differences were seen between the groups or sexes regarding age, family income, gestational age or current body mass index Z scores. A generalized linear model regression showed an interaction between sex and continuous BWR on the percent calories derived from fat in the habitual food intake [Wald=4.949; df=1; p=0.026], in which boys showed an increased intake of this macronutrient as BWR decreases [B=-4.988, CI -10.276; 0.299], with no correlation in girls [B=3.695, CI - 2.166; 9.555]. Food control, encouragement and restriction rules were not different between groups. **Conclusion:** IUGR boys have increased preference for high-fat diets and parental food rules do not seem to play a specific role on this behavior. It is likely that biological factors such as fetal programming of homeostatic and/or hedonic pathways functioning are involved.

**Keywords:** Low birth weight, feeding behavior, children.
**Financial Support:** Canadian Institutes of Health Research (CIHR INC-110726).

## CLI02 - Low birth weight is associated with altered food choice and brain activation in adolescents.

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Individuals with intrauterine growth restriction (IUGR) have typical food preferences and it could explain in part their increased risk for developing metabolic disorders during life course. Food memory leads to a greater awareness of the intake, which helps control the next meal consumption. The aim was to investigate if food choice, an indirect aspect of food memory, could be related with their unbalanced feeding behavior. Adolescents who have studied near HCPA could choose foods offered in a snack bar. Before eating it, a photograph of the snack was taken. Months after, 4 photos of snacks and the question: "If you eat now, which of the following snacks would you choose?" were shown to them. They did not know, but one of pictures was of their own snack eaten months before. Feeding behavior was assessed by 24h Dietary Recall, Food Frequency and Dutch Eating Behavior questionnaires. After this, subjects underwent fMRI scans while viewing palatable foods and neutral objects pictures. Fetal growth was based on birth weight ratio (BWR) and those in lower tertile of BWR distribution were considered with IUGR. 69 individuals were evaluated and 24 had IUGR. IUGR individuals chose with less frequency their own snack in comparison to

normal birth weight group. For those who did not choose their own snack, the lower the BWR, the more active is cuneus and the less active are precuneus and inferior and middle frontal gyri when visualize palatable food. For boys who do not choose the snack, the lower BWR, the greater intake induced by external stimuli. IUGR seems to be associated with a change in food memory, which may be leading these individuals to greater external intake. Brain activation changes in regions involved in visuospatial processing, memory, expectation of reward and awareness endorse this evidence.

**Keywords:** External eating, food memory, eating programming, fMRI, fetal restriction.

**Financial Support:** CNPq and FIPE/Hospital de Clínicas de Porto Alegre (HCPA).

## CLI03 - Comparison of Growth Charts in the Diagnosis of Small for Gestational Age Newborns.

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**Introduction:** The birth weight is an important predictor of perinatal morbidity and mortality. The application of a suitable reference chart is important to determine the cutoff point for monitoring of metabolic problems that can affect the quality of life of newborns (NBs). The aim of this study was to compare two growth charts, from Alexander and Fenton, in the diagnosis of small for gestational age (SGA) newborns (NBs). **Methods:** Retrospective study performed with data from 293 unique pregnancies live NBs from March to May 2015 in a public maternity hospital in São Luís (MA). The growth charts from Alexander and Fenton and birthweight below 10th percentile for gestational age were used for diagnosis of SGA NBs. The NBs were divided into gestational age groups: 32-35, 36-37, 38-39 and 40-41 weeks. The Kappa method was applied for the agreement analysis of the growth charts, adopting the significance level of 5% ($p<0.05$). Results: The NBs presented average gestational age, weight and stature of 37,7±6,5 weeks, 3154,5±555g and 48,3±2,6cm. As for gender and delivery type, 56,2% (n= 168) were male and 54% (n=162) were natural delivery. The growth charts showed substantial agreement (k=0,71; $p<0,001$). Alexander growth chart detected a higher number of SGA NBs, 17,9% (n=52) than Fenton growth chart, 13,6% (n= 40). When stratified by gestational age and gender group, Alexander growth chart diagnosed highest percentage of SGA NBs in all surveyed groups and male NBs. **Conclusion:** Fenton growth charts are tools which were developed with the latest data and are specific to the genre. However, Alexander growth chart detected higher prevalence of NBs SGA with gestational age of 32 to 41 weeks and both genders.

**Keywords:** Growth charts, birth weight, infant, small for gestational age.

## CLI04 - Maternal obesity is associated with metabolic and inflammatory profile of the offspring at birth.

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**Background:** The effect of maternal obesity on the metabolic and inflammatory state of their offspring at birth remains to be fully defined. Aim: The aim of this study was to compare offspring cord blood insulin, leptin, adiponectin and cytokines from normal weight and obese mothers, and relate these to maternal and neonatal biological characteristics. Subjects and **methods:** A group of healthy pregnant women, obese (BMI >30 kg/m2) and normal weight (18.5 and 24.9 kg/m2) at <14 wks gestation were recruited at the time of delivery (36 – 31 wks) after signing an informed consent. Cord blood samples were obtained at birth on all healthy neonates with birth weight >2500 g. Umbiliacl cord plasma served to determine concentrations of insulin, leptin, cytokines (Milliplex® Human Cytokine/Chemokine and Human Adipokine, Merck Millipore, Billerica, MA, USA), and adiponectin (ELISA, HMW & Total Adiponectin ELISA. ALPCO, USA). Distribution of variables was assessed with Shapiro Wilk test. The comparison between groups was done using t-test and chi2 tests. Pearson served to assess correlations between variables. Multiple linear regression models were used to examine the association between the neonatal outcomes and maternal BMI. P-value <0.05was considered statiscally significant. Results: Offspring of obese mothers had higher birth weight (3560 g vs. 3426 g) and concentrations (log(pg/mL)) of insulin (10.85 vs. 9.91), leptin (95.01 vs. 77.14), adiponectin (33.68 vs. 28.69), TNFα (4.13 vs. 3.96) and IL12p40 (7.53 vs. 7.09), at birth. Maternal variables were associated with increase cord plasma leptin, adiponectin, TNFα and IL12p40 in the offspring, at birth. **Conclusion:** Maternal obesity in early pregnancy was associated with higher concentrations of insulin, leptin, adiponectin, TNFα and IL12p40 in the offspring at birth.

**Keywords:** Maternal obesity, metabolic profile, inflammatory profile, offspring at birth.

**Financial Support:** Becas CONICYT (CONICYT - PCHA/ Doctorado Nacional/2014-201463140222) and Proyecto FONDECYT #1141195.

## CLI05 - Physical Activity and Associated Factors among Schoolchildren in São Luís, Maranhão, Brazil.

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**Background:** The aim of this study was to evaluate the prevalence of physical activity and associated factors in students from São Luís, Maranhão, Brazil. **Methods:** This is a cross-sectional study conducted with 140 students aged 10 to 19 years from public schools. The study was a pproved by the Ethical Committee of the HUUFMA (protocol No. 251/11). Statistical analyzes were performed using the statistical software package SPSS® version 19 for Windows, p valeus <0.05 were considred statistically significant. **Results:** The prevalence of overweight in the sample was 24.3% (n = 34), 48.5% (n = 68) of participants have one to three cardiometabolic risk factors. The prevalence of physical activity was higher in boys 56.7% (n = 38). After the sample divided into two groups, stratified by the criterion of physical activity they are denominated: physically active-PA (n = 67) and not physically active - NPA (n = 73). When comparing the averages of age, height, weight, body mass index (BMI), waist-to-height ratio (WHtR), body fat percentage (BF%) and systolic blood pressure (SBP) and diastolic (DBP) per group, only the variable weight showed a statistically significant difference (p = 0.42). The prevalence of overweight 29.9% (n = 20), abdominal obesity 17.9% (n = 12) and participation in physical education class 46.3% (n = 31) was higher in group practice physical activity, but the prevalence of WHtR changed 14.9% (n = 10), high BP 11.9% (n = 8), high BF% 43.3% (n = 29) was lower among physically active. **Conclusion:** The prevalence of risk factors such as WHtR changed, high BP and % BF was lower among physically active. It emphasizes the importance of physical activity as a means of prevention and treatment of obesity among children and adolescents.

**Keywords:** Physical activity, obesity, risk factors, adolescents.
**Financial Support:** Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Estado do Maranhão.

## CLI06 - Oxidative Damage in Pregnant Women and its Association with Obesity.

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**Background:** Obesity is a health problem worldwide that is increasing among pregnant women. This condition leads to metabolic complications associated to oxidative stress and inflammation. Adverse events during intrauterine life can lead to fetal programming and determine diseases in adulthood. Objective: To evaluate maternal oxidative damage to lipids and proteins in the third trimester of pregnancy in normal weight, overweight and women with obesity. **Methods:** This is a secondary analysis from a large cross-sectional study done at the Instituto Nacional de Perinatologia (Mexico City, 2012-2014). Healthy women were included during the third trimester of pregnancy. Pregestational weight was reported to calculate body mass index (p-BMI). Oxidative stress was quantified in plasma; lipid damage was assessed with lipohydroperoxide (LHP) and malondialdehyde (MDA), and protein damage with carbonylation of proteins (PC). Descriptive statistics (mean±SD), One-way ANOVA and Bonferroni's multiple comparison test were performed according to their p-BMI weight category (SPSS, v.20). **Results:** A total of 80 women were studied, 28 were normal weight (N), 26 were overweight (OW) and 26 were obese (OB). Women were 30.3 ± 8.33 years old. Oxidative stress biomarkers were higher in women with obesity when compared to overweight and normal weight women: LHP (OB: 0.035 ± 0.012 vs OW:0.026 ± 0.005, N:0.021 ± 0.005 nmol I3/mg dry weight, p<0.0001), MDA (OB:0.22 ± 0.11 vs OW:0.12 ± 0.04, N:0.11 ± 0.03 nmol carbocyanine/mg dry weight, p<0.0001) and PC (OB:17.02 ± 4.0 vs OW:10.64 ± 2.28, N:9.73 ± 1.36 nmol DNPH/mg protein, p<0.0001). There was a trend for higher levels in overweight women when compared to normal weight, without achieving statistical significance. **Conclusion:** Pregnant women with obesity show higher levels of lipid and protein oxidative damage than overweight and normal weight women. This damage may result in higher risk for adverse perinatal outcomes or fetal programming.

**Keywords:** Overweight, lipohydroperoxide, malondialdehyde and carbonylation of proteins.

## CLI07 - Longitudinal Association of 25-hydroxyvitamin D with Markers of Glucose Metabolism among Brazilian Pregnant Women.

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**Background/Aims:** Lower levels of vitamin D have been associated to increased risk of adverse outcomes such as gestational diabetes. It is suggested that vitamin D influences the glucose metabolism. The aim is to evaluate the association between 25-hydroxyvitamin D [25(OH)D] and insulin, glycaemia and homeostatic model assessment of insulin resistance

(HOMA-IR) throughout pregnancy. **Methods:** A prospective cohort of 182 pregnant women from Rio de Janeiro was followed at 5-13th, 22-26th and 30-36th gestational weeks. Blood samples were drawn in each trimester of gestation. Plasma 25(OH)D concentration (nmol/L) was measured using liquid chromatography-tandem mass spectrometry, insulin (mU/mL) by enzyme-linked immunosorbent assay method and glycaemia (mmol/L) by enzymatic colorimetric method. HOMA-IR was calculated based on the product of insulin and glycaemia divided by 22.5. Sample characteristics were described using medians and interquartile range (IQR) and frequencies (%). 25(OH)D concentration lower than 75 nmol/L was classified as inadequacy status. Longitudinal linear mixed effects models [β; 95% Confidence Intervals (95%CI)] adjusted for age, gestational age, seasons and Body Mass Index (BMI) were performed to evaluate the association between 25(OH)D and markers of glucose metabolism. Results: At baseline, women presented a median of 26.0 years of age (22.0-31.0) and pre-pregnancy BMI 23.7 kg/m² (21.9-27.0). Plasma concentrations of glycaemia, insulin, 25(OH)D and HOMA-IR were 83.0 mg/dL (78.0-88.0), 4.36 µU/ml (3.01-6.48), and 25.5 nmol/L (21.0-30.0), 0.86 (0.571.36), respectively. Vitamin D inadequacy was observed in 70.3% of women. Glycaemia showed an inverse association with 25(OH)D during pregnancy (β=-0.104, 95%CI:-0.207; -0.001, p=0.048). Insulin and HOMAIR showed no significant association with 25(OH)D. **Conclusion:** The high prevalence of vitamin D inadequacy in this population raises the concern regarding pregnant women's health since it was observed that glycaemia increases with decreases 25(OH)D. This is relevant due to the risk of adverse maternal-fetal outcomes related to higher glucose level during pregnancy.

**Keywords:** Pregnancy, vitamin d, glucose, metabolism.
**Financial Support:** The present study was supported by Carlos Chagas Filho Research Foundation from the State of Rio de Janeiro (FAPERJ) (grant numbers E-26/111.400/2010, E-26/110.681/2012; E-26/112.181/2012; E26/111.698/2013).

## CLI08 - Effect of Maternal Smoking on Overweight and Growth in the First Six Months of Life.

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**Background/Aims:** Among the maternal variables related to child growth, smoking during pregnancy is shown negatively associated to intrauterine and postnatal growth in the short and long term. Therefore, the objective of this study is to evaluate the association between smoking during pregnancy and the occurrence of growth deficit and overweight in children in the first six months of life. **Methods:** cohort study with an initial sample of 460 children. The children were evaluated in four times, being measured weight and length in all evaluations to be converted to length for age (L / A) and body mass index for age (BMI / A) indexes in z-score. The cutoff points recommended by WHO were used to classify the indexes. It was applied a semi-structured questionnaire with sociodemographic and pregnancy-related information. To assess the association between smoking during pregnancy with the growth deficit occurrence time and overweight in children up to the sixth month it was used survival analysis with Hazard Ratio calculation for both outcomes by Cox regression, adjusted for confounding variables selected by Directed Acyclic Graphs (DAG). **Results:** The percentage of smoking during pregnancy was 7.6%. Survival time until the occurrence of stunting (p <0.004) and overweight (p <0.012) was lower in children whose mothers smoked during pregnancy. Smoking during pregnancy was an independent risk factor for length deficit (HR = 2.84; 95%CI = 1.42 to 5.70) and overweight (HR = 1.96; 95%CI = 1.09 to 3.53) among children, even after the adjustment for family income, maternal education and number of prenatal visits. **Conclusion:** smoking during pregnancy is a modifiable risk factor associated with the development of early anthropometric deviations in child growth.

**Keywords:** Smoking, pregnancy, infant, growth disorders, overweight
**Financial Support:** Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

## CLI09 - Interaction Between Birth Weight And The PLIN4 rs8887 Variant on Impulsivity Phenotype

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**Background:** PLIN4 is a member of the PAT family of lipid storage droplet (LSD) proteins. Interaction at human PLIN4 single nucleotide polymorphism (SNP) rs8887 and omega-3 polyunsaturated fatty acids (n-3 PUFAs) on obese phenotypes suggests dietary n-3 PUFAs protective effect is dependent on the rs8887 A allele presence. Small for gestational age (SGA) individuals are also more sensitive to the n-3 PUFAs effects. SGA children exhibit less food fussiness and external eating when consuming higher n-3 PUFAs. This study questioned if the A allele presence/absence of the rs8887 SNP (in responsiveness to n-3 PUFAs) interacts with birth weight influencing inhibitory control in children. **Methods:** 254 five-year-old children taking part in a birth cohort study in Canada were genotyped and administered a computerized neuropsychological test including the Stop-Signal Reaction Time (SSRT). Birth weight ratio (BWR) was used to characterize fetal growth. **Results:** There were no significant differences between carriers and non-carriers of the A allele in main confounders such as birth weight, gestational age, breastfeeding duration, gender, maternal schooling and income, smoking during gestation and n-3 PUFAs intake in infancy. There was a significant interaction between BWR and the presence of the A allele on SSRTs (p=0.014), in which lower birth weight is associated with poorer inhibitory control scores only in the A allele non-carriers individuals (B=-586.81, beta=-

1.452, t=2.019, p=0.045). In A allele carriers, which have higher responsivity to dietary n-3 PUFAs, the effect of low birth weight on inhibitory control is abolished. **Conclusions:** This study evidences a relevant interaction between the polymorphism rs 8887 and SGA children on poor inhibitory control and the n-3 PUFAs seem to be important moderators of this association. These results have significant implications in primary prevention of several medical conditions often seen in the SGA population, such as altered feeding and psychological behaviors.

**Keywords:** Inhibitory control, small for gestational age, omega-3 polyunsaturated fatty acids, PLIN4 single nucleotide polymorphism, feeding behavior.

**Financial Support:** Acknowledgments and financial support: CIHR (Canadian Institutes of Health Research), Sackler Foundation, JPB group, Capes.

## CLI10 - Leptin polymorphism is associated with serum lipids change during pregnancy independently energy and fat intake.

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**Background/Aims:** Serum lipids are associated with adverse pregnancy outcomes. However, little is known about how dietary intake and leptin polymorphisms interact to affect lipid changes during pregnancy. Thus, the aim of this study was to evaluate the association between leptin gene single nucleotide polymorphism (SNP), dietary fat intake and lipid concentrations during pregnancy. **Methods:** Prospective cohort of 154 pregnant women followed in Rio de Janeiro, Brazil, during pregnancy (5-13th, 20-26th and 30-36th weeks). Serum high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC) and triglycerides (TG) were measured by enzymatic colorimetric method and low-density lipoprotein cholesterol (LDL-c) was calculated. DNA was extracted by phenol-chloroform protocol and leptin SNP (G2548A, rs7799039) was genotyped using real time PCR method. Dietary intake was assessed using a food frequency questionnaire. Statistical analyses included linear mixed-effect models, adjusted for BMI, age, education, skin color, parity, physical activity, smoking habit, fasting glucose and energy intake and the interaction between SNP and time. **Results:** The lipid concentrations increased significantly during pregnancy trimesters (TC 139.6% and TG 198.8%). Adjusted longitudinal models showed that women with the AA genotype of leptin SNP presented significantly higher concentrations of TC (β=27.1 mg/dL; p=0.006) and LDL-c (β=16.6 mg/dL; p=0.038) during the second and third trimester compared with those with at least one G-allele. There was a significant interaction between LEP SNP and gestational week in the association with TG (β=1.1; p=0.026), in which women with the AA genotype presented a higher increase per week in TG compared with those with AG/GG genotypes. We did not observed any significant interaction between leptin SNP and dietary fat intake during pregnancy. **Conclusion:** Women homozygote for the A-allele of the leptin SNP (G2548A) had significantly higher concentrations of TC and LDL-c during pregnancy and presented a higher increase in TG concentrations/gestational week, compared with AG or GG genotypes.

**Keywords:** Leptin gene polymorphism, Cholesterol, Lipids, Dietary intake, Pregnancy.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

## CLI11 - Metabolome and Metilome Characterization in Children Exposed to Adverse Pregnancy Conditions: preliminary results

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**Background/Aims:** The metabolic phenotype in humans may be conditioned by environmental exposures during pregnancy such those present in maternal obesity and obstetrical complications (preeclampsia and preterm labor). Preliminary evaluation of metilome and metabolome in children from a perinatal cohort in Mexico City was done. **Methods:** Five children under two years old selected from normal (CG) or complicated pregnancies (EG) were included. Fasting samples of serum and after a standardized meal consumption were collected. Amino acids and acylcarnitines were measured by tandem mass spectrometry and the 450,000 CpGs islands microarray by Ilumina was used for methylome description using Genome Studio software. **Results:** Fasting EG children showed significant differences in acylcarnitines C2, C8, C10, and C12 concentrations compared with the CG, as well as C10 in the postprandial condition. Marginal differences were found in insulin, proline, alanine and urea between groups. Trends of global methylation analyses showed a hypermethylation in genes with low β values (0.05-0.15) and down-methylation in genes with high β values (0.8-0.95) in exposed children. The list of involved genes will be showed. **Conclusion:** Young children exposed to pregnancy disorders may use lipid substrates in a differential way compared to non-exposed children, suggesting a distinct metabolic phenotype. Those changes could be associated to extensive changes in the genome methylation.

**Keywords:** Metabolome, methylome, pregnancy disorders.

**Financial Support:** Instituto Nacional de Medicina Genómica (project 10/2015/I).

## CLI12 - Birth weight and blood pressure according to overweight in brazilian children and adolescents.

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**Introduction:** Low birth weight has been associated with an increased risk of hypertension and overweight in children and adolescents1,2,3. Unclear is whether this finding could be modified by overweight in students. We investigated the association between birth weight and blood pressure considering body mass index (BMI) as a potential effect modifier. **Methods:** Cross-sectional study evaluated students at public schools from 6 to 14 years in Niteroi city (RJ), Brazil, 2010. Students were classified as eutrophic (-2,00 ≤ Z ≤ + 1,00) and overweight (+ 1,01 ≤ Z > + 2,00), based on Z-scores of BMI (kg/m²) for age and gender. Blood pressure (BP) measurements ≤ 90th percentile (P90) were classified as normal; above P90 up to P95 was minor hypertension and above P95 major hypertension, according to gender and age. Birth weight (BW) was retrieved from medical records, national system of live births and mother interviews. Prevalence rates of low birth weight (LBW<2500g), hypertension and overweight were estimated. Association between BW and BP was evaluated considering overweight. Logistic regression model were use to test the interaction effect adjusted by age, gender and year of birth. **Results:** We evaluated 645 students: 52.4 % were female, 62.3% range from 10 to 14 years. The prevalence rates of hypertension and overweight were 12.6% and 30.6%, respectively. 6.2% students with hypertension were born with BW. The prevalence ratio for the BW/BP association varied according to overweight (overweight: 2.3 versus Eutrophic: 0.5). Multivariate analysis found 7.5 times odds for hypertension at low birth weight in students overweighted (RP=7.5; p-value=0.05), but without interaction term RP=0.4 (p-value=0.22). **Conclusion:** BW was not associated with BP and this could be possibly due to the size of the sample studied. Nevertheless, the presence of the effect modifier accentuates the effect of BW on BP, corroborating the fetal programming hypothesis.

**Keywords:** Hypertension, birth weight, overweight, students.
**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) — (Edital MCT/CNPq nº 15/2007 — Universal) e Bolsa Pós-Doutorado Júnior (PDJ) a JCPL (Processo nº 151359/2013-0), Financiadora de Estudos e Projetos (FINEP) — encomenda vertical do DECITFINEP (Projeto Ref. 0436/08), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) (Edital nº 04/2008) — apoio às instituições de pesquisa sediadas no Rio de Janeiro e Bolsa de Doutorado nota 10 a JCPL (Processo nº E-26/100.438/2011), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) — Bolsa de Doutorado a JCPL (2009/2010).

## CLI13 - Risk Factors Associated Among Schoolchildren from São Luís, Maranhão, Brazil.

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**Background:** To evaluate the presence cardiometabolic risk factor in adolescents. **Methods:** Cross-sectional study with 198 adolescents between 10 and 19 years of age of 16 public schools in the state of Maranhão, conducted from December 2011 to April 2013.Anthropometric analyses were undertaken, as well as measuring at-rest blood pressure. The study was approved by the Ethics Committee of the Federal University of Maranhão through the protocol number 251/11.Statistical analyses were performed using the statistical software package SPSS® version 19 for Windows. P values <0.05 were considered statistically significant. **Results:** The prevalence of abdominal adiposity, elevated blood pressure and excess weight in the sample were 21.4 % (n = 44), 15.8 % (n = 29) and 30.8 % (n = 61), respectively. The mean age, BMI, WC, SBP and DBP were respectively: 15.1 ± 2.4 years, 21.67 ± 4.53 kg/m², 70.43 ± 11.36 cm, 106 ± 11.42 mmHg and 69.04 ± 10.38 mmHg. After the sample was divided into two groups, stratified by nutritional status, and called eutrophic (normal weight) and excess weight (overweight and obesity). The mean values BMI ($p < 0.001$), WC ($p < 0.001$), SBP ($p < 0.021$) and DBP ($p < 0.004$) variables showed a statistically significant difference between groups. The prevalence of abdominal adiposity (65%), elevated BP (23.5%), physical activity (58.3%) and presence of CRF in family (72.1 %) were higher in excess weight group. **Conclusions:** The prevalence of cardiometabolic risk factor was higher in adolescents with excess weight. We recommend the implementation of measures to prevention/explanation in schools in order to reduce the prevalence of overweight in this age group.

**Keywords:** Obesity, adolescent, risk factors.
**Financial Support:** Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Estado do Maranhão.

## CLI14 - Obesity, gestational weight gain and maternal metabolic risk: a longitudinal study in pregnant mexican women.

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**Background/Aims:** Obesity during pregnancy increases the risk of adverse clinical outcomes, due to metabolic alterations and low chronic grade inflammation. The aim of this study was to describe prospectively maternal metabolic risk and

inflammation during pregnancy by age, obesity and gestational weight gain and evaluate their association with birthweight in a group of pregnant Mexican women. **Methods:** Prospective cohort; healthy pregnant women <14 weeks of gestation, receiving prenatal care at National Institute of Perinatology (Mexico, 2009-2013). Serum analysis of metabolic and inflammatory markers were done each trimester. Statistics included descriptives, correlations Pearson/Spearman, mean differences (ANOVA, Student T-test), longitudinal differences (repeated measures ANOVA) (SPSS, 20.0). **Results:** A total of 180 women were studied (20.8% desertion). Mean age was 27.02±8.43 years old (27.1% were adolescents). Thirty-eight percent (n=67) of women were overweight or had obesity; 33.1% (n=58) showed excessive gestational weight gain. Higher lipids were observed in adult women when compared to adolescents ($p<0.05$); adult women had also lower TNF-alpha in the 2nd trimester and lower leptin and adiponectin in the 3rd trimester. During pregnancy, insulin, lipids, leptin and interleukin 6 (IL-6) increased in all women ($p<0.05$). Longitudinal differences were observed in C-reactive protein (CRP) and IL-6 between normal weight and overweight/obese women. Pregestational body mass index (BMI) correlated with insulin, leptin, triglycerides (TG) and CRP (all $r>0.237$; $p<0.002$). Excessive gestational weight gain was associated with higher insulin and HOMA and higher birthweight ($p<0.05$). Gestational weight gain, p-BMI and TG, in addition to gestational age at birth, were main determinants of birthweight ($R2=.4$). **Conclusions:** Leptin, insulin, lipids and some inflammatory markers are increased during pregnancy in Mexican women and are associated with obesity and weight gain. Obesity, weight gain, and TG during the 3rd trimester were the main determinants of birthweight, together with age at birth.

**Keywords:** Pregnancy, adipokines, inflammation, insulin resistance, birthweight.

**Financial Support:** This project was in part funded by the Consejo Nacional de Ciencia y Tecnología (CONACYT) (Fondo Sectorial en Salud, Project No. 86840).

## CLI15 - Processed Dietary Pattern is Associated with Body Mass Index and Adipokines throughout Pregnancy.

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**Background/Aims:** This study aims to evaluate the association between dietary patterns (DP) and body mass index (BMI), adiponectin and leptin throughout pregnancy. **Methods:** Prospective cohort of adult pregnant women (n=176), conducted in Rio de Janeiro/Brazil, at three moments: 5-13th, 22-26th, 30-36th gestational weeks. A food frequency questionnaire was administered at the third trimester, with 6 months as the time frame. Three DP were previously identified using principal component analysis: Healthy (milk, dairy products, fruit, fruit juice, green vegetables/legumes, fish, cakes/cookies-crackers and tea), CommonBrazilian (rice, beans, vegetable spices, eggs and bread/fats) and Processed (meats, candies/sugar, pasta, roots/tubers, fast food/snacks, sausages/deli meats, soft drinks, and inversely related to beef and coffee). BMI and plasma adipokines were assessed in all trimesters. Leptin (ng/dl) and adiponectin (µg/mL) were measured using ELISA kits. Statistical analysis included Student's t-test (1st+2nd vs. 3rd tertiles of DP adherence), means and standard deviation and longitudinal linear mixed effects models [β; 95% Confidence Intervals (95%CI)]. Two multiple models were fitted. The first included per-capita household income, total energy intake and gestational weeks. The second further adjusted for pre-gestational BMI. **Results:** Women with higher adherence to the Processed pattern presented higher means of BMI and leptin comparing to those in the 1st/2nd tertiles [BMI=25.6 (4.9) vs. 24.5 (3.8) kg/m2, P=0.044; leptin=21.7 (13.2) vs. 18.5 (10.9) ng/dl, P=0.043]. There were no differences in the adiponectin concentrations between the groups. The Processed pattern was positively associated with BMI (β=1.21, 95%CI: 0.70; 1.73, P<0.001) and leptin (β=2.86, 95%CI: 0.54; 5.17, P=0.016), and negatively with adiponectin (β=-0.90, 95%CI: -1.46; -0.35, P=0.001). The association with adiponectin remained significant after adjusting for pre-gestational BMI but lost significance for leptin. **Conclusions:** The Processed DP was positively associated with BMI and leptin, and inversely with adiponectin, showing that a processed diet may be a negative factor for maternal health.

**Keywords:** Food habits, pregnancy, body mass index, leptin, adiponectin.

**Financial support:** The present study was financially supported by Carlos Chagas Filho Research Foundation from the State of Rio de Janeiro (FAPERJ) (grant numbers E-26/111.400/2010, E-26/110.681/2012; E-26/112.181/2012; E26/111.698/2013).

## CLI16 - Urinary interleukin-10 as biomarker in Type 1 Diabetes Mellitus nephropathy.

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Patients with type 1 diabetes mellitus (DM1) show a subclinical and chronic inflammatory condition. The aim of the present study was to investigate the association between the urinary interleukin-10 (IL-10) levels and biomarkers of nephropathy, endothelial damage and oxidative stress in patients with DM1. The sample was composed by 35 healthy individuals (control group), 63 DM1 patients with normoalbuminuria - group 1A (<30 mg of albumin/g of creatinine) and 62 DM1 patients witch micro- and macroalbuminuria – group 2A (≥ 30 mg of albumin/g of creatinine). Urinary IL-10 (corrected by urinary creatinine) and thrombomodulin levels were determined

by ELISA. Lipid peroxidation was evaluated through plasma thiobarbituric acid reactive species (TBARS) concentration. Fasting glucose and urinary creatinine were determined by enzymatic method and HbA1c by immunoturbidimetry. The groups were compared using the Mann-Whitney test. The variables were correlated using Spearman's test. It was considered significant value of p <0.05. The age observed in group 1A was 32.84 ± 9.54 years, in group 2A was 34.56 ± 10.13 years, while in control group was 32.80 ± 8.63. The median levels of IL-10 in group 1A – 6,89 (10.87) pg/g Cr - were higher than in control group - 4.36 (7.60) pg/g Cr (p = 0.006). Also, urinary levels of IL-10 was higher (p = 0.038) in group 2A – 7.04 (16.49) pg/g Cr when compared with control group. Finally, urinary IL-10 levels proved positive correlation with fasting glucose, HbA1c, thrombomodulin and TBARS. These data suggest an increased IL-10 kidney production or excretion simultaneously of nephropathy progression.

**Keywords:** Diabetes, albuminuria, interleukine-10, oxidative stress, endothelial damage.
**Financial Support:** FAPEMIG, CNPq.

## CLI17 - Urinary TNF-α levels are associated with nephropathy in patients with Type 1 Diabetes Mellitus.

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Patients with type 1 diabetes mellitus (DM1) present a chronic and subclinical inflammatory condition. The aim of the present study was to investigate the association between the urinary levels of TNF-α and biomarkers of renal function. The sample was composed by 35 healthy individuals (control group), 63 DM1 patients with normoalbuminuria - group 1A (<30 mg of albumin/g of creatinine) and 62 DM1 patients witch micro- and macroalbuminuria – group 2A (≥ 30 mg of albumin/g of creatinine). Urinary TNF-α and serum cistatin-C were determined by ELISA. Serum levels of creatinine and urea were determined by enzymatic method. First-morning urine samples was used for urinary albumin excretion determination. Urinary albumin and TNF-α was corrected by urine creatinine. Urinary albumin was evaluated by immunoturbidimetry and urinary creatinine was determined by enzymatic method. The estimated glomerular filtration rate was calculated using the abbreviated modification of diet in renal disease formula (Levey, et al. 1999). The groups were compared according to the Mann-Whitney test. The correlation between markers was performed by Spearman test. The significance level was p <0.05. The age observed in group 1A was 32.84 ± 9.54 years, in group 2A was 34.56 ± 10.13 years, while in control group was 32.80 ± 8.63. When compared to group 2A (0.43 (0.59) pg/g Cr), individuals with normoalbuminuria (0.23 (0.24) pg/g Cr) and control group (0.17 (0.27) pg/g Cr) presented significantly lower TNF-a urinary levels. Moreover, urinary levels of TNF-a were positively correlated with plasma levels of cystatin C, creatinine, urea and albuminuria, while they were negatively correlated with estimated glomerular filtration rate. Also, urinary TNF-a levels were independently associated with the presence and severity of macroalbuminuria, after logistic regression analysis. This finding suggests that urinary TNF-a level determination may be helpful to evaluate progression to nephropathy in DM1 patients.

**Keywords:** Diabetes, albuminuria, TNF-α, oxidative stress, endothelial damage.
**Financial support:** FAPEMIG, CNPq.

## CLI18 - Cardiovascular Risk in Patients that use Antipsychotic a Psychosocial Care Center.

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**Introduction:** Antipsychotic drugs are an important component in the medical management of many psychotic conditions, however, its use has been associated with increased cardiovascular risk because of other complications such as weight gain, diabetes mellitus and dyslipidemia. **Objective:** analyze the predictors of cardiovascular risk in patients that use antipsychotic drugs. **Methodology:** quantitative, retrospective study, conducted from February to July 2016 in the St. Louis CAPSad, Maranhão. Were evaluated the anthropometric parameters (weight, height, body mass index, waist circumference and waist-hip ratio), demographic data, clinical aspects (consumption of psychoactive substance used medication and comorbidity) and laboratory results (glucose, triglycerides and total cholesterol). Results: We interviewed 25 people with prevalence of men (23), average 36 years old, non-white (100%), most without occupation, without a partner and with over 8 years of study. Anthropometric parameters were equal to average BMI 25,19 kg/m2, waist circumference 89,84 cm and waist hip ratio 0,90. Eleven (44%) participants were overweight. The alcohol was prevalent (92%), as well as tobacco (64%) and other drugs (72%). The psychoactive drugs most used were carbamazepine, diazepam, bupropion, disulfiram, naltrexone and chlorpromazine. The average results of laboratory aspects were 85,2 mg/dL blood glucose, 188,96 mg/dL for capillary cholesterol and 169,94 mg/dL for capillary triglycerides and 14 (56%) patients with dyslipidemia. Only one patient had diagnose of hypertension and none had diabetes. **Conclusion:** Patients surveyed showed 44% of overweight or obese and 61% with abnormal triglyceride values. The monitoring of patients might contribute to changing eating habits and practice exercises in order to modify the risk factors observed.

**Keywords:** Antipsychotics, risk factors, alcoholism, drug abuse.
**Financial Support:** FAPEMA.

# 5TH INTERNATIONAL SYMPOSIUM ON METABOLIC PROGRAMMING AND STRESS AND THE 2ND MEETING OF IBERO-AMERICAN DOHAD CHAPTER

# EPIDEMIOLOGY SESSION

## EPI01 - Different Patterns of Longitudinal 25-hydroxyvitamin D Durin g Pregnancy According to Season at recruitment: A Prospective Cohort.

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**Background:** Vitamin D inadequacy in pregnant women is highly prevalent worldwide and associated with an increased risk of maternal and fetal outcomes. We hypothesize that vitamin D during pregnancy may be influenced by season at recruitment, even in tropical countries. Objective: To estimate the prevalence of 25-hydroxyvitamin D [25(OH)D] inadequacy and to explore the effect of season at recruitment in longitudinal changes of 25(OH)D in Brazilian pregnant women. **Method:** A prospective cohort of 229 apparently healthy pregnant women from Rio de Janeiro followed between 5th-13th, 20th-26th and 30th-36th gestational weeks. 25(OH)Dnmol/L was measured by liquid chromatography-tandem mass spectrometry and categorized as adequate (≥75 nmol/L) or inadequate (<75nmol/L). Statistical analyses were performed using longitudinal linear mixed-effects models reported regression coefficients (β) and 95% Confidence Intervals (CI). This model was adjusted for parity, education, self-reported skin color and pre-pregnancy body mass index (BMI). We also tested interactions between gestational age and season at recruitment. **Result:** The women presented a mean age of 26.6 years and 40.2% had pre-pregnancy BMI ≥ 25 kg/m2. The prevalence of vitamin D inadequacy was higher during the first trimester compared to second and third trimesters (70.4, 41.0% and 33.9%, respectively). There was an increase in 25(OH)D (β=0.869; 95% CI, 0.723 to 1.014; p< 0.001) during pregnancy. Women that started the study in winter (β=1.441; 95% CI, 1.066 to 1.816, P<0.001), spring (β=1.126; 95% CI, 0.758 to 1.493, P<0.001) or autumn (β=0.398; 95% CI, 0.044 to 0.752; P=0.028) had greater longitudinal increases in 25(OH)D than women that began the study during summer. Conclusion: Vitamin D inadequacy was high in Brazilian pregnant women, especially in the first trimester. There was an influence of season at recruitment on the longitudinal patterns of vitamin D concentrations during pregnancy. This result brings new evidence regarding 25(OH)D longitudinal changes during pregnancy.

**Key words:** Vitamin D, pregnancy, cohort, tropical country, seasons.

**Financial Support:** The present study was financially supported by Carlos Chagas Filho Research Foundation from the State of Rio de Janeiro (FAPERJ) (grant numbers E-26/111.400/2010, E-26/110.681/2012; E-26/112.181/2012; E-26/111.698/2013).

## EPI02 - Association between Plasma Vitamin D Concentrations Throughout Pregnancy and Birth Weight.

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**Background/Aims:** Inadequateconcentrationsofvitamin D [25(OH)D] duringpregnancy are associatedwith adverse neonatal outcomes such as low birth weight (BW). The aim of this study is to assess the association of plasma 25(OH) D throughout pregnancy with BW z-score. **Methods:** Prospective cohort of 194 pregnant women followed at a public health care center in Rio de Janeiro, Brazil. Women met the following eligibility criteria: age between 20 and 40 years old, <13 gestational weeks and free from chronic communicable diseases (except obesity). Plasma concentrations of 25(OH) D (nmol/L) were analyzed using liquid chromatography-tandem mass spectrometry and early pregnancy status was categorized as adequate (≥75 nmol/L) or inadequate (<75nmol/L). BW z-score for gestational age at birth and sex was calculated according to the International Fetal and Newborn Growth Consortium for the 21st Century curves (Intergrowth-21st). Women and newborn characteristics were described as means (standard deviations). A multiple linear regression model (with respective betas and confidence intervals) was used to test the associations between vitamin D concentrations and BW z-score. Variables regarding 25(OH) (intercept and slope) were estimated using linear mixed effects models and predicted by the Best Linear Unbiased Prediction (BLUP) method. The model was adjusted by age, schooling, pre-gestational body mass index, gestational weight gain and self-reported skin color. Results. The mean BW of neonates born to women who presented adequate (30%) and inadequate 25(OH)D concentrations in early pregnancy were 3186.1 (±568.6) and 3283.0 (±561.5) grams, respectively. The regression model revealed a direct association between 25(0H)D slope throughout pregnancy (refers to the longitudinal variation) with BW z-score (β=0.32;

95% CI=0.02-0.63; p=0.034). No association was observed for the intercept. **Conclusions:** Lower increases in maternal 25(OH)D concentrations during pregnancy may be associated with an increased risk of low BW. Early preventive measures during pregnancy should be taken to reduce the impact on childhood.

**Key words:** Birth weight, vitamin D, pregnancy.
**Financial Support:** FAPERJ, CNPq.

## EPI03 - Social Sanitary Profile and Anthropometry in Basic Attention Users in a Health Unit.

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**Aims:**To describe the social sanitary profile and verify the anthropometric data of patients registered in the e-SUS Primary Assistance, assisted by a team of the Family Health Strategy in São Luís. **Methods:** cross-sectional study with non-probabilistic sample, composed of 171 male and female patients, above 18, with hypertension and/or diabetes mellitus, linked to a Basic Health Unit in São Luís. Social demographic and lifestyle data, such as smoking, drinking consumption alcohol and physical activity, were analyzed. Anthropometric measurements such as body mass index (BMI), abdomen circumference (AC), waist circumference (WC) and waist vs hip ratio (WHR) were also evaluated. **Results:** The study showed a predominance of females (69.59%), self-declared brown color (56.14%), age average of 60.53 (± 11.41), incomplete primary education (47.37%), low family income of ½ to 1 minimum wage (44.44%) and married (38.59%). The data show that 77.77% do not use alcohol, 88.88% do not use tobacco and 76.02% do not practice regular physical activity. Most participants do not consider themselves healthy. Those who had only hypertension were more prevalent (57.3%), followed by those who had the combination of the two diseases (30.4%) and those who were only diabetics (12.3%). Regarding the BMI, higher prevalence occurred among overweight people (48%), followed by obese ones (28%). It was also observed the prevalence of cardiovascular risk for both sexes evaluated by the waist / hip ratio with 86.5% female and 13.5% male and waist circumference with 98.31% for females and 71.15% for males. **Conclusion:** In the studied population there was increased cardiovascular risk, predominantly female, elderly and hypertensive. Thus, it is important to know the community profile in order to adjust the services offered, improve the services to the population and work on measures to improve health indicators, especially those related to cardiovascular risk.

**Keywords:** Anthropometry, risk factors, diabetes mellitus, arterial hypertension.
**Financial Support:** FAPEMA-PPSUS.

## EPI04 - Weight Gain Pregnancy And Child Body Mass Index: Path Analysis In BRISA And Generation XXI Cohort.

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Childhood obesity is one of the most serious public health challenges in the twenty-first century. The problem is global and affects different levels of income countries. This study evaluated the direct and indirect effects of gestational weight gain in body mass index (BMI) among children from two birth cohorts with different levels of socioeconomic development. They were followed 3742 children from two cohorts: 3202 were from BRISA cohort (Brazil) and 540 were from Generation XXI cohort (Portugal). The variables used were BMI for age, family income, maternal education, pre-pregnancy BMI, gestational weight gain, birth weight and duration of breastfeeding. The model was adjusted for path analysis that allowed us to assess the total, direct and indirect effects of the explanatory variables on the child BMI. Gestational weight gain had a positive total effect on the child BMI in the Brazilian cohort (standardized coefficient (SC) = 0.094; $p < 0.001$) and in the Portuguese cohort (SC = 0.129; $p = 0.003$). In addition, pre-pregnancy BMI (SC = 0.127, $p < 0.001$; SC = 0.252, $p < 0.001$) and birth weight (SC = 0.164, $p < 0.001$; SC = 0.230, $p < 0.001$) also had direct effects on child BMI in both cohorts, respectively. Family income had a positive total effect (SC = 0.056, $p = 0.004$) only in BRISA cohort. Thus, increasing gestational weight gain, pre-pregnancy BMI and birth weight are risk factors for increased child BMI. The increase in household income was a risk factor for the increase on child BMI only in Brazilian cohort, showing that inequalities in developing countries is still a factor to be taken into account in the prevention of childhood overweight.

**Key words:** Weight gain, pregnancy, pediatric obesity.

## EPI05 - Association Between Caffeine Consumption During Pregnancy a nd Low Birthweight or Preterm Birth.

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**Background/Aims:** Maternal exposures such as excessive caffeine consumption during pregnancy is likely associated to low birth weight (LBW) and preterm birth. This issue has been the subject of several epidemiological studies. However, the results of such studies are contradictory due to different methodologies and samples. The objectives of this study were: to describe the caffeine intake during pregnancy on birth cohort of Ribeirão Preto in 2010 and the association between caffeine consumption during pregnancy with preterm birth and LBW. **Methods:** A cohort study, inserted in a thematic study.

Data collected included 7609 pregnancies in RibeirãoPreto and their newborns. The independent variable was caffeine consumption from coffee drink during pregnancy, whereby high consumption of caffeine was defined as ≥300mg /day and the dependent variable were LBW - defined as <2500 grams at birth - and preterm birth - defined as <37 weeks. Bivariate risk was calculated using the Relative Risk (RR), with a confidence interval of 95%. RR were estimated adjusted in four multiple models: biological variables and maternal socio-demographic ; obstetric history; the current pregnancy and all variables. **Results:** 4908 mothers (64.5%) consumed coffee and 143 (2.9%) had high caffeine consumption. No association was found between caffeine consumption and preterm birth and LBW in both unadjusted (RR 1.45, 95% CI 0.91 to 2.32 and RR 1.16, 95% CI 0.77-1.75, respectively) and adjusted analyses (RR 1.42, 95% CI 0.85-2.38 and RR 1.03, 95% CI 0.65-1.63, respectively). Mothers without partners, history of preterm birth and stillbirth, gestational hypertension, threat of preterm delivery and smoking were risk factors for LBW and preterm birth, according to analyses. **Conclusion:** In this cohort, the high caffeine consumption was not a risk for LBW and preterm birth.

**Key words:** Coffee, caffeine, low birth weight, preterm birth, Cohort study.

**Financial Support:** Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Conselho Nacional de Desenvolvimento Científico e Tecnológico (Capes), Fundação de Apoio ao Ensino, Pesquisa e Assistência.

## EPI06 - Birth weight and overweight associations in students between 6 and 14 years olds from two public schools in Niterói, Rio de Janeiro, Brazil.

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**Background/Aims:** There are evidences that factors from the prenatal period to adolescence are important determinants of overweight throughout the life course. The aim of this study was investigate the association between birth weight and overweight of students from 6 to 14 years olds. **Methods:** A cross-sectional study was conducted in two public schools in Niterói(RJ), Brazil in 2010. All students aged 6 to 14 years were eligible to participate. Students (n=795) were weighed and measured by trained staff. Overweight students were defined as a Z-score for BMI/age/sex > +1.00 (students with Z-score for BMI/age/sex < -2.00 were excluded, n=15). Maternal information at student's birth (color, education and age) and student information (type of delivery, weight (g) and length (cm) at birth, prematurity, age, gender and exclusive breastfeeding) were collected by self-report questionnaires and medical records. Prevalence rates of overweight according to categorical maternal and student characteristics and summary statistics (continuous variables: weight and length at birth, maternal ages) were calculated. Poisson regression with a robust variance was used to test associations. Variables with a statistical significance (p value<0.25) were selected in the univariate analysis for the multivariate analysis model. The final model considered covariables with statistical significance (p value<0.05). **Results:** Overweight occurred in 30.3% of the students. In the univariate analysis, excepted student gender and prematurity, all covariates were associated with overweight. In multivariate analyses, only the birth weight was positively associated with overweight. (coef. 0.0003, 95%IC: 0.0001-0.0006, p value=0.019).**Conclusions:** Birth weight was positively associated with overweight of students from 6 to 14 years olds. Others factors as catch-up growth and life-style determinants should be tested as potential effect modifiers in fetal programming analysis.

**Key words:** Birth weight, overweight, students, fetal programming.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) — (Edital MCT/CNPq nº 15/2007 — Universal) e Bolsa Pós-Doutorado Júnior (PDJ) a JCPL (Processo nº 151359/2013-0), Financiadora de Estudos e Projetos (FINEP) — encomenda vertical do DECITFINEP (Projeto Ref. 0436/08), Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) (Edital nº 04/2008) — apoio às instituições de pesquisa sediadas no Rio de Janeiro e Bolsa de Doutorado nota 10 a JCPL (Processo nº E-26/100.438/2011), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) — Bolsa de Doutorado a JCPL (2009/2010).

## EPI07 - Factors of the First 1000 Days of Life Associated with the "Asthma Phenotype": Brisa Cohort, Brazil.

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**Background:** Asthma is the most prevalent nontransmissible chronic disease during childhood and is characterized by recurrent episodes of wheezing breath that vary in frequency and severity among individuals (WHO, 2016). In children, asthma is a complex syndrome of difficult diagnosis (Papadopoulos et al., 2012). **Objective:** To analyze environmental factors of the first 1000 days of life associated with the "asthma phenotype" in childhood. **Methods:** A prospective study involving three time points was conducted on the BRISA Cohort, São Luís, Brazil (n=1150): prenatal period, birth and second year of life. The "asthma phenotype" was a construct consisting of four indicators (a medical diagnosis of asthma, wheezing, emergency care due to wheezing, and rhinitis). A theoretical model based on prenatal factors (socioeconomic construct, pregestational BMI and life habits), birth factors (gestational age, birth weight, type of delivery) and second year factors (breastfeeding and BMI z-scores) was analyzed in association with the "asthma phenotype" using structural equation modeling. **Results:** The "asthma phenotype" formed a good construct. It was observed that, the higher the pregestational BMI (Standardized Coefficient – SC = 0.118; p-value - p = 0.021) and the soft drink consumption during pregnancy (SC = 0.117; p = 0.042) and by the infants born by cesarean section without labor (SC = 0.146; p = 0.021), the higher the values

of the “asthma phenotype”. In contrast, the higher the birth weight (SC = -0.173; p = 0.030) and for babies exclusively breastfed for 6 months (SC = -0.146; p = 0.017), the lower the values of the “asthma phenotype”. **Conclusion:** The present findings support the hypothesis that childhood asthma seems to be defined early, with the involvement of environmental factors present before conception and during the first 1000 days of life.

**Key words:** Asthma, environmental factors, one thousand days of life, structural equation modeling.

**Financial Support:** Maranhão State Research and Scientific and Technological Development Foundation (FAPEMA), São Paulo State Research Foundation (FAPESP), and National Council for Scientific and Technological Development (CNPq).

## EPI08 - Factors associated with disadvantages in the mothers-child relationship in Sao Luis - Cohort BRISA.

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**Background/Aims:** The development of the mother-child relationship is a crucial process and can be affected by various interferences that do not occur in isolation. This study aimed to evaluate factors associated with losses in the mother-child relationship in a capital of northeastern Brazil. **Methods:** Cohort Study of 3,215 mothers of children between 15 and 36 months of age. Losses in the mother-child relationship, rated by Postpartum Bonding Questionnaire (PBQ), was the outcome variable and the explanatory variables were demographic, socioeconomic, reproductive health and mental health of mothers and the birth status of children. We used multivariate regression analysis with hierarchical approach. **Results:** The prevalence of losses in the mother-child relationship was high (12.6%) compared to studies carried out in countries with high social indicators1,2 and were associated risk factors to lower maternal education (RR=1.64), having unplanned pregnancy (RR=1.42), alcohol consumption during pregnancy (RR=1.42) and maternal stress symptoms (RR=1.88) and depression (RR=2.00). Women with less education are in settings with higher incidence of negative patterns in their ability to respond to the needs of children, compromising the quality of maternal interaction3. The maternity brings various changes and occurs when no suitable time, it becomes a stressful event4. In addition, mothers with symptoms of stress and depression may also have difficulties to link training with child5,6. There were no other studies on association between losses in the mother-child relationship and consumption of alcoholic beverages during pregnancy. **Conclusions:** Lower education and elements related to mental health were risk for damage in the mother-child relationship. It is likely that they are not necessarily less favorable living conditions, but the lack of intellectual resources, translated by less education, which influence the occurrence of damage in the mother-child relationship.

**Key words:** Mother-child relations, psychosocial impact, association.

**Financial Support:** The BRISA received funding from the National Scientific and Technological Development Council (CNPq), Foundation for Research and Scientific and Technological Development of Maranhão (FAPEMA) and the Support Program for Centers of Excellence (PRONEX).

## EPI09 - Sociodemographic Factors are Associated with Dietary Patterns of Women in the Pre-pregnancy Period: the ProciAr Cohort Study.

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**Background:** During reproductive age and pregnancy, the women’s dietary intake has serious implications on health of children, both in utero and during childhood. Objective. To characterize dietary patterns of women in pre-pregnancy period and to investigate factors and nutrients associated with these patterns in the ProcriAr Cohort Study conducted in São Paulo/Brazil, 2012. **Methods:** Pre-pregnancy dietary patterns of women (n=454) were investigated by principal component factor analysis, based on intake reported on a validated 110-item food frequency questionnaire. Multiple linear regression was used to assess sociodemographic and lifestyle factors related to dietary patterns. Spearman's correlation coefficients identified the association between dietary patterns and nutrient intake. **Results:**The four dietary patterns retained were named "P1-Lentils, whole grains and soups," "P2-Snacks, sweets and soft drinks," "P3-Seasoned vegetables and low-fat meats", "P4-Sweetened juices, bread and butter, rice and beans." P2 could be considered the most harmful dietary pattern by being composed of alcoholic, sugar-sweetened beverages, industrialized and takeaway food, and food rich in sugar, fat, energy and synthetic folate. Higher education (βi=0.26;95%CI=0.06,0.45) was positively related to P2, whereas age (βi=-0.02;95%CI=-0.04,-0.01), lack of formal work (βi=-0.39;95%CI=-0.59,-0.18) and being born in Northeast region (βi=-0.31;95%CI=-0.53,-0.09) were negatively related to P2. **Conclusions:** In the ProcriAr study, being younger, more highly educated, employed and born in Southeast Brazil were related to the dietary pattern most deleterious to healthy pregnancies. Not only should these factors be considered to implement health promotion practices in nutrition directed to women, but also to foster an adequate environment for the fetus in advance.

**Key words:** Factor analysis, dietary pattern, preconception care, pregnancy, sociodemographic factors

**Financial Support:** Sao Paulo Research Foundation (FAPESP, nº 2009/17315-9 and nº 2014/12647-1), and the National Council for Scientific and Technological Development (MCT/CNPq/FNDCT/CAPES/FAPESP, nº 2008/57717-6).

## EPI10 - Phenotypic frequency systems: ABO and Rh donors HEMOMAR, São Luís – MA.

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**Background / Aims:** The ABO system is considered the most important system of blood groups in clinical medicine for blood transfusion. It consists of the blood groups: A, B, AB and O. The objective of this study was to evaluate the frequency of alleles of blood donors of Hematology Center and Hematology of Maranhao - HEMOMAR, in February 2012, with a total 3006 of employees assigned to a, B, AB and O, besides the positive and negative Rh factors. **Methods:** To analyze the data to understand the allelic frequency of individuals and how they behave, used the gene frequency of calculation cases of autosomal polialelismo (when there is dominance and recessive). **Results:** Of the total of 3006 donors individuals were found 864 (28.742%) belonging to blood group A, 374 (12.608%) for the blood group B, 76 (2.528%) for the AB group and 1687 (56.121%) for the O group. To group according to the distribution table of chi-square, the population met the value was less than the tabulated (X2 = 1,844). **Conclusions:** So we come to the conclusion by means of specific calculations, that this group is in Hardy Weinberg equilibrium, showing no evolutionary factor action. Furthermore, there was a prevalence of group O Rh positive and factor.
**Key words:** Hardy weinberg, abo system, Rh factor.

## EPI11 - Violence During Pregnancy Affects the Mother-Child Relationship?Brisa Cohort.

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**Background / Aims:** Violence against women is recognized as a serious public health problem, and may even affect children of women subjected to ill-treatment. The aim of this study was to analyze the effects of violence against pregnant women in the mother-child relationship in early childhood. **Methods:** A prospective cohort study started with 1447 pregnant women interviewed in São Luís, in 2010 and 2011, had the final sample 1140 mothers interviewed again from 2011 to 2013. Violence during pregnancy was measured by the instrument World Health Organization Violence Against Women. The Postpartum Bonding Questionnaire (PBQ) was used to investigate the mother-child relationship. In the proposed model, socioeconomic status occupied the most distal position, determining demographic, violence against pregnant women, social support and depression symptoms in women, which determined the outcome losses in the mother-child relationship. This model was estimated using structural equation modeling. **Results:** The rate of violence against pregnant women was 48.46% and losses in relation to their children was 6.14%. The proposed model has good fit according to the RMSEA (0.021), IFC (0.976) and TLI (0.975) indicators. Violence against pregnant women resulted in losses in the mother-child relationship via symptoms of postpartum depression (load factor CF = 0.178; p <0.001). Pregnant women with lower social support (CF = -0.196; p <0.001) in unfavorable socioeconomic status (CF = -0.131; p = 0.002) and non-residents with an intimate partner (CF = 0.129; p = 0.003) had more losses in mother-child relationship. **Conclusions:** Violence against pregnant mediated symptoms of postpartum depression had a negative effect on the mother-child relationship, suggesting that should be investigated in prenatal care.
**Key words:** Cohort studies, factor analysis, statistical, mother-child relations, pregnancy, violence.
**Financial Support:** His project was funded by FAPESP (Portuguese acronym for the São Paulo State Research Foundation), FAPEMA (Portuguese acronym for the Maranhão State Research Foundation) and CNPq (Portuguese acronym for the Brazilian National Research Foundation).

## EPI12 - Exploring Obesogenic Pathways Linked to Asthma in Adult Life: 1978/79 Ribeirao Preto Cohort, Brazil

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**Background/Aims:** To analyze the obesogenic pathways throughout the life cycle and its association with asthma in adults. **Methods:** Birth cohort study from 1978/79, Ribeirão Preto, Brazil (n=1982). This cohort was studied in three stages: birth (baseline), school age (1st follow-up) and adult age (2nd follow-up). A theoretical model was proposed to analyze the obesity pathways and its association with asthma in adults, through structural equation modeling. The following variables were used: baseline: family socioeconomic status – SES at birth (construct formed by maternal education, maternal occupation and family income), type of delivery and adequacy of birth weight for gestational age; 1st follow-up: BMI z-score at 7-8 years; 2nd follow-up: current adult SES (construct formed by adult education, adult occupation and monthly family income), current BMI, history of parental obesity and asthma in adults (construct formed by medical diagnostic of asthma, wheezing in the last 12 months and bronchial hyperresponsiveness). **Results:** Higher SES at birth (CP=0189; p<0.001) and parental obesity (CP=0.137; p=0.004) were associated with being overweight at birth. Higher SES at birth (CP=0.169; p<0.001), parental obesity (CP=0.177; p<0.001), and cesarean section (CP=0.153; p=0.002) were associated with being overweight at 7-8 years. In adult life, lower adulthood SES (CP=-0199; p=0.005), parental history of obesity (CP=0.240; p<0.001), caesarean delivery (CP=0.137; p<0.001); and being overweight at school age (CP=0.554;

p<0.001) were associated with higher adult BMI. Parental obesity, being overweight in infancy and adulthood were the variables of the obesogenic pathway that explained asthma in adults (CP=0.112; p=0.044); while having higher SES at birth or in adulthood were protective factors for overweight. **Conclusions:** Obesogenic pathways starting from parental obesity are associated with higher weight over the life cycle and asthma.

**Key words:** Asthma, obesity, life cycle, structural equation modeling.
**Financial Support:** National Council for Scientific and Technological Development (CNPq), Aid to Education Foundation, Research and University Hospital Assistance RibeirãoPreto Medical School, University of São Paulo (HCFMRP-USP) and Foundation for the São Paulo State Research Paulo.

## EPI13 - Social Mobility and Insulin Sensitivity and Secretion in Young Adults in a Brazilian Cohort.

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**Background:** Studies in high-income countries have associated upward social mobility with decreased insulin resistance. However, in low and middle-income countries the results are controversial. We studied associations between family income or social mobility with insulin sensitivity or insulin secretion by pancreatic beta cells in the 1978/79 RibeirãoPreto birth cohort, Brazil. **Methods:** 2,063 subjects were evaluated at birth and at the age of 23/25 years. Family income was defined in two moments of life as low, medium and high based on tertiles of the minimum wage. Social mobility from birth to young adulthood was based on family income - which was categorized into low and high, with the cutoff point in the median - and classified as low-low (persistent poor), high-high (persistent rich), low-high (upward social mobility) and high-low (downward social mobility). Multiple linear regression models with adjustments for caloric and fat intake, alcohol use and smoking, physical inactivity, birth weight, body mass index and waist circumference were used to estimate associations. **Results:** Women who had low family income at birth or in early adulthood, those who remained with low family income in these two moments of life and those who showed upward social mobility had lower insulin sensitivity and increased insulin secretion by pancreatic beta cells. These associations were mediated by body mass index and waist circumference. There were no significant associations among men. **Conclusions:** Having low family income at birth or in early adulthood or having low income at both moments or showing upward social mobility were risk factors for increased insulin resistance and secretion in young adult women. Socially constructed patterns regarding body image, mediated by dieting and physical activity, may explain our different findings according to sex.

**Key words:** Insulin resistance, social mobility, family income, young adult.
**Financial Support:** This work was supported by the São Paulo State Research Foundation (FAPESP in the Portuguese acronym–nos. 93/0525-0, 97/09517-1, and 00/09508-7), by the Support Teaching, Research and Service Foundation from the University Hospital, Faculty of Medicine, University of São Paulo and by the CNPq (Portuguese acronym for the Brazilian National Research Council-grants nos. 523474/96-2 and 520664/98-1).

## EPI14 - Descriptive analysis of pregnant women in Uruguay (national data from 2010-2012).

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**Background:** There is evidence that gestational weight gain (GWG) is related to pregnancy outcomes. For example, low birth weight (LBW) is mainly associated with low body mass index (BMI) women and reduced GWP, meanwhile macrosomia is mainly associated with high BMI of obese women and excessive GWG. 1,2,3,4,5,6 In Uruguay, more than half of non-pregnant women have overweight or obesity.7 this study aims to describe the nutritional status of Uruguayan pregnant women. **Methods:** Cohort study of women covered by the health care services in years 2010, 2011 and 2012. Information from their first health control in pregnancy to their delivery in public and private maternity hospitals was registered. The national Perinatal Information System (SIP in Spanish) collected all the data. Values are mean (SD) for continuous variables, and frequencies expressed as percentages for categorical variables. **Results:** A sample of 45.257 pregnant women was included with mean age 27.86 ± 6.17 years. GWG 12.77kg ± 4.91, and BMI (24.52 ± 4.5); means of GWG and BMI were normal according to recommendations of the US Institute of Medicine, 2009 (IOM, 2009). Mean values of newborn variables were: 3411.23 ± 432.46 g for birth weight, 39.08 ± 0.99 weeks for gestational age, and 49.18 ± 2.53 cm for birth length. BMI in early pregnancy was positively associated with birth weight. The prevalence of LBW was 16%, being higher in women of normal BMI in early pregnancy (66.1%) and normal GWG 11,90 kg ± 4.36. The prevalence of macrosomia was 9%, being higher among women with normal BMI 46.8% and normal GWG 15.59 ± 4.74. **Conclusion:** The prevalence of LBW and macrosomia had the higher frequencies when BMI and GWG were normal in early pregnancy according to the IOM recommendations, 2009. These results suggest evaluating with other guidelines initial maternal nutritional status.

**Key words:** gestational weight gain, birth weight, maternal weight, body mass index.

## EPI15 - Low Weight at Birth Effect on the Human Capital of Young Adults.

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There is growing evidence that early factors exert influence on human capital in adulthood. Birthweight was important marker for verification of human capital, considering the possibilities of influence in education and work. The goal was to determine the effect of low birth weight in the human capital of young adults. In this prospective longitudinal study, data met coming from the first study of birth cohorts, started 37 years ago in RibeirãoPreto, São Paulo, Brazil. We analyzed all young adults entered the fourth phase of the cohort, aged 23 and 25, totaling 2,063 individuals (31.8% of the original cohort). We used a standard questionnaire that gathered data on socio-economic aspects, family history, risk factors, family and environmental backgrounds. The analysis was based on the verification of the low weight effect in human capital. Therefore, we used modeling with structural equations to determine the effect, adopting a significance level of 5%. human capital was defined as a latent variable composed of income, occupation and education. These steps were performed with the Mplus program version 7.31. Search examined and approved by the Ethics and Research Committee of the HCRP HCFMRP- USP No. 7606/99 process. We obtained data from 2,063 young adults, males (51.5%), white (66.2%), single (67.9%), with 9 to 11 years of education (50.3%), performing activities unskilled manual (23.6%) income of 10 to 20 minimum wages (36.7%). The low weight represented 7.2% of the sample (n = 492) and has had a direct effect on human capital (0.85 / p <0.01) reducing the human capital accumulation in adulthood. The low weight (by direct way) was able to negatively influence the human capital of young adults. This knowledge is essential to measure the health sector to prioritize and address situations that may produce improvements in exhibitions such as low birth weight.

**Key words:** Low weight at birth, human capital.

## EPI16 - Streptococcus mutans in Mother-Child Dyads and Early Childhood Caries: Examining Factors Underlying Bacterial Transmission

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This study investigated the association between colonization of mother-child dyads with Streptococcus mutans (SM) and early childhood caries (ECC) using a theoretical model that included more causally distal variables. Four hundred mothers and their preschool children attending daycare centers in São Luís, Brazil, were included in the study. A diagram based on directed acyclic graphs was elaborated to analyze the association between SM colonization of the mother and child SM and ECC. Other maternal [socioeconomic, waist circumference (WC), sugar consumption, DMFT index, and visible plaque] and child factors [sugar consumption, visible plaque, and child age] composed the theoretical model. A total effect model (maternal SM on ECC) and a direct effect model adjusted for the mechanism of SM transmission (maternal SM via child SM on ECC) were analyzed by Poisson regression. The Paramed test was used to analyze mediation. The following variables were associated with ECC in the total effect model: maternal SM, maternal WC ≥ 80cm, DMFT, maternal visible plaque, child age ≥ 4 years, and increased sugar consumption of the child (> 3 times/day). In the direct effect model, high maternal SM levels remained associated with ECC; while moderate and high colonization of the child with SM was also associated with ECC. Child SM colonization just partially mediated the effect of maternal SM on ECC (33%). Factors other than transmission of these microorganisms, including obesogenic factors, sugar consumption, hygiene practices and a family history of caries, should be considered in mother-child interactions linked to ECC.

**Keywords:** Early childhood caries, *Streptococcus mutans*, mother-child interactions, epidemiology.
**Financial Support:** FAPEMA.

## EPI17 - Association Between Pre Natal and Postpartum Maternal Depression and Child Malnutrition or Excess Weight.

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**Background:** The prevalence of overweight and obesity has increased worldwide. This trend is also observed among children. The role of maternal depression on child development has been studied. Studies show that about one-fifth of women during pregnancy have depressive symptoms. AIM: To verify the association between prenatal and postpartum maternal depressive symptoms with malnutrition or excess weight among children. **Methods:** It's a prospective study with data from the BRISA Prenatal Cohort in São Luís - MA, obtained in 2009/10 when the women were with 22 to 25 weeks of gestational age and in 2010/12 when the children were with 12 to 32 months of age. Maternal depressive symptoms were identified by the Center for Epidemiologic Studies Depression Scale (CES-D) ≥ 22 points (prenatal) and by the Edinburgh Postnatal Depression Scale (EPDS) ≥ 12 points. In the evaluation of the excess weight we used the BMI for age z-score> +2 and for child malnutrition we used the Z score of height for age < -2. Confounding factors were identified in directed acyclic graphics made in the DAGitty program. To estimate the association between the maternal depressive symptoms and the nutritional status of the children we used the $\chi^2$ test (chi2), with a significance level of 0,05 and logistic regression models. **Results:** The prevalence of prenatal maternal depressive symptoms was 17.6% and in the postpartum period 19.8%. The malnutrition rate was 6% and the excess weight rate was 10.9%. Prenatal depressive symptoms weren't associated with malnutrition (OR 1,09; CI 0,62 – 1,89) or excess weight (OR 0,84; CI 0,54 – 1,31). Postnatal depressive symptoms were also not associated with malnutrition (OR 0,96; CI 0,51 – 1,80)

or excess weight (OR 1,07; CI 0,67 – 1,71). **Conclusions:** We didn't find evidence that prenatal or postpartum maternal depressive symptoms influence malnutrition or excess weight in the children.
**Key words:** Depression, malnutrition, overweight, infant, pregnant women

**Financial Support:** Fundação de Amparo à Pesquisa do Estado de São Paulo grant 2008-53593-0; Conselho Nacional de Desenvolvimento Científico e Tecnológico 471923/2011-7 e 561058/2010-5; Fundacão de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão grants 0035/2008, 00356/11 e 01362-11.

# 5TH INTERNATIONAL SYMPOSIUM ON METABOLIC PROGRAMMING AND STRESS AND THE 2ND MEETING OF IBERO-AMERICAN DOHAD CHAPTER

# EXPERIMENTAL SESSION

## EXP01 - Maternal Time Restricted Feeding Programs Glycemic Dysfunction in Adult Rat Offspring.

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**Background/Aims:** Time restricted feeding during the wrong phase can cause circadian rhythm disruption; and this behavior is associated with the onset of obesity and metabolic dysfunction. Cardiometabolic diseases can be programmed at an early phase of development. Gestation is very sensitive window for programming. Thus, the aim of this work was to verify whether time restricted feeding during the active phase (dark) or resting phase (light) in rats could program the metabolism of the offspring to metabolic diseases onset latter in life. **Methods:** Female Wistar rats with 70 days-old were bred with male rats with 80 days of life. The pregnant rats were randomly assigned in 3 experimental protocols: Normal phase group (free access of normal commercial diet all day-NP) light phase group (access of normal commercial diet only during the light phase-LP) and dark phase group (access of normal commercial diet only during the dark phase-DP). After deliverance, dams had free access to commercial chow during all day. After weaning offspring received ad libitum normal commercial diet until 180 days-old. With 150 days of life, part of animals were submitted to the intolerance intraperitoneal glucose test (ipGTT) and insulin tolerance test (ipITT). The other rats from both groups were euthanaized at 180 days. **Results:** Restriction feeding during light and dark phase did not alter the body weight of males and females offspring at 180 days of age. LP and DP increased fasting glycemia in males and females. Males showed glucose intolerance in DP and LP groups compared to NP group; while females had greater susceptibility to glycemic dysfunction than males. The insulin tolerance test showed an increase in insulin sensitivity for DP and LP groups in males and females. **Conclusion:** Time restricted feeding during gestation programs glycemic dysfunction in offspring adulthood to both sex; however, female showed more susceptibility to programming than male rats.

**Keywords:** Time restricted feeding, pregnancy, glucose intolerance, circadian rhythm, metabolic programming.

**Financial Support:** CNPq, CAPES.

## EXP02 - IUGR associated with palatable diet leads to differential food memory and insulin resistance in rats.

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Intrauterine growth restriction (IUGR) is associated with insulin resistance (IR), preference for palatable foods, and changes in hypothalamus and hippocampus. Possibly, this insulin imbalance is centrally changing the dietary pattern on IUGR. Here, metabolic profile and memory related to food were analyzedin rats induced to IUGR associated with a palatable diet. On 10th day of pregnancy, rats were divided into control group (Adlib), which continued with standard chow ad libitum, and experimental group (FR), which received 50% of the chow intake of Adlib. At birth, male pups were adopted by Adlib mothers and, at 60 days, half of offspring from each group received diet rich in fat and sucrose (HFS) and half continued with standard diet (CON). At 140 days, behavioral tasks started. At 200 days of age, animals were killed with 4h of fasting. Animals were weighed weekly and abdominal fat, on the day of death. During all the experiment, there was interaction between time, diet and IUGR in evolution of body weight. There was no effect of IUGR, diet, neither interaction between them in time on periphery and in crossing on open field, and in new object/food recognition indexes. All groups explored more the new object and FR-HFS group was the only one to explore more the new food. On chocolate localization task, HFS took more time and ate less chocolate. Abdominal fat, triglycerides, glucose and serum leptin were higher in HFS. Insulin and HOMA-IR were higher in HFS and there was a tendency to interaction between diet and IUGR. There was an interaction between diet and IUGR and isolated effects of them in hypothalamic SOCS3 concentration. It seems that IUGR associated with palatable diet leads to differential food memory andperipheral and central IR. Hippocampal analyzes are being made to better understand this altered eating behavior.

**Keywords:** Eating behavior, metabolism, hippocampus, hypothalamus, fetal restriction.

**Financial support:** CNPq and FIPE/Hospital de Clínicas de Porto Alegre.

## EXP03 - Glucose homeostasis and insulin secretion in adult off spring after maternal Roux-en-y gastric bypass operation.

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Maternal obesity has negative consequences on female health and in the development of offspring. Interventions that reduce obesity and improve the metabolic health of the mother will have long-lasting impact of childhood health and adult health. Roux-en-Y gastric bypass (RYGB) operation is the most effective procedure for sustained weight loss. Herein we investigated the effect of maternal RYGB in obese rats by cafeteria diet and its relationship with glucose homeostasis of the adult offspring. Female Wistar rats were allocated in two groups: control (CTL) and western diet (WD) which received standard and cafeteria diet for 15 weeks, respectively. Then, WD group was submitted to sham-operation (WD-Sham) or RYGB operation (WD-RYGB). Five weeks after surgery, female rats were housed with single male rats for mating period. The offspring was designated as the treatment of mother. The glucose tolerance test, fasting glycemia and plasma insulin followed by insulin secretion were verified in adult offspring on 120 days of life. Fasting glucose and glucose tolerance were similar between the groups. However WD-Sham-F1 were hyperinsulinemic showing an increase the plasma insulin levels compared to CTL-F1. WD-RYGB-F1 demonstrated partial reduction of plasma insulin levels compared to WD-Sham-F1. When we evaluated the release of insulin at a stimulatory glucose concentration, 8.3, 11.1 and 27.0mM, did not differ between CTL F1, WD-Sham-F1 and WD-RYGB-F1 islets. Nonetheless, in the presence of 16.7, 22.0mM glucose, insulin secretion was 30% and 35% higher, respectively, in WD-Sham than in CTL-F1 islets. RYGB-F1 operation partial reduction insulin release in response to 16.7 and 22.0mM glucose compared to WD-Sham-F1 islets. Although fasting glucose and glucose tolerance were similar between the groups, WD-Sham-F1showed increased plasma insulin levels and presented higher insulin secretion at 16.7 and 22.0mM glucose. The maternal RYGB operation provides partial improvement in the plasma insulin levels and insulin secretion.

**Keywords:** Maternal obesity, Roux-en-Y Gastric Bypass operation, insulin secretion.

**Financial Support:** Capes, CNPQ, Fundação Araucária.

## EXP04 - Effect of a Maternal Low Protein Diet During Gestation in Gene Expression of Transcriptional Factors PDX1 and MafA in Pancreatic Islets of Male Rat Offspring.

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Protein restriction during gestation causes several damages in endocrine pancreas of the offspring, such as impaired glucos estimulated insulin secretion. Wehave shown previou sly that maternal low protein diet during gestation in creases insulin gene expression. Theaim of this work was to study the effect of a maternal low protein diet in the expression of transcription al factors Pdx-1 and MafA in the pancreas of the offspring, which are involved in development and maintenance of beta cell and are necessary for regulation of insulin gene. We studied male offspring at postnatal days (PND) 36 and 90 from rats fed control (C: 20% casein) orrestricted (R: 10% casein) diet during pregnancy. Islets isolation was performed by collagenase digestión then, total RNA was extracted and gene expression of Pdx-1 and MafA was assessed by qPCR. Blood insulin was quantified by radioimmunoassay and fasting serum glucose was measured using the hexokinase method. Blood insulin concentration was significantly higher at PND 90 than in PND 36, while there were no changes in glucose concentration, this data could suggest there is insulin resistance in olderrats. At 36 PND, levels of mRNA of MafA and Pdx-1 were significant ly higher in R group compared to C group, while at PND 90 there were no changes between groups. These results could suggest that at PND 36 there is an adaptation mechanism to survival increasing the expression of these genes in R groups to up regulate insulin expression to reach normal levels. Itis known nutritional stimulican modify DNA methylation, and itcould be one of the mechanisms that regulate expression of these transcription alfactors, in this regard, further investigation is needed and is currently under way in our laboratory.

**Keywords:** Protein restricted diet, rat, gene expression, pancreas.

**Financial Support:** CONACYT (National Council of Science and Technology, Mexico) CB177624.

## EXP05 - Early Chronic Treatment With Glibenclamide Blocks Metabolic Dysfunctions Onset and Improves Vagus Nerve Hypertonia in Obese MSG-rats.

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**Background/Aims:** Glibenclamide is an antidiabetic used in the treatment of type 2 diabetes. This sulphonylureia stimulates insulin secretion from pancreatic beta cells Autonomic nervous system (ANS) imbalance is associated with metabolic diseases. There is scarce data concerning ANS activity in diabetic patients, treated with glibenclamide. The goal of this work was to test whether glibenclamide can improve ANS activity and the muscarinic acetylcholine receptors subfamily M3 (M3AChR) functionality in pre-diabetic-rats. **Methods:** Pre-diabetes was induced by treatment with monosodium L-glutamate (MSG) in neonatal rats. MSG and control groups were treated with glibenclamide (2 mg/kg body weight/day), from weaning to 100-day-old. After the end of glibenclamide treatment, animals were sacrificed to biometric and biochemical evaluation. The vagus and sympathetic nerve electrical activity were recorded. Insulin secretion was measured in isolated islets challenged with glucose, acetylcholine and selective antagonist to M3AChR. **Results:** Glibenclamide treatment prevented the onset of obesity, insulin resistance, hyperinsulinemia and glucose intolerance; normalized parasympathetic activity, and increased the glucose and cholinergic insulinotropic effect and decreased the activity of M3AChR in islets from MSG groups. **Conclusion:** Although; glibenclamide, as a sulphonylureia that classically has a target pancreatic beta-cell to enhance insulin secretion, early glibenclamide treatment prevents metabolic dysfunction in pre-diabetic MSG-rats, associated to improvement of ANS and beta-cell activity.

**Keywords:** Glibenclamide, autonomic nervous system, MSG, pre-diabetic rats, hyperinsulinemia.

F**inancial Support:** Brazilian agencies:CAPES and CNPq.

## EXP06 - Caloric Abundance Is a Trigger to Show Later Disruption in Offspring Metabolism from Mothers Malnourished During Later Pregnancy.

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**Background/Aims:** Nutritional insult throughout gestation and lactation periods can program to long-term obesity and metabolic dysfunction in offspring, particularly when they are nourished with a hypercaloric diet during early postnatal life, constituting long periods of insults and therefore the consequences are easily observed. However, dependent on maternal period and insult types it can provoke different phenotypes and sometimes no dysfunction is observed in adult offspring. In the present study, we aimed to assess whether metabolic dysfunction induced by high fat diet in adulthood can be aggravated by malnutrition induced by protein-caloric restriction diet during late gestation in rats. **Methods:** Rat dams at last 1/3 pregnancy, received low protein diet (4%; LP group). Controls received normoprotein diet (23%; NP group). After birth, dams and their offspring from both groups consumed standard diet (C). Male offspring with 60-days-old of both groups were submitted to C diet or high fat diet (HFD; 35% of lard). At 90-days-old, body weight, food intake, fat tissue accumulation, glucose and insulin homeostase tolerance and insulin secretion by isolated pancreatic islets were evaluated. The vagus and sympathetic nerve electrical activity was recorded to evaluate autonomous nervous system (ANS) function. **Results:** Maternal protein-caloric restriction diet provoked low birth weight of pups (-30%; $P<0.05$). However, at weaned no difference among groups was observed in BW. Adult animals from both groups submitted to HFD presented obesity associated to altered insulin secretion in vitro, glucose intolerance, hyperinsulinemia, insulin resistance, hypertriglyceridemia, hypercholesterolemia and high parasympathetic activity, ($P<0.05$); however, LP-HFD showed low sympathetic tonus and higher magnitude of dysfunctions than NP-HFD ($P<0.05$). Conclusion: Malnutrition during later pregnancy program offspring for metabolic dysfunction almost revealed on abundance caloric offer. Metabolism impaired might be associated to pancreatic beta-cell and ANS imbalanced function.

**Keywords:** Late pregnancy, malnutrition, metabolic programming, hypercaloric diet, rats.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) andthe Paraná Science Foundation (Fundação Araucária).

## EXP07 - Intrauterine Growth Restriction Increase Contratile Response Offspring: Possible Role of NO.

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**Objective:** To evaluate the effects of intrauterine growth restriction (IUGR) in vascular reactivity in carotid female adult offspring. Methods: Pregnant Wistar rats received ad libitum or 50% of ad libitum diet throughout gestation. At birth, pups were

weighted. Indirect blood pressure (BP) was evaluated in adult female offspring (14 age) from both groups in estrus cycle. Foll study. Concentration-response curves to Acetylcholine (ACh: 10 10-9M-10-6M), and Phenylephrine (Phe 10 inhibitor (L-NAME 10-4 M). Results are show the mean ± SD, AUC test were used to analyze the vascular reactivity (CEUA: 479028). Results: Body weight at birth (C: 7.01 ± 0.34g vs. R: 4.3 ± 0.08g), confirmed IUGR. IUGR increased BP levels (C: 122 ± 4mmHg; R: 130± 2mmHg). Restricted group exhibited normal vascular response to ACh (C: 321.1 ± 118.6 vs. R: 311.3 ± 137.9). There were differences in the vascular vasodilatation (C: 592.0 ±70.42 vs R: 688.9 ± 76.83) and the contract the restricted group had higher vasoconstriction compared to the control group (C: 2.98 ± 0.80 vs R: 4.34 ± 1.57). On the other hand, when it was added L both groups (C: 8.82 ± 2.64 vs R: 8.91 ± 3.38). Conclusion: Our data suggests that IUGR leads to increase the contractile response to phenilephrine, at least in part due to changes on NO pathway, as inhibition of NOS resulted in similar contractile response in both groups.

**Keywords:** Intrauterine growth restriction, carotid artery, contractile response, nitric oxide, phenilephrine.
**Financial Support:** FAPESP, CNPq.

## EXP08 - Parental Obesity Programs Pancreatic Islet Dysfunction in Male Rat Offspring.

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**Background/Aims:** Pancreatic beta-cell has been consider one target of metabolic programming. Parental obesity is associated with the transmission of obesity to their offspring. The aim of this work was to investigate whether parental obesity programs insulin secretion dysfunction in their adult offspring. **Methods:** Normal litter rats were bred and the offspring was divided in two groups, Normal Litter (NL) and Small Litter (SL). This offspring were bred at 90 Days Old (NL vs NL; SL vs SL; different parents and litters) and had their offspring separated in four experimental groups, normal litter offspring from normal litter (NLNL), small litter offspring from normal litter (NLSL), normal litter offspring from small litter (SLNL) and small litter offspring from small litter (SLSL). At 90 days old, the animals were euthanized and their pancreatic islets were isolated by the collagenase method. The islets were incubated with different muscarinic and adrenergic receptor agonists and antagonists to study their effects on insulin secretion. **Results:** Early overfeeding induced by litter size reduction (SL) lead to metabolic dysfunction and obesity. It was observed an increased insulin secretion in isolated pancreatic islets stimulated by different glucose concentrations in SL groups when compared to NL groups. Cholinergic response was reduced in SL-groups when compared with NLNL. Using M3 muscarinic receptor antagonist, 4-DAMP, cholinergic response of islets from SL-groups was more inhibited than NL-rats. The adrenergic inhibition of insulin secretion was increased in islets from NLSL, but parental obesity lead to a reduction in the adrenergic response. Using yohimbine, a blocker of adrenergic Alpha2 receptor, adrenergic secretion response was diminished by parental obesity, independent of early overfeeding, suggesting a sympathetic dysfunction. **Conclusion:** Parental obesity programs progeny to obesity associated to increase glucose-induced insulin secretion and disrupting reception of autonomic signals in pancreatic beta-cell.

**Keywords:** Pancreatic islets, parental obesity, metabolic programming, insulin.
**Financial Support:** CNPq, CAPES.

## EXP09 - Altered urinary sodium excretion response after central adrenergic microinjection in lateral cerebral ventricle of gestational protein-restricted offspring.

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**Background:** The gestational low protein diet in rat models leads to low birth weight and reduced nephron number that has been related to development of arterial hypertension and end-stage renal disease in adulthood life. Although not fully elucidated various mechanisms has been identified as directly or indirectly involved in the genesis of renal disorders. Previous studies have shown that change in salt and water metabolism with sodium retention is involved in this process. Since the kidney is the main hydroelectrolyte control organ and its function is thoroughly modulated by the nervous system, sympathetic neural alterations may have a key role on arterial hypertension development. **Aims:** This study evaluates the implications of intracerebroventricular (ICV) noradrenergic microinjection, mediated by α-adrenoceptors, on blood pressure and urinary sodium excretion in gestational protein-restricted adult male offspring. **Methods:** In adulthood, these offspring underwent an intracerebroventricular cannula implantation towards microinjection of α1 and α2 adrenoceptors antagonists during the evaluation of blood pressure and renal function by creatinine and lithium clearances. **Results:** The low-protein (LP) offspring showed significant reduction in the birthweight and increased systolic blood pressure compared to control (NP) group. Also, the central sympathomimetic stimuli by epinephrine before α2-blockade with Yohimbine (YOH) promoted marked antidiuresis associated with increased natriuresis in LP compared to NP group. This effect was blockage by Prazosin. The study also shows that renal sodium retention occurs in the proximal and post-proximal nephron segments without changes in glomerular filtration. In programmed offspring, the increased natriuresis and antidiuresis response to YOH occurs, at least in part, by increased activity and/or number of central α2-adrenoceptors, alone or in conjunction with changes in α1-adrenoceptors-mediated signaling in the central nervous system in programmed animals. **Conclusion:** Here, we demonstrated that changes in central catecholaminergic modulation might play an important role in the hypertension development in gestational protein-restricted offspring.

**Keywords:** Fetal programming, gestational protein restriction, arterial hypertension, renal function, central catecholaminergic stimuli.
**Financial Support:** Fapesp: 2013/20539-1 and 2013/12486-5.

## EXP10 - N-Acetylcysteine, a Glutathione Precursor, Reverses Vascular Dysfunction and Endothelial Epigenetic Programming in IUGR Guinea Pigs.

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**Background/aims:** In humans, intrauterine growth restriction (IUGR) is associated with vascular dysfunction, oxidative stress and signs of endothelial programming of the umbilical vessels. We aim to determine the effects of maternal antioxidant treatment with N-acetyl cysteine (NAC) on fetal endothelial function and eNOS programming in IUGR guinea pigs (GP). **Methods:** Pregnant GP at mid gestation were submitted to a surgery for implanting ameroid constrictors on both uterine arteries (IUGR). Half of the sows of each group received NAC (500mg/Kg/day) in the drinking water starting at day 34 until term (~ 60 days). Fetal biometry and umbilical artery resistance were followed by ultrasound. At term, fetuses were extracted by C-section, dissected and weight. Umbilical arteries and fetal aorta were isolated to assessed vascular function by wire-myography. Primary cultures of endothelial cells from fetal aorta, femoral and umbilical arteries were performed to determine the levels of eNOS mRNA by qPCR and analyze the DNA methylation of 12 CpG sites in Nos3 promoter by pyrosequencing. **Results:** Doppler ultrasound measurements showed that NAC reduced placental vascular resistance in IUGR and this effect was associated with a recovery in fetal weight and increasing fetal-to-placental ratio at term (~40%) compared with untreated IUGR. Additionally, NAC restored eNOS-dependent relaxation determined by wire myography in aorta and umbilical arteries, and normalized eNOS mRNA levels in primary cultures of endothelial cells (EC) from aorta, femoral and umbilical arteries. Pyrosequencing analysis showed that IUGR-derived EC have a decreased methylation (~30%) at CpG -170 (from the TSS) and this epigenetic signature was absent in fetuses treated with NAC. **Conclusions:** These data show that IUGR-EC have common molecular markers of programming in umbilical and systemic arteries. Notably, maternal treatment with NAC restores fetal growth by increasing placental efficiency and reversing the functional and epigenetic programming of the endothelium in IUGR GP.

**Keywords:** Endothelial function, epigenetics, eNOS, IUGR.
**Financial Support:** Funded by grants nº 1130801 and 115119 from the National Fund for Scientific and Technological Development (FONDECYT-Chile).

## EXP11 - Early and sustained exposure to high-sucrose diet triggers hippocampal ER stress in young rats.

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**Background:** Early-life environmental insults have been shown to promote long-term development of chronic non-communicable diseases, including metabolic disturbances and mental illnesses. As such, premature consumption of high-sugar foods has been associated to early onset of detrimental outcomes, whereas underlying mechanisms are still poorly understood. Aims: In the present study, we sought to investigate whether early and sustained exposure to high-sucrose diet promotes metabolic disturbances that ultimately might anticipate neurological injuries. **Methods:** At postnatal day 21, weaned male rats started to be fed a standard chow (10% sucrose, CTR) or a high-sucrose diet (25 % sucrose, HSD) for 9 weeks prior to euthanasia at postnatal day 90. **Results:** HSD did not alter weight gain and feed efficiency between groups, but increased visceral, non-visceral and brown adipose tissue accumulation. HSD rats demonstrated elevated blood glucose levels in both fasting and fed states, which were associated to impaired glucose tolerance. Peripheral insulin sensitivity did not change, whereas hepatic insulin resistance was supported by increased serum triglyceride levels, as well as higher TyG index values. Assessment of hippocampal gene expression showed endoplasmic reticulum (ER) stress pathways were activated in HSD rats, as compared to CTR. HSD rats had overexpression of unfolded protein response sensors, PERK and ATF6; ER chaperone, PDIA2 and apoptosis-related genes, CHOP and Caspase 3; but decreased expression of chaperone GRP78. Finally, HSD rats demonstrated impaired neuromuscular function and anxious behavior, but preserved cognitive parameters. **Conclusions:** Our data indicate that early exposure to HSD promote metabolic disturbances, which disrupt hippocampus homeostasis and might precociously affect its neurobehavioral functions.

**Keywords:** High-sucrose diet, metabolic syndrome, unfolded protein response, neurological impairment, developmental origins of health and disease (DOHaD).
**Financial Support:** Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão – FAPEMA and Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq.

## EXP12 - Rat Maternal Obesity Programs Male Offspring Fat Cell Size: Effects of Maternal or Offspring Exercise.

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**Background:** Maternal Obesity (MO) leads to offspring adverse metabolic disturbances, which can be reduced by Maternal Exercise (MEX) or Offspring Exercise (OEX) interventions. Increased Fat Cell Size (FCS) has been

related to dyslipidemia and insulin resistance. Offspring from obese mothers exhibit increased adiposity with greater and heterogeneous FCS. However, the effects of MEX or OEX interventions over offspring FCS heterogeneity has not been established. **Aim:** Determine by statistical distribution analysis the FCS heterogeneity in offspring of obese mothers with MEX or OEX interventions. **Methods:** Female Wistar rats were weaned whether on chow (C) or high energy obesogenic diet (MO), and bred at Postnatal Day (PND) 120; half of each group was assigned to MEX intervention from PND 90 until the end of pregnancy. Male offspring from all groups (n=8 litters/group) were weaned to C diet at PND 21 (C, C-MEX, MO and MO-MEX ). One male of C and MO litters received OEX intervention from PND 50 to 110 (C-OEX and MO-OEX). Males were euthanized at PND 110, Adiposity Index (AI=Total Visceral Fat Weight×100/Body Weight) calculated, FCS determined as cross sectional area in retroperitoneal adipose tissue histologic slides and characterized by gamma distribution scale parameter (data spreading) and shape parameter (large/small adipocyte proportion). **Results:** Increased AI and FCS in MO offspring were reduced by MEX and OEX. However, increased FCS spreading in MO offspring was only reduced by OEX and higher proportion of large adipocytes in MO was reduced by MEX and OEX. **Conclusions:** The data spreading in MO group suggests a lack of FCS regulation, that can be modified by OEX. Moreover, the increased proportion of large adipocytes suggests an increase in adipocyte differentiation, that was prevented by MEX and compensated by OEX. These findings suggest that MO programming of FCS has several mechanisms regarding adipocyte proliferation and differentiation.

**Keywords:** Fat cell size, Exercise

## EXP13 - High-Fat Diet during Adolescence in Male Rats Promotes Increased Adiposity in Adulthood: Effect of Exercise Intervention.

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**Background:** Adverse metabolic disorders can be post natally programmed, during several stages of development, such as adolescence. However, theeffects of dietary habits related to obesity during the adolescence window over adult physiology and metabolism are not well established, and even more whether later exercise intervention could counter balance the adverse adolescence metabolic programming. **Aim:** To evaluate the effects of High-FatDiet (HFD) during adolescence and laterexercise intervention over adult physical fitness, insulin resistance and adiposity. **Methods:** Male adolescent Wistar rats were fedwith Normal Fat Diet (NFD=Fat 5%) orwith HFD=Fat 30% from Postnatal Day (PND) 32 until PND 62. Body Weight (BW), food and energy in take were determined weekly. After PND 62 untiltheend of experiment, both group sreceived NFD and from PND 70 to 100 weres plitin to sedentary (SED) groups (NDF-SED and HFD-SED) and exercised (EXC) group swith 50 min of treadmill training/day/3 times/week (NFD-EXC and HFD-EXC). Around PND 100, physical fitness was evaluated by their maxima loxygenup take (VO2 max), intravenousglucose tolerance test was performed and Adiposity Index (AI=total visceral fat weigthx100/BW) calculated in euthanized males (n=9-10/group). Different letters denotes P<0.05. **Results:** Food and energy in take were lower in HFD group during adolescence (P<0.05 from PND 32-50). However, after adolescence BW washigher in the HFD-SED and HFD-EXC groups. Around PND 100, VO2 max in NFD-EXC was high erthan NFD-SED, while in HFD-EXC was similar to HFD-SED. Glucose tolerance waslower in HFD-SED and HDF-EXC. Increased AI in HFD group was parti ally reducedby EXC, (NFD-SED=2.9±0.2a, NFD-EXC=2.5±0.1a, HFD-SED=3.9±0.3b, HFD-EXC=3.4±0.2c). **Conclusions:** HFD during adolescence programs deficient physical conditioning, reduce dglucose tolerance and excessive fat accumulation in adulthood. However, moderate intensity exercise prior to adultho odonsetisable to reduce partial lythein crease dadiposity program medduring adolescence, which could be linked to a better lipid metabolism.

**Keywords:** Adolescence, High-Fat Diet, Adiposity, Exercise.

**Financial Support:** CA. Ibáñez-Chávez received an international fellowship from Programa Latino americano para la Investigación en Salud Sexual y Reproductiva (PLISSER).

## EXP14 - Early onset of Non-Alcoholic Fatty Liver Disease and transition to Non-Alcoholic Steatohepatitis in monosodium L-glutamate-induced obese mice.

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**Introduction:** Monosodium L-glutamate (MSG)-induced obese rodents have been largely used in pre-clinical tests investigating drugs, extracts or probiotics effects on nonalcoholic fatty liver disease (NAFLD)/ nonalcoholic steatohepatitis (NASH), whereas there are few studies focusing on the underlying mechanisms for this condition on this model. Besides, there is no agreement about at what age NAFLD/NASH onset is triggered. This study aimed to characterize the time-course of NAFLD features and its progression to NASH in MSG obese mice. **Methods:** Pulps of Swiss mice 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. Thereafter, each group was divided to three subgroups. Animals was weighted twice a week and took the Lee' Index every thirty days. They were euthanized at 60, 120 or 180 living days, according their subgroups, and samples of serum, liver and periepididymal and retro-abdominal fats were collected.Fats and liver were weighted, serum biochemistry evaluation was taken and samples of liver were used to ascertain the lipid profile and histopathological analysis. **Results:** MSG-induced obese mice developed hypertriglyceridemia and obesity, but only 120 and 180 days

old mice were diabetic with statically difference in TyG value. The serum and hepatic cholesterol values had no difference between MSG and lean group, such as serum cytokines concentration. The histopathological analysis showed that 60 days old MSG-mice had microvesicularsteatosis with rared ballooning, while 120 old ones had NASH. 180 days old MSG-mice had NASH and enhance of hepatic triglycerides in relation to 120 days old ones. **Conclusion:** These results show that MSG-induced obesity causes nonalcoholic fatty liver disease in young animals, which promptly evolves to NASH. However, there is still a gap concerning the main molecular targets involved in this pathophysiological mechanism.

**Keywords:** Non-alcoholic fatty liver disease, monosodium L-glutamate, obesity, non-alcoholic steatohepatitis, metabolic syndrome.

**Financial Support:** FAPEMA, CNPq.

## EXP15 - Metformin early treatment inhibits obesity onset and improves autonomic nervous system in pre-diabetic rats.

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**Background/Aims:** Metformin is an antidiabetic used currently for metabolic syndrome treatment. Autonomic nervous system (ANS) imbalance is associated with metabolic diseases. The aim of study was to test whether chronic metformin treatment could improve ANS activity in pre-diabetic rats. **Methods:** Pre-diabetic rats were obtained by neonatal treatment with monosodium L-glutamate (MSG), 4 mg/Kg body weight during the first 5 days of life. Metformin was gavaged, 250 mg/kg body weight/day, from weaning to 100-days-old. Controls received saline. After treatment, animals were sacrificed to biometric and biochemical evaluation. Electrical activity of superior vagal and sympathetic nervous were recorded. **Results:** While, metformin treatment decreased hyper vagal activity, sympathetic one was increased in MSG rats. Insulin secretion stimulated by glucose in isolated islets was increased in MSG rats; while, acetylcholine (Ach) induced lower insulin release. Metformin treatment did not change glucose insulinotropic response; however, cholinergic response increased. Insulinostatic effect of M3mAChR selective antagonist was significantly high in both groups. Although, M2mAChR selective antagonist decreased cholinergic response in metformin treated MSG-rats; response in islets from MSG untreated animals was increased. **Conclusion:** Chronic metformin treatment was effective to alleviate obesity, leading to an ANS activity balanced in pre-diabetic rats.

**Keywords:** Metformin, MSG, pre-diabetic rats, obesity, insulin secretion.

**Financial Support:** CAPES and CNPq.

## EXP16 - Pancreatic islet morphometry in adult offspring after maternal roux-en-y gastric bypass operation in obese rats.

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**Introduction:** Fetal exposure to maternal obesity increases the prevalence of obesity in childhood and adulthood, besides acting negatively in physiology and metabolism of offspring. Roux-en-Y gastric bypass (RYGB) operation is the most effective procedure for sustained weight loss. The question is whether RYGB can reverse the deleterious effects of obesity in female health and subsequent offspring. **Objectives:** Here, we evaluated the morphology and morphometry of pancreatic islets in the male offspring from obese dams submitted to RYGB. **Methods:** Female Wistar rats were allocated in two groups: control (CTL) and western diet (WD) which received standard and cafeteria diet for 15 weeks, respectively. Then, WD group was submitted to sham-operation (WD-Sham group) or RYGB operation (WD-RYGB group). Five weeks after surgery, females rats were housed with single male rats for mating period. The offspring was designated as the treatment of mother. The pancreases were used for immunohistochemistry for insulin or glucagon (120 days of life). **Results:** The pancreas weight, pancreatic islet architecture and islets mass were similar in all groups. The area and β-cell mass was similar between WD-Sham-F1 and CTL-F1 animals. However, WD RYGB-F1 rats showed an increase of 17% in β-cell area compared to WD-Sham-F1, without alterations in β-cell mass ($P < 0.05$). Although the α-cell mass did not alter in WD-Sham-F1 animals compared to CTL group, these animals displayed a reduction of 26% in α-cell area ($P < 0.05$). No alteration was observed in this parameter in WD-RYGB-F1 offspring than WD-Sham-F1 group. The distribution of the number of islets by size was not altered in all experimental groups. **Conclusion:** Offspring from WD-Sham dams presented a reduction in α-cell area while WD-RYGB-F1 offspring showed an increase in β-cell area.

**Keywords:** Maternal obesity, metabolic programming, bariatric operation.

**Financial Support:** CAPES, CNPq, Fundação Araucária

## EXP17 - Metabolic and reproductive profile of obese rats treated with Syzygiumcumini (L.) SKEELS.

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**Background:** Metabolic syndrome (MS) is defined as a set of interrelated risk factors that contribute to type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). MS also causes the harmful effects on the reproductive system, especially for women, reducing ovulatory rates, increasing the number of abortions, late pregnancy complications, which increase the risk of infertility. **Aim:** Through these actions, we sought to investigate whether the hydroalcoholic extract of the leaves of S. cumini (EHSyz) improves the metabolic changes and consequently, changes in reproductive function in rats with induced obesity L-monosodium glutamate (MSG). **Methods:** Wistar female newborns rats were induced obesity L-monosodium glutamate (MSG 4g/Kg/day) for 10 day. Divided into the following groups: CTRL group (treated with NaCl 0.9% 0.1 ml / 100g / day v.o,); MSG group (treated with NaCl 0.9% 0.1 ml / 100g / day V.O.); EHSyz obese group (treated with EHSyz at a dose of 500mg / kg / day, V.O.), each for 60 days. **Results:** The administration EHSyz promoted retention of weight gain, reduction Lee index and improved glycolipid profile, with reduced serum triglyceride levels by 60.7% and 29.7% compared to cholesterol total ($p < 0,05$). The EHSyz even avoided introduction resistance table in the treated rats. However, despite the improvement in oligociclicidade, the extract was not able to improve reproductive impairment of the treated rats. **Conclusion:** Thus, we conclude that treatment with EHSyz produced marked effects on metabolic parameters in obese rats without interfering with the reproductive capacity of the same.

**Keywords:** Fertility, metabolic syndrome, L-glutamate monossodic, alternative medicine, jambolan.
**Financial Support:** CAPES, FAPEMA and CNPq.

## EXP18 - Maternal Exposure to Fluoxetine Alters Nitric Oxide and Prostacyclin Pathways Leading to Decreased Aortic Contraction.

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Fluoxetine (FLX) is prescribed during gestation and lactation for depression and anxiety disorders' treatment. Recently, we demonstrated that maternal FLX treatment during gestation and lactation causes aortic hypo-contraction and increases plasmatic nitric oxide (NO) levels in adult female rat offspring. The study's aim was elucidate the mechanism involved in aortic hypo-reactivity induced by FLX exposure. Wistar female rats were gavaged daily with FLX (5mg/kg/day) or water (CTL) during pregnancy and lactation. In adult female offspring, thoracic aorta was removed and cut in two rings, with (E+) and without (E-) endothelium. Cumulative curves to phenylephrine (Phe-1nM-30μM) were constructed in absence or presence of: L-NAME (1μM), L-NIL (1μM), catalase (100U/mL), indomethacin, (INDO-10μM), NS-398 (1μM) or tranylcypromine (tranyl-10μM). NO was measured in plasma, Griess method. Aortic expression of endothelial NO synthase (eNOS) and COX1 were assayed, Western blot. Results expressed as mean±SEM, (n) is the number of rats/group. For Phe, results were expressed as maximal response (Rmax, grams). Statistical analysis: one or two-way ANOVA and Tukey's test, $p<0.05$. E+ aortic rings from FLX rats (1.52±0.11 (10)) presented reduction in Rmax to Phe comparing to CTL (2.47±0.19(10)). Endothelium removal increased vasoconstriction, eliminating difference between groups (CTL=3.12±0.17 (10) vs FLX=3.30±0.26 (10)). L-NAME increased the Rmax to Phe in both groups, (CTL=3.20±0.20 (7); FLX=2.97±0.33 (7)). Neither L-NIL, catalase nor NS-398 interfered with vasoconstriction. INDO (CTL=2.14±0.08 (7) vs FLX=2.27±0.12 (7)) and tranyl (CTL=2.22±0.23(7) vs FLX=2.23±0.28(7)) increased the Rmax to Phe in FLX rats, equaling Rmax between CTL and FLX. NOx levels were increased in FLX group (5.7±0.40nM (8)) compared to CTL (3.8±0.22nM (7)). There was no difference in eNOS and COX1 aorta's expression. Intrauterine and neonatal FLX exposure causes reduction in aortic contractile response in female adult offspring, involving endothelium, NO and prostanoids, probably through eNOS and COX1 increased activity, but not expression.

**Keywords:** Vascular reactivity, nitric oxide, endothelium, fluoxetine, maternal treatment.
**Financial Support:** CAPES/CNPq.

## EXP19 - Early Exercise Effect Associated with Treatment of GLP-1 analog in Adiposity of Obese Rats Obtained by Cafeteria Diet.

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Body fat excess is directly related to insulin resistance. Beginning to exercise early in life, right after weaning, seems to cause beneficial effects in adulthood. This study aims to evaluate the effect of treatment with GLP-1 analogue associated with exercise in obese rats obtained by cafeteria diet intake. Male animals were obtained from the vivarium of the State University of Ponta Grossa - PR. At age of 21 days, animals were divided into 8 groups, 4 groups associated

with exercise: Group cafeteria diet (DIET EXE), Group with commercial diet (CONT EXE.), and 4 groups without exercise: Group cafeteria diet (DIET SED) Group with commercial diet (CONT. SED). Subsequently they were divided into groups of animals that received subcutaneous injections of GLP-1 at age of 80 days: GLP-1 DIET EXE, CONT. EXE GLP-1, GLP-1 DIET SED and CONT. SED GLP-1. At age of 90 days the animals were sacrificed, blood was collected and so as white adipose tissue (WAT) stores to assess obesity. The diet caused an increase in WAT compared to the control group. Early exercise caused decreased perigonadal stocks (28.8%) and decrease in triglycerides for the groups treated with exercise about 48.85% lower than in the sedentary group. Longer treatment with the sedentary group associated with the drug analog of GLP-1 caused decrease in both the control group and the obese group, triglyceride levels were lower in the diet group that received the drug. Groups treated with exercise plus the drug was observed decrease in weight of fats, but not considered significant decrease in triglycerides for exercising control group plus the drug. Therefore, the effect of prematurely started exercise is the best treatment and prophylaxis of diseases that lead to metabolic syndrome.

**Keywords:** Obesity, diabetes, exercise, incretins, GLP-1.
**Financial Support:** CNPq.

## EXP20 - Shunting diabetes: Neonatal metformin treatment protects against obesity onset.

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**Background/Aims:** Antidiabetic metformin has been used worldwide to treat metabolic diseases. Perinatal phases are known as window to program adulthood metabolism. The goal of this study was verified whether metformin treatment during lactation could attenuate early overnutrition, (small litter) induced obesity. **Methods:** After birth normal litter size (NL) were adjusted to 9 pups or small litter (SL) with 3 pups per dam. From the first to the 12th day rat offspring received intraperitoneal injection of metformin, 100 mg/kg body weight (bw)/day, controls received saline. From weaning until 90-days-old, body weight (bw) and food intake were taken. It was also evaluated fat pad stores, blood glucose and insulin levels during intravenous glucose tolerance test (ivGTT). **Results:** As expected SL animals showed increased food consumption and bw compared to NL group. SL rats presented glucose intolerance and hyperinsulinemia ($p<0.05$). While, metformin did not alter food intake and bw of NL group, to SL rats these parameters were reduced ($p<0.05$). Fat tissue accretion was also decreased in SL rats by metformin early treatment ($p<0.05$). Glucose intolerance and hyperinsulinemia were normalized by metformin comparing to untreated-SL and -NL rats ($p<0.05$). **Conclusion:** Antidiabetic metformin treatment during lactation might attenuate early overnutrition-induced obesity.

**Keywords:** Metformin, obesity, small litter, lactation, hyperinsulinemia.
**Financial Support:** National Council for Scientific and Technological Development (CNPq), Training Coordination Higher Education Personnel (Capes), Paraná Science Foundation (Araucaria Foundation).

## EXP21 - Effects of Maternal Exposure to Valeriana officinalis During Lactation on Physical and Neurobehavioral Development of Rat Offspring.

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**Background-Aims:** Valeriana officinalis is used in herbal medicine of many cultures as mild sedatives and tranquilizers. It is belived that these effects derive from interactions with GABA receptors and metabolism. Animal studies have shown that exposure in neonatal life to drugs that act on the GABA system can cause changes in neurodevelopment. Our aim was analyze the effects of treatment with valerian during lactation on offspring development. **Methods:** Approved by CEEA/UFJF (Protocol number 014/2015). 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). All litters were standardized to eight pups (4 males — 4 females). The physical parameters evaluated included: date of eye opening, ear unfolding, appearance of lanugo and hair, superior and inferior incisor eruption, testis descent and vaginal opening. To evaluate reflex development: grasping reflex, righting reflex, cliff avoidance and negative geotaxis, were performed daily, 15 sec each, from postnatal day one until the day of appearance. Weight gain of pups was also measured at 2, 4, 6, 10 and 25 days old. **Results:** No significant differences were observed on weight gain, physical and reflex development analyzed. **Conclusions:** These findings suggest that maternal treatment with valerian during lactation did not cause changes on postnatal development evaluated.

**Keywords:** Lactation, postnatal development, maternal treatment.
**Financial Support:** Universidade Federal de Juiz de Fora.

## EXP22 - Maternal Exposure to Metformin did not Interfere with Aortic Endothelial Function of Male Adult Offspring.

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Metformin (MET) is used for the treatment of pregnant with polycystic ovary syndrome or gestational diabetes. Although the MET crosses the placenta and has been detected in the umbilical cord at similar concentrations of maternal blood, it is considered a safe drug throughout gestation. It was demonstrated that maternal exposure to MET increases body weight, visceral fat deposit, the fasting blood glucose and glucose intolerance, when the offspring is exposed to high-fat diet, indicating that MET may cause in the adult offspring metabolic syndrome such as obesity and diabetes. Metabolic syndrome is strongly related to the development of endothelial dysfunction. Thus, the aim of this study was investigate if maternal exposure to MET could cause endothelial dysfunction. Wistar female rats were treated with metformin 293mg/kg/day, by gavage from gestational day (GD) 0 to the GD 21 (METG) or water by gavage at the same period (CTRG). It was evaluated in male offspring (75 days) the aortic reactivity to phenylephrine (Phe), acethylcoline (Ach) and sodium nitroprussiate (SNP) in the presence (E+) or absence (E-) of endothelium. Data were expressed as mean±SEM and compared by one-way ANOVA (*p<0.05). The contraction induced by Phe in rings E+ or E- was similar between METG and CTRG [E+: 2.23±0.11 (10) vs 2.18±0.23 (8); E-: 3.64±0.46 (7) vs 3.45±0.27 (8)]. The % of relaxation to Ach was similar between METG and CTRG groups [91.40±2.18 (8) vs 90.36±2.19 (6)] and as well as the response to SNP [METG: 94.29±0.94 (10) vs CTRG: 94.56±0.81 (7)]. These results suggest that maternal exposure to metformin did not interfere with the vascular endothelial function in adult male offspring.
**Keywords:** Vascular reactivity, endothelial dysfunction, metformin, maternal treatment, metabolic syndrome.
**Financial Support:** CAPES.

## EXP23 - Effect of Undernutrition on the Morphology of Masticatory Muscles in Experimental Model of Cerebral Palsy.

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**Background/aim:** Commonly children with cerebral palsy (CP) have feeding difficulties resulting from multiple orofacial changes, including damages in masticatory muscles. In this context, the nutritional intake during early stages of life appears to play an important role on the maturation of craniofacial complex. So, the aim of this study was to investigate the effect of perinatal undernutrition on the morphology of masticatory muscles in rats submitted to CP experimental model. **Methods:** The project was approved by the Ethics Committee on Animal Use UFPE,N: 23076.025165 / 2014-10. A total of 20 male Wistar rats were randomly distributed into four groups: Nourished (NC, n = 5), Nourished - CP (NCP, n = 5); Undernourished (UC, n = 5) and undernourished - CP (UCP, n = 5). Animals of PC group were subjected to an experimental model based on the combination of perinatal anoxia associated with sensorimotor restriction of the hind paws. On the twenty-ninth day of life, animals were euthanized to remove digastric and masseter muscles for analysis of weight, relative weight and distribution of the types of muscle fibers. The results were expressed as mean and standard error. To compare the means of the experimental groups, we used the Anova Two-Way test ($p < 0.05$). **Results:** The relative and muscle weight of digastric and masseter was lower in UCP group compared to the NCP group. In relation to fibers types proportions, animals in the UCP group, showed an increase in the proportion of type IIA fibers in masseter and digastric compared to the NCP group. Furthermore, in the digastric, was observed reduction in type I fibers in animals UCP group compared to NCP group. **Conclusion:** Perinatal undernutrition modifys the morphology of masticatory muscles in rats with CP, which may impair the grinding function, indispensable for adequate digestion.
**Keywords:** Cerebral Palsy, Undernutrition, Chewing.
**Financial Support:** FACEPE.

## EXP24 - Postnatal Overfeeding Combined to Maternal Low-protein Diet Disturbs Long-term Glucose Homeostasis in Rats.

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**Background/Aims:** Adults glucose homeostasis is affected by the nutritional status on the early stages of life. Nevertheless, so far these disturbs have been considered separately. We investigate the long-term effects on obesity and glucose homeostasis in the offspring of dams fed with low-protein diet exposed to overfeeding, during lactation. **Methods:** Wistar rats' delivering was considered the post-natal day 0 (PN0), the dams were divided in control diet (NP) and low-protein diet (LP), on PN2 litters were adjusted to 9 (NL) or 3 (PO) pups, originating 4 groups: NL+NP, PO+NP, NL+LP and PO+LP. After PN14 until weaning, and from weaning to PN80, animals, dams and offspring respectively, were supplied with control diet; food consumption and body weight (BW) were monitored. On PN81, animals from all the 4 groups were subjected to an Intravenous Glucose Tolerance Test (IvGTT), followed by euthanasia and fat collection. **Results:** Compared to the control group (NL+NP), while the NL+LP rats present lower BW (-14,9%) fat accumulation (-23%) and fasting glycemia

(-14%) and insulinemia (-28%); the PO+NP group exhibited higher food intake (14%), BW (16%), fat accumulation (43%) and fasting insulinemia (38%). Differently, the PO+LP group seems similar to the NL+NP in all these parameters. On IvGTT, NL+LP and PO+NP show higher AUC of glycemia compared with NL+NP (NL+NP vs NL+LP, 26%; NL+NP vs PO+NP, 24%), and lower AUC of insulinemia (NL+NP vs NL+LP, -21% NL+NP vs PO+NP, -32%). PO+LP group shows the highest AUC scores for glycemia (NL+NP vs PO+LP, 56,4%) and the lower insulinemia (NL+NP vs PO+LP,-61%). **Conclusions:** The combination of lactate low-protein diet with postnatal overfeeding did not lead offspring to obesity on adulthood; however it cause increased damage on glucose homeostasis compared to each of the different insults placed separately on the same period.

**Keywords:** Postnatal overfeeding, low-protein diet, Lactation, Glycemia, Insulinemia.

**Financial Support:** CNPq, CAPES.

## EXP25 - Maternal high-fat diet alters adipose tissue development in early life.

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**Background/Aims:** The observation of functional brown adipose tissue (BAT) in adult humans combined with the recent understanding that subcutaneous white adipose tissue (sWAT) can develop into brown-like adipocytes may provide an opportunity to increase the whole-body energy expenditure, combatting obesity. This study aims to assess the effects of maternal high-fat diet (HFD) on the early stages of BAT and sWAT development. **Methods:** Sixty day-old female Sprague Dawley rats (n=20) were divided into 2 groups; a control normal fat diet (NFD), or high-fat diet (HFD). After 3 weeks, rats were mated and continued on the diet throughout pregnancy and the suckling period. At 10 days postnatal (PN10), pups were weighed and euthanized; adipose tissue was collected from subcutaneous and interscapular depots for histology and gene expression. **Results:** Offspring of HFD fed dams demonstrated higher body weight (n=6, $p<0.05$) and fat mass (N=6, $p<0.05$) compared with controls at PN10. Blood leptin (N=6, $p<0.05$) and glucose (N=6, $p<0.05$) concentrations were increased in offspring of HFD rats. Subcutaneous white adipose tissue (sWAT) from HFD offspring exhibited larger adipocytes compared with controls (N=4, $p<0.01$). Although brown adipocytes from interscapular depot (iBAT) did not vary in size, the white adipocytes found within iBAT was larger in HFD pups than in NFD (N=4, $p<0.05$). Maternal HFD increased the expression of Leptin in sWAT (N=4, $p<0.05$) and lowered the gene expression of LeptinR, PPAR gamma, PPAR alpha and PRDM16 in iBAT of HFD rats. **Conclusions:** Offspring of fat fed dams demonstrate altered morphology and gene expression in iBAT and sWAT during earliest stages of WAT development, which may lead to a dysfunctional adipose tissue later in life with long-term health implications.

**Keywords:** Maternal diet, high-fat diet, early life, adipose tissue.

**Financial Support:** CNPq.

## EXP26 - Study of rate re-epithelialization and revascularization on the wound healing skin of rats submitted to low protein diet during lactation.

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**Introduction:** The Lactation is a crucial period of development, the restriction of dietary protein can interfere with growth, development and repair of tissues. The wound healing, in turn, is achieved through a dynamic cellular proliferation, migration and differentiation process and epigenetic signaling plays a key role in coordinating the activities of a varied type of cells that act on the skin repair process, however the epigenetics mechanisms that control skin healing remain not understood. Aim:The objective of this study was to evaluate the healing process of wounds excisional in adult rats whose mothers were fed during the first fourteen days in milk, with a low protein-diet 4% protein. **Method:** After the birth of the puppies, in the first fourteen days of lactation, the mother has had a low protein diet containing 4% protein, from day 15 to day 21 of lactation, mothers returned again to receive normal chow. Were used 20 Wistar male rats, suckled by mothers who received low protein feed during the first fourteen days, At 21 days the pups were weaned and reach 50 days, the male pups were separated for wound healing experiments. Skin excisional wounds were made, On the right side was applied gel base for treatment, and the left side, insulin gel. The animals were sacrificed after 4, 7, 10 and 14 days of treatment. The skin samples were collected for histological analysis and H&E staining for histologycal study of re-epithelialization and revascularization. **Results:** The programation metabolic influenced the mitogenic response of atypical reepithelization tongues in periods initial, there wasn't statistical difference in mitogenic analysis and vessel formation as well. **Conclusion:** the malnutrition of lactating rats during the first 14 days of lactation promoted morphological changes in the epidermis and dermis.

**Keywords:** Maternal protein restriction, metabolic programming, re-epithelialization, vessel, insulin.

**Financial Support:** CNPq and CAPES.

## EXP27 - Rxrα Hypermethylation and Downregulation in Rat Male Offspring Exposed to Maternal High-Fat Diet Induced Obesity.

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**Background/Aims:** Variations in methylation of the retinoid X receptor alpha (Rxrα) promoter have been associated to maternal diet composition during pregnancy and this related to adiposity in the offspring. We evaluated a rat model of exposition to a high-fat diet and modulation of methylation of the Rxrα gene promoter, as well as expression of the gene and protein. **Methods:** 21 days old female Wistar rats were fed with a diet enriched in saturated fat and at day 120 were mated and pregnancy confirmed. Rat continued on the same diet along pregnancy. Rats of the same age eating a standard diet were used as controls. Pools of umbilical cord from Wistar rat litters (n=12) were collected forming four groups: 1. Female control group (♀CO); 2. Female exposed group (♀MO); 3. Male control group (♂CO) and, 4. Male exposed group (♂MO). Six pools per group were examined. DNA, RNA and protein were isolated to analyze a sequence of Rxrα gene promoter near to early growth response-1 (EGR-1) transcription factor binding-site and mRNA and protein expression. Methylation sensitive high resolution melting (MS-HRM), reverse transcription quantitative polymerase chain reaction (RT-qPCR) and western blotting, were used respectively. Direct sequencing was used to validate Rxrα methylation results. **Results:** ♂MO but not ♀MO, showed a significant hypermethylation near the sequence of EGR-1 binding compared with the control group. Direct sequencing of DNA modified samples of each group validated these results. A significant low expression of Rxrα gene and protein in ♂MO compared to the other groups was also observed. **Conclusions:** Male offspring from obese rats exposed to a high-fat diet before and during pregnancy show increased Rxrα methylation that is correlated to decreased expression of the protein. A Sexually dimorphic response to maternal high-fat diet was observed in umbilical cord of the offspring.

**Keywords:** DNA methylation, Rxrα, sexual dimorphism, maternal obesity.

**Financial Support:** Instituto Nacional de Medicina Genómica (project 10/2015/I) and Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.

## EXP28 - Intrauterine Growth Restriction (IUGR) the Place Conditioning in Rats?

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**Background/Aims:** Studies demonstrated that certain perinatal factors, such as intrauterine growth restriction (IUGR), influence physical activity levels, as well as increase the risk of metabolic and cardiovascular disorders in adulthood. Furthermore, it is suggested that running wheel has a conditioning effect in rodents. The objective of this research was to investigate if IUGR affects the preference for physical activity in adulthood when the animals are exposed to a running wheel throughout life. **Methods:** 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 w ere randomly allocated to two groups: unlocked or locked running wheel (access or not to physical activity). In adulthood, the conditioning place preference (CPP) test was performed, in which the running wheel was the reward. **Results:** IUGR animals exposed to the locked running wheel during development spent less time in the side of the apparatus with the reward (running wheel) when compared to control animals [IUGR: median = 17.71 (-12.21; 31.20); controls: median = 55.59 (26.60; 61.87)], showing less conditioning in IUGR animals. However, the groups exposed to unlocked running wheel (access to physical activity ) showed no difference in the conditioning [IUGR: median = 31.04 (-25.50; 73.90); controls: median = 0.78 (-13.87; 94.99)]. **Conclusions:** The exposure to physical activity throughout development was able t o make the conditioning difference between the control and IUGR group, observed when the animals were not exposed to physical activity (locked running wheel), disappear. Physical activity might modulate some systems, such as the dopaminergic system, changing the response to the CPP test in animals with IUGR. This hypothesis will be investigated in this animal model.

**Keywords:** Intrauterine growth restriction, physical activity, conditioning place preference.

**Financial Support:** Brazilian National Council for Technological and Scientific Development (CNPq), Foundation for the Coordination of Higher Education and Graduate Training (CAPES) and Fundo de Incentivo à Pesquisa e Eventos do Hospital de Clínicas de Porto Alegre (FIPE/HCPA).

## EXP29 - Methylglyoxal Treatment in Lactating Mothers Leads to Type-2 Diabetes Phenotype in Rat Offspring at Adulthood.

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**Background/Aims:** Environmental and nutritional disorders during perinatal period cause metabolic dysfunction in the progeny and impairs human health. Advanced glycation end-products (AGEs) are primarily produced during metabolism of excess blood glucose, which is observed in Diabetes. Methylglyoxal (MG) is a precursor for the generation of endogenous AGEs, which disturbs the metabolism. This work aimed to investigate if the maternal MG treatment during lactation programs the progeny to metabolic dysfunction later in life. **Methods:** Female Wistar rats were divided into two groups: control group (C) treated with saline and MG group treated with MG (60 mg/kg/day) by gavage throughout lactation period. Both mothers and offspring were fed a standard chow. At weaning, breast milk composition was analyzed and mothers euthanized for blood and tissue samples collections. At 90-day-old offspring were submitted to glucose tolerance test (ivGTT) and euthanized for blood and tissue samples collection. **Results:** MG mothers showed increase in glucose and fructosamine levels; however, they showed low insulin levels and failure in β-cell function ($p<0.05$). MG mothers also showed dyslipidemia ($p<0.05$). Moreover, breast milk had elevated levels of glucose, triglycerides, cholesterol and fructosamine, and low insulin ($p<0.05$). Interestingly, MG offspring had increased body weight and adipose tissue at adulthood, they also showed glucose intolerance and failure in β-cell function ($p<0.05$). Besides, MG offspring showed dyslipidemia ($p<0.05$) increasing cardiovascular diseases risk. **Conclusions:** Maternal MG treatment malprograms their male rat offspring leads to type 2 diabetes and dyslipidemia in later life, possibly by changes on breast milk composition.

**Keywords:** Diabetes, AGEs, methylglyoxal, lactation, metabolic programming.

**Financial Support:** Fundação de Amparo á Pesquisa do Estado de Goiás (FAPEG), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes).

## EXP30 - Postnatal Early Methylglyoxal Treatment Induces Hepatic Metabolism Disruption in Young Rat Offspring.

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**Background/Aims:** Increased levels of Advanced Glycation End products (AGEs) in the organism is associated with hyperglycemia, which is due to AGE-induced cell dysfunction. Therefore, our aim was to study the effects of chronic administration of an AGE precursor, Methylglyoxal, on the metabolism and pancreatic islet function of the offspring treated with MG during the two first weeks of lactation. **Methods:** After birth, rat offspring were divided into 2 groups: Control Group (CO, n=10) saline injection treated (0.9% Kg of BW/day) and the Methylglyoxal Group (MG, n=10), Methylglyoxal injection treated (6 mg/Kg of BW/day) during the first 15 days of the lactation period. At 21 days-old, male offspring were submitted to pyruvate tolerance test and euthanized for tissue collection. **Results:** Treatment with MG decreased body weight, liver weight, periepididymal and mesenteric fat pads as compared with the CO group. MG group developed dyslipidemia with increased plasma levels of LDL, VLDL, total cholesterol and triglycerides ($p<0.05$). Furthermore, pyruvate tolerance test showed an increase in gluconeogenesis in the MG group as compared to CO group ($p<0.05$). **Conclusions:** Treatment with Methylglyoxal in the first two weeks of lactation period promoted metabolic programming inducing alterations in hepatic glucose and lipid metabolism.

**Keywords:** Methylglyoxal, AGE, metabolic programming, dyslipidemia, lactation, gluconeogenesis.

**Financial Support:** Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes).

## EXP31 - Effect of Short-Term Moderate Caloric Restriction on the Systemic and Liver Metabolism of Glucose.

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**Aims:** To evaluated biometric and metabolic characteristics and the hepatic metabolism of glucose, in rats of reduced litters (RL) with (GR) or without (GL) post-lactation calorie restriction (CR) at 60 days of age. **Methods:** Newborn litters of Wistar

rats were organized in the following groups: Control (GC): rats from nine-pups litters; RL with free diet (GL): rats from three-pups litters; RL with CR (GR): rats from three-pups litters with chow reduced by 30%. Biometric assessments were made at 60 days of age. The in vivo (oral glucose tolerance, oGTT, and insulin-induced hypoglycemia, IIH) and in vitro (primary hepatocytes incubations) assays were made at the age of 60 days. Isolated hepatocytes were used to assess liver glucose release in the absence (basal) or in the presence of the gluconeogenic precursors alanine, glutamine, lactate or glycerol (5 mM). The significance level for the statistical comparisons was 5%. **Results:** Body weight increased in small litters and normalized after caloric restriction, while the relative visceral fat was higher in both groups than in the control group (GC). They had changes on the kinetics of the blood glucose after oral glucose administration (oGTT) or insulin injection (HII). The basal glucose production increased and gluconeogenesis decreased in small litters after restriction (GR). The hepatocytes of this group had higher basal glucose production and lower gluconeogenesis-derived glucose. **Conclusions:** Caloric restriction after litter size reduction did not decrease adiposity and changed glucose homeostasis during oGTT and impaired insulin-induced glucose uptake during the HII. Changes in liver glucose handling due to caloric restriction probably contributed to the in vivo glucose changes.

**Keywords:** Caloric restriction, gluconeogenesis, liver, reduced litter, blood glucose.

**Financial Support:** Fundação de Apoio ao Desenvolvimento Científico.

## EXP32 - Fetal Programming Of Polycystic Ovary Syndrome: Prenatal Hyperandrogenism Disrupts Ovarian Functionality And Causes Reproductive Derangements.

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Prenatal hyperandrogenism is hypothesized as one of the main factors contributing to polycystic ovary syndrome (PCOS), an endocrine-metabolic disorder. We aimed to study the impact of prenatal hyperandrogenism on ovarian functionality at pubertal age. Pregnant rats were hyperandrogenized with testosterone and a Control group was obtained by vehicle injection. The prenatally hyperandrogenized (PH) female offspring (N=150) and control offspring (N=96) were characterized according to the estrous cycle as ovulatory (PHov) and anovulatory (PHanov) phenotypes at pubertal age. We evaluated ovarian histology, testosterone and estradiol serum levels. The mRNA levels of adipokines (Leptin, Adiponectin and Chemerin), steroidogenic enzymes and LH and FSH receptors were quantified by qPCR. None of the groups displayed body weight differences ($p > 0.05$). In three independent repetitions, Control rats showed (100%) regular estrous cycle. 43–51% of PH group showed irregular estrous cycles (PHov), whereas 27–39% presented anovulatory cycles (PHanov). Ovaries from the PH offspring presented cysts and an excess of small antral follicles. Testosterone levels were increased in both, PHov and PHanov groups ($p<0.01$), while estradiol was decreased only in PHanov ($p<0.05$). Leptin levels were lower in PHanov group than in Control and PHov groups ($p<0.01$). Adiponectin levels were higher in PHov group than in Control and PHanov groups ($p<0.01$). Chemerin levels were higher in PHov vs Control and PHanov ($p<0.05$). Regarding steroidogenesis, StAR levels were increased in PHanov group ($p<0.05$) and aromatase levels were lower in PHanov than in Control and PHov ($p<0.05$). LH-R was increased in PHanov ($p<0.05$); FSH-R was lower in PHov but remained unaltered in PHanov as compared to Control ($p<0.05$). In conclusion, fetal programming causes alterations in ovarian functionality altering steroidogenesis and adipokines secretion, even in the absence of overweight. The differential deregulations of adipokines, steroidogenesis and LH-R and FSH-R are involved in the alterations displayed in PCOS phenotypes.

**Keywords:** Fetal Programming, prenatal hyperandrogenism, polycystic ovary syndrome, steroidogenesis.

**Financial Support:** This study was supported by Agencia Nacional de PromociónCientífica y Tecnológica (Grant 577/2012 and Grant 689/2013). G.A.A. and M.F.H. are supported by a doctoral fellowship awarded by CONICET and A.B.M. is a Principal Researcher from CONICET.

## EXP33 - Topical treatment with insulin on cell migration and collagen deposition the wound healing skin in pre-diabetic MSG-rats.

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**Introduction:** Diabetes is accompanied by delayed wound healing and insufficient granulation tissue formation, possibly due to fibroblast disfunction. The insulin hormone can promove cell division and growth through its mitogenic effects. Aim: To evaluate the effectiveness of base gel containing insulin in the healing of excisional skin wounds in insulin-resistent rats. **Method:** 20 MSG- male Wistar rats at 50 days old were used, two parallel demarcations were made with aid of a 1 $cm^2$ metal delimiter, after excision, the wounds on the right side (control), were treated with the base gel and those on the left side were treated with insulin gel. The animals were sacrificed after periods of 4, 7, 10 and 14 days. Two hours before death, the animals were injected vincristine sulfate intravenously, a blocker of the mitotic spindle, for study of cell proliferation. The skin with the wounds was removed, fixed and stained with hematoxylin and eosin (HE), used for study of the migration of the epidermis and Sirius-Red to collagen deposition after 14 days. **Results:** After 7 days, we found a reduced keratinocytes migration, insulin gel showed better effect on the migratory activity of keratinocytes. 10 days later, it is possible to infer a peak in migration of keratinocytes and again, in the increased keratinocytes

migration in insulin treated animals, in both groups there were the same deposition of type I collagen, however, in control animals, there was a greater mature collagen type III, which increases the tensile strength of the fabric which was not observed in the wounds animals treated with gel containing insulin. **Conclusion:** The MSG-animals showed disadvantage in relation keratinocytes mitogenic activity and insulin resistance involves the deposition process and maturation of collagen fibers Type III, presenting a trouble the structural reorganization of the extracellular matrix and consequent increased tissue tensile strength.

**Keywords:** MSG-model, diabetes, insulin, cell migration, collagen.

**Financial Support:** CNPq and CAPES.

## EXP34 - Repercussions of Gestational Protein Restriction on Cardiac Morphology, MiRNA Expression Profile and Predicted Target Genes Expression.

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**Background:** Maternal malnutrition predisposes offspring to low birthweight, cardiac disorders and hypertension in adulthood. Epigenetic mechanisms are involved in fetal programming and miRNA regulation could play an important role. Aims: Evaluate the miRNAs expression pattern and their predicted targets on cardiac left ventricle (LV) of gestational protein restricted rats. **Methods:** Pregnant Wistar rats were allocate in two groups, according to protein supply during pregnancy: NP(17%) or LP(6%). Offspring body weight and systolic blood pressure (SBP) was measured weekly. Cardiac LV weight, myocytes cross sectional area (MCA), collagen fraction (CF) and the miRNA and mRNA predicted target expression were evaluated in male offspring at 12-days (12d) and 16-weeks (16w) after birth. **Results:** LP offspring had low birthweight (16%; $p<0.001$), followed by rapidly body weight recovery on second week of life ($p=0.223$), and hypertension development from the ninth to sixteenth week ($p<0.001$). LP-12d and LP-16w had similar LV weight versus NP-12d ($p=0.337$) and NP-16w ($p=0.259$), respectively. However, LP-16w had increased MCA (53%) and CF (82%) versus NP-16w ($p<0.001$). LP-12d had significantly increased miR-184(177%), miR-192(152%), miR-376c(60%), miR-380-3p(1444%), miR-380-5p(426%), miR-451(175%), miR-582-3p(32725%) and significantly decreased miR-547(37%) and miR-743a(58%) versus NP-12d. LP-16w had significantly increased let-7b(18%), miR-125a-3p(4425%), miR-142-3p(86%), miR-182(9616%), miR-188-5p(172%) and significantly decreased let-7g(12%), miR-107(81%), miR-127(98%), miR-181a(23%), miR-181c(72%), miR-184(91%), miR-324-5p(55%), miR-383(83%), miR-423-5p(89%) and miR-484(14%) versus NP-16w. Target prediction was performed for miRNAs differentially expressed between groups. LP-12d had increased Dnmt3a(130%), Oxct1(49%), Rictor(43%) and Trps1(56%) expression and decreased Bbs1(34%) and Calml3(49%) expression versus NP-12d. LP-16w had increased Adrbk1(28%), Bbs1(50%), Dnmt3a(54%), Gpr22(112%), Inppl1(46%), and Oxct1(32%) expression versus NP-16w. **Conclusions:** Gestational protein restriction leads to offspring low birthweight, increased SBP and impaired cardiac morphology in adults. Furthermore, it is related to early heart miRNAs expression changes that perpetuates into adulthood and which are associated with regulation of critical genes involved in cardiovascular development, heart morphology, function, and metabolism.

**Keywords:** Fetal programming, Heart, Hypertension, Epigenetics, MiRNAs.

**Financial Support:** Capes, Fapesp.

## EXP35 - Protein expression of hepatic lipid metabolism in male offspring from obese rats undergo bariatric operation.

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**Introduction:** Maternal obesity has long-term consequences for the offspring. Roux-en-Y gastric bypass (RYGB) surgery is the most effective procedure for sustained weight loss and ameliorates comorbidities associated of the mother and the health of the child. Objectives: Herein, we investigated the effects of RYGB on hepatic lipid metabolism in male offspring from obese female rats undergo bariatric operation. **Methods:** Female Wistar rats were allocated in two groups: control (CTL) and western diet (WD) which received standard and cafeteria diet for 15 weeks, respectively. Then, WD group was submitted to sham-operation (WD-Sham group) or RYGB surgery (WD-RYGB group). Five weeks after surgery, female rats were housed with single male rats for mating period. The offspring was designated as the treatment of mother in CTL-F1, WD-SHAM-F1 and WD-RYGB-F1 group. The expression of proteins involved in hepatic lipid metabolism was verified in adult offspring (120 days of life). **Results:** The protein expression of Microsomal Triglyceride Transfer Protein (MTTP) and phosphorylation of Acetyl-CoA carboxylase (pACC) was reduced in WD-SHAM-F1 offspring rats compared to CTL-F1 animals. In addition the protein expression of fatty acid synthase (FASN) and stearoyl-CoA desaturase-1 (SCD-1) was higher in WD-SHAM-F1 rats than CTL-F1 animals. WD-RYGB-F1 animals displayed MTTP protein expression higher than WD-SHAM-F1 group, partial improvement in protein expression of FASN and pACC. The protein expression of Acetyl-CoA carboxylase, SCD-1 and carnitine palmitoyl transferase 1 was similar between WD-RYGB-F1 and WD-SHAM-F1 offspring. **Conclusion:** RYGB and cafeteria diet offered to mothers can alters the functioning of pathways involved in hepatic lipid metabolism of male offspring.

**Keywords:** RYGB, Maternal obesity, hepatic lipid metabolism
Financial Support: CAPES, CNPq and Fundação Araucária.

## EXP36 - Low-protein Diet During Lactation Program to an Imbalanced Adrenergic Response in Pancreatic Islets in Rats Fed with a High-fat Diet in Adulthood.

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**Background/aims:** Obesity and metabolic syndrome in adulthood has been correlated with insults in perinatal life, which induces pancreatic islets dysfunction. Protein restriction during lactation programs lean phenotype later in life associated to low insulin secretion. We aimed to study islets function from rat malprogrammed by low-protein diet during lactation that received high-fat diet at adulthood. **Methods:** Lactating dams were fed with a low-protein diet (LP, 4%) during 2/3 of lactation, while control dams received a chow diet (NP, 23%). In adulthood, male rats received a high-fat diet (NP/HF and LP/HF groups) or normal-fat diet (NP/NF and LP/NF groups). At 90-days-old, offspring rats were sacrificed. Pancreatic islets were isolated and incubated with agonists and antagonists of muscarinic and adrenergic receptors to study insulin secretion. **Results:** Islets from NP-HF group stimulated by glucose secreted more insulin than islets from NP-NF; however, HF diet did not change glucose response in LP rats. Cholinergic response was decreased in islets from all animal groups submitted to HF diet; however, LP-rats were less responsive. Using an antagonist for M3 muscarinic receptor, 4-DAMP, as expected, cholinergic response was inhibited in islets from all groups, while, LP groups showed less inhibition. Submitting islets to a M2 muscarinic receptor antagonist, MTT, as expected, cholinergic response were increased in all groups; however, LP groups presented greatest magnitude. Adrenaline inhibited glucose response in all islets groups. Yohimbine, an alpha 2 adrenergic antagonist, blocked adrenaline inhibition in islets from NP-NF; however, HF diet avoided yohinbine response in LP and NP rats. **Conclusions:** Adult rat malprogrammed by protein restriction during lactation fed with HF diet in adulthood presented low insulin secretion associated with reduced adrenergic response in pancreatic islets, suggesting altered sympathetic nervous system activity. This alteration can be a protective mechanism for the dysfunctions caused by HFD.

**Keywords:** Lactation, insulin secretion, low-protein diet, cholinergic system, adrenergic response.
**Financial Support:** CNPq, CAPES.

## EXP37 - Study of rate fibroplasia and cell death in the wound healing skin of rats submitted to low protein diet during lactation.

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**Introduction:** The Lactation is a crucial period of development, the restriction of dietary protein can interfere with growth, development and repair of tissues. **Aim:** evaluate the healing process of wounds excisional in adult rats whose mothers were fed during the first fourteen days in milk, with a low protein-diet 4% protein. **Method:** After the birth of the puppies, in the first fourteen days of lactation, the mother has had a low protein diet containing 4% protein, from day 15 to day 21 of lactation, mothers returned again to receive normal chow. Were used 20 Wistar male rats, suckled by mothers who received low protein feed during the first fourteen days, At 21 days the pups were weaned and reach 50 days, the male pups were separated for wound healing experiments. Skin excisional wounds were made, On the right side was applied gel base for treatment, and the left side, insulin gel. The animals were sacrificed after 4, 7, 10 and 14 days of treatment (n=5). The skin samples were collected for histological analysis Sirius red study fibroplasia and immunohistochemical stained by peroxidase method for detecting TUNEL technique the occurrence of programmed cell death **Results:** Wounds of 4 and 7 days showed large number of apoptotic cells, especially fibroblasts, keratinocytes and endothelial cells, in wounds treated or not. After 10 days the apoptotic number cells decreased. Analysis by type of collagen type I and III demonstrated that the insulin gel favored group maturation of collagen. **Conclusion:** It was also found the occurrence of nuclear fragmentation typical of apoptosis in hypertrophic keratinocytes, reinforcing the epidermis was one of the tissues most affected by malnutrition during lactation.

**Keywords:** Maternal protein restriction, metabolic programming, re-epithelialization, fibroplasia, cell death.
**Financial Support:** CNPq and CAPES.

## EXP38 - Methyl Jasmonate chronic treatment modulates the insulin metabolism during the chemically induced experimental colitis.

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**Introduction:** The main endocrine manifestations of inflammatory bowel disease (IBD) includes metabolic stress, high inflammation levels, changes in carbohydrate metabolism and insulin resistance increased in patients. The Methyl jasmonate (MeJA) is a plant hormone, this substance shows protaglandin similar structure with potent inhibitory on the production of pro-inflammatory effects. Aim: The goal was to check the potential MeJA in the modulation of insulin's serum levels in a model of experimental colitis chemically induced during 28 days, a cronic period. **Method:** It was used 30 male Wistar rats, we use six groups (n=5): (a) control without treatment; (b) control treated with corn oil; (c) control treated

with MeJA, (d) TNBS without treatment, (e) TNBS treated with corn oil and (f) TNBS treated with MeJA. the animals received TNBS enema containing solution (0.3 ml) dissolved in 30% ethanol with 28 days diary MeJA-treatment by gavage. After the euthanase, the blood was collected and the distal colon macroscopic evaluation analyses were scored from 0 to 5, according kind of injury. The insulin levels were measured by radioimmunoassay (RIA). **Results:** Macroscopic analysis showed the model is effective in the experimental colitis model induced. MeJA treatment was effective in reducing levels of colic in TNBS animals presenting intestinal morphology similar to those animals with control animals. Similarly, insulin levels were high in untreated TNBS animals, however, after treatment with MeJA, insulin levels were modulated. **Conclusion:** In addition to the anti-inflammatory potential, maintenance of basal insulin levels during IBD, prevents the maintenance of a possible tissue insulin resistance, this process could blocking colonic mucosal repair.

**Keywords:** IBD, Insulin, MeJA, TNBS, colitis.
**Financial Support:** CNPq and CAPES.

## EXP39 - Impact of Litter Reduction During the Lactation Period on Maternal Morphophysiology and its Repercussion on the Offspring.

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Metabolic programming is a phenomenon triggered by nutritional and/or hormonal changes at critical stages of development, such as lactation. The study aimed to characterize the effect of handling the number of pups in the litter on biometric, metabolic and maternal histological parameters and their impact on the offspring at different stages of lactation. Female Wistar rats (n = 64) were mated so as on the 3rd day after birth the number was set to 9 rat pups, Normal Litter (NL), and 3 pups, Short Litter (SL). The mothers or Dams-NL and Dams-SL and the Offspring-NL and Offspring-SL were studied on the 7th, 14th and 21st day of lactation. Monitoring of body weight of dams and offspring was performed, including the feed intake of dams, breast milk analysis, serum biochemical tests and histological analysis of dams and offspring. The results demonstrated decreased food consumption, together with higher stock of retroperitoneal fat and reduced fat droplets in brown adipose tissue (BAT), suggesting increased thermogenic activity throughout lactation in Dams-SL. The mammary gland in Dams-SL showed lower degree of alveolar development with increased adiposity in breast tissue, resulting in milk with higher calorie content. Dams-SL also exhibited reduction in size of the pancreatic islets, liver weight reduction, with increased cell count and increased blood glucose. Offspring-SL had higher body weight, accompanied by increase in BAT with lower thermogenic activity evidence. In addition, these animals showed an increase in pancreatic weight during lactation and elevated blood glucose and serum protein at certain stages of lactation. The study confirmed that the litter reduction during the lactation period promotes morphophysiological changes in mothers affecting body weight and metabolism of offspring, events that can be programming markers with complications throughout life.

**Keywords:** Metabolic programming, lactation, dams, offspring.

## EXP40 - Acute restraint stress increases carotid reactivity from type-I diabetic rats by increased activity of Nox4/NADPH-oxidase.

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**Background/Aims:** Hyperglycemia increases the generation of reactive oxygen species (ROS) and affects systems that regulate the vascular tone. Behavioral stress could exacerbate intracellular oxidative stress during diabetes upon the activation of angiotensin AT1/NADPH-oxidase pathway, which might accelerate diabetic cardiovascular complications. **Methods:** Type-I Diabetes was induced in Wistar by intraperitoneal injection of streptozotocin. 28 days after, the animals underwent to acute restraint stress for 3h. Cumulative concentration–response for angiotensin II (AngII) (10pmol/l–1mmol/l) were obtained in endothelium intact (E+) or endothelium-denuded (E-) carotid rings in the presence of hydrogen peroxide (H2O2) scavenger (PEG-Catalase 250U/ml), and inhibitors of Nox4 (VAS2870 5.0µmol/l), Cyclooxygenase-1 (SC560 1nmol/l) and Cyclooxygenase-2 (SC236 0.1nmol/l) added 30min prior to AngII. Nox4 expression and activity were assessed by western blotting and lucigenin chemiluminescence. The role of Nox4 on ROS generation was evaluated by Amplex Red assay. Cyclooxygenases expression was assessed by real-time polymerase chain reaction. **Results:** Acute stress increased AngII maximum contraction in Stressed Diabetic (SD) (E+)(Emax:0,88±0,05) or (E-)(Emax:1,38±0,06) when compared to Diabetic(E+) (Emax:0,70±0,04) and (E-)(Emax:1,01±0,03). In the presence of PEG-Catalase Emax of SD(E+)(Emax:0,64±0,03), SD(E-) (Emax:1,21±0,05) and Diabetic(E+)(Emax:0,51±0,02) were reduced. VAS2870 reduced the AngIIEmax in Diabetic(E+) (Emax:0,54±0,04), SD(E+)(Emax:0,66±0,03) and SD(E-) (Emax:1,24±0,02). Western blotting showed increased expression of Nox4 in carotid of SD compared to Diabetic and Stressed normoglycemic. H2O2 levels were higher in AngII-stimulated carotid arteries from SD when compared

to Diabetic group. VAS2870 reduced H2O2 levels from SD, without changing levels from Diabetic rats. In presence of SC236 or SC560 it was also observed reduced of Emax from Diabetic(E+) and SD(E-) to the same levels obtained in carotid from normoglycaemic rats which were accompanied with an increased gene expression of Cyclooxygenase-2. Conclusion: Our findings suggest that acute restraint stress exacerbates the contractile hyperreactivity to AngII in Diabetic rat carotid by enhancing Nox4-driven generation of H2O2, which evokes contractile tone by cyclooxygenases-dependent mechanisms.

**Keywords:** Type-1 diabetes; acute restraint stress; reactive oxygen species; nitric oxide synthases; renin-angiotensin-system.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico CNPq (protocol nº 470142/2012), the Núcleo de Apoio à Pesquisa em Doenças Inflamatórias (NAP-DIN protocol nº 11.1.21625.01.0) and São Paulo Research Foundation (FAPESP, grants #2012/09019-3, #2012/00647-0, #2014/17740-0, #2011/11205-7 and #2013/08216-2, Brazil).

## EXP41 - Enhanced peroxynitrite formation during acute stress in type-1 diabetic rats by increased activity of eNOS.

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**Background/Aims:** High glucose levels enhance superoxide anion (O2-) generation, which leads to a pro-oxidant environment. Behavioral stress could exacerbate intracellular oxidative stress during Diabetes upon the upregulation of NADPH-oxidase, which contributes to the development of diabetic cardiovascular complications. **Methods:** Type-I diabetes was induced in Wistar rats by intraperitoneal injection of streptozotocin. 28 days after, the animals underwent to acute restraint stress for 3h. Cumulative concentration–response for angiotensin II (AngII) (10 pmol/l–1mmol/l) were obtained in endothelium-intact (E+) or endothelium-denuded (E-) carotid rings in the presence of O2- scavenger (Tiron 100µmol/l), Nox1 inhibitor (ML171 0.5µmol/l) and eNOS inhibitor (L-NNA, 100µmol/l), added 30 min prior to AngII. Protein expression of Nox1, peroxynitrite by 3-Nitrotirosine, eNOS and eNOSphospho-Ser1177 were assessed by Western blotting. The O2- generation was evaluated by flow cytometry. **Results:** Acute stress increased AngII maximum contraction in Stressed Diabetic (SD)(E+) (Emax: 0,88±0,05) or (E-)(Emax: 1,38±0,06) when compared to Diabetic(E+)(Emax: 0,70 ± 0,04) and (E-) (Emax: 1,01±0,03). In the presence of TironEmax of SD(E+) (0,51±0,04), SD(E-)(1,17±0,05) and Diabetic(E+)(0,51±0,03) were reduced. ML171 reduced the AngIIEmax in Diabetic(E+) (0,50±0,04), SD(E+)(0,50±0,05) and SD(E-)(0,99 ± 0,05) to the same levels obtained in normoglycaemic rats. Western blotting showed increased protein expression of Nox1 in carotid of Diabetic and SD compared to normoglycemic. The basal levels of O2- from Diabetic and SD rat carotid were higher than normoglycaemic. In presence of L-NNA it was also observed reduced of EmaxAngII Diabetic(E+)(0,69±0,04) and SD(E+)(0,68±0,03) which were accompanied with an increased protein expression of eNOSphospho-Ser1177 in the SD group. 3-Nitrotyrosine expression was increased in Diabetic rat carotid that was higher in the SD. **Conclusion**: Our findings suggest that the increase nitric oxide generation by eNOS activation during acute stress under increased levels of O2- induced by diabetic hyperglycemia enhances peroxynitrite formation, which leads to AngII contractile hyperreactivity in rat carotid.

**Keywords:** Type-1 diabetes; acute restraint stress; reactive oxygen species; nitric oxide synthases; renin-angiotensin-system.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico CNPq (protocol nº 470142/2012), the Núcleo de Apoio à Pesquisa em Doenças Inflamatórias (NAP-DIN protocol nº 11.1.21625.01.0) and São Paulo Research Foundation (FAPESP, grants #2012/09019-3, #2012/00647-0, #2014/17740-0, #2011/11205-7 and #2013/08216-2, Brazil).

## EXP42 - Early and sustained exposure to a high-sucrose diet induce changes of adaptive pathways to apoptosis on endoplasmic reticulum.

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**Background/Aims:** Premature consumption of high-sugar foods has been associated to early onset of metabolic syndrome and affect the homeostasis of the endoplasmic reticulum (ER), promoting a condition of ER stress. Thereby, our study aimed to investigate the effects of high sucrose diet in promotes metabolic disorders and the involvement of ER stress to development of these disturbances. **Methods:** Weaned Swiss mice were randomized in two groups which received standard chow (CTR) or high-sucrose diet (HSD) and followed for two periods, 30 (CTR30/HSD30) and 60 (CTR60/HSD60) days. At the end of each period, the blood, liver and adipose tissue (visceral, non-visceral and brown adipose tissue) were collected. **Results:** The HSD30 group showed a weight gain with impaired feed consumption and increase of fat deposit on body and liver. The HSD60 showed the same characteristics and additionally a higher lee index. The fat deposits on liver of HSD60 are composed by high levels of triglycerides. Both groups had an increase of fasting and fed glucose levels, dyslipidemia, glucose intolerance (GTT), nevertheless only HSD60 showed increase of serum free fatty acids and insulin tolerance (ITT) and resistance (TyG index). The HSD60 showed hyperinsulinemia and insulin resistance by HOMA index and insulin measurement on HSD30 are not evaluated yet. Assessment of liver gene expression in HSD30 showed increased of endoplasmic reticulum stress

pathways (IRE1α, ATF6, PERK), chaperones (GRP78, PDI) and factor related to antioxidant defense (NRF2). On the HSD60 the expression of all markers were decreased compared to HSD30 and, additionally, the CHOP expression (an apoptotic marker) on HSD60 showed increased. **Conclusions:** We conclude that early exposure (30 days) with HSD was successful to promote metabolic dysfunctions and the sustained exposure (60 days) lead to a loss of adaptive function mediated to ER and increase of apoptotic pathways, resulting in consolidation of metabolic disorders.

**Keywords:** Metabolic syndrome, high-sucrose diet, endoplasmic reticulum stress.

**Financial Support:** Fundação de Amparo à Pesquisa do Estado do Maranhão (FAPEMA).

## EXP43 - Glibenclamide treatment attenuates the Walker-256 tumor growth in prediabetic rats.

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**Background/Aims:** Glibenclamide is widely used in the treatment of type 2 diabetes. Beyond its antidiabetic effect, a low incidence of certain types of cancer in diabetic population have been observed. However, the mechanisms remain unclear. In the present study, we aimed to test the protective effect of glibenclamide on the tumor growth in a well-established prediabetic rat model. **Methods:** Prediabetic rats were obtained by neonatal treatment with monosodium L-glutamate (MSG). Control and MSG groups were treated with Gli (2 mg/kg body weight/day), from weaning to 100-day-old. After Gli treatment, the control and MSG rats were grafted with Walker-256 tumor cells. After 14 days, grafted rats were euthanized and tumor weight as well as glucose homeostasis were evaluated. Results: Treatment with glibenclamide normalized tissue insulin sensitivity and glucose tolerance, suppressed fasting hyperinsulinemia, reduced fat tissue accretion in MSG rats and was able to attenuate tumor growth by 27% in control and MSG rats. In morphological analysis, glibenclamide treatment revealed a large reduction in PCNA positive cells. **Conclusion:** Glibenclamide prevents Walker-256 tumor growth and this effect is not related to metabolism improvement, suggesting an antiproliferative effect on cancer growth.

**Keywords:** Diabetes, glibenclamide, Walker-256 tumor, MSG rats.

**Financial Support:** National Council for Scientific and Technological Development (CNPq), Training Coordination Higher Education Personnel (Capes), Paraná Science Foundation (Araucaria Foundation).

## EXP44 - Adolescent Rats Exposed to High Fat Diet Show Hypertension in Adulthood.

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**Background/Aims:** High fat diet exposition during gestation and lactation periods lead to hypertension later in life. It have been suggested that adolescence is, as well, a susceptible phase for programming to metabolic syndrome. In this context we hypothesised that high fat diet during adolescence may lead to hypertension. **Methods:** Adolescent Wistar rats (30 to 60 day-old) were exposed to a high fat diet (HFD, 35% of lard). Control animals had access to normal commercial chow (NFD). Blood pressure, heart rate and pulse pressure were recorded in 120-day-old rats. Student t-test was used to compare groups. **Results:** HFD animals showed greater systolic blood pressure levels compared with control animals (127 ± 2.1 vs. 119 ± 1.5 mmHg, respectively, $p<0.05$); while diastolic blood pressure was unchanged (HFD: 74 ± 2.0 and NFD: 71 ± 2.1 mmHg, $p=0.27$). Pulse pressure tended to be greater in HFD animals compared with control animals (51.7 ± 0.8 vs. 48 ± 1.9 mmHg, respectively, $p=0.05$). Heart Rate was similar between groups (HFD: 342 ± 13 and NFD: 361 ± 17 bpm, $p=0.4$). **Conclusion:** High fat diet exposition during adolescence programs to higher systolic blood pressure later in life, which is an important predictor for risk of cardiovascular and renal disease.

**Keywords:** Programming of cardiometabolic disease, adolescence, hypertension, high fat diet.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPQ; Science With out Bourders Program, PVE process number 400762/2014-5.

## EXP45 - Feeding behavior changes in detrained young adult rats exposed to high-fat-sugar diet intake.

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**Introduction:** Detraining is considerate the period following physical training interruption. It is possible to maintain the beneficial effect of exercise or not, causing health troubles because training lack. Feeding behavior is very sensitive to lifestyle modifications and it has a complex control involving central and peripheral pathways. The objective of this study was to analyze the feeding behavior in detrained animals feed or no with high fat sugar diet during young adult life and checking to potential central mechanisms involved. Materials and **Methods:** Sixty-day-old rats were subjected to moderate exercise, three times a week, for 30 days. After that, trained rats received a HFS (EXE-HFS) or a commercial normal diet (EXE-NFS) for 30 more days. Sedentary animals also received the diets (SED-HFS and SED-NFS). Body weight was measured weekly. On 120 days of life, food intake behavior was analyzed with a BioDAQ Systems. Following euthanasia biochemical and molecular analyzes were performed. Statistical analyses were performed using two-way ANOVA and the Tukey post-test. **Results:** Body weight gain and fat pad accumulation were decreased in detrained animals. HFS increased fat pad stores, glycemia, cholesterol and triglycerides. Food intake was reduced during light period in EXE-NFS animals. Furthermore, HFS animals showed decrease on food intake. This profile was maintained during changed diet test. Satiety and dopaminergic activity on striatum nucleus were increased in detrained animal. HFS decrease expression of SOCS-3 protein. **Conclusion:** Previous exercise blocks obesity onset induced by HFS diet. Detraining also induces a better control of food intake rhythm by activation dopaminergic systems on striatum nucleus. However, HFS diet attenuated these benefits of previous exercise on feeding behavior.

**Keywords:** Feeding behavior, treadmill exercise, detraining, high-fat-sugar diet.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

## EXP46 - Characterization of Ascites during Ehrlich Tumor Development.

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**Background/Aims:** To elucidate molecular mechanisms involved in tumor development and progression experimental animal models has been studied. One of the most used is Ehrlich Ascites Tumor, which is a murine mammary adenocarcinoma with fast growth and aggressive behavior. Therefore, the present work aims to characterize aspects related to tumor ascites and animals. **Methods:** Swiss mice separated into three groups (n=4/group) were used. Tumor inoculation was performed with 200µL of 2.106/mL tumor cells in Phosphate Buffered Saline (PBS) into peritoneal cavity. Animals were euthanized 6, 9 and 12 days after tumor inoculation. Ascites were evaluated for its volume and aspect. For cellularity and viability evaluation, cells were counted in optical microscope (40x) with Neubauer chamber and stained with Tripan Blue. Spleen was collected, macerated with PBS and stained with crystal violet, cellularity was evaluated as described above. Animals weight variation (day 0 to days 6, 9 and 12) was expressed by difference of final and initial weight and considered mean of each group. **Results:** A weight gain is observed as tumor growths. Total cell number into ascites increases with tumor progression, as well as volume and erythrocytes (bleeding). However, a reduction in cellular viability and number of spleen cells was observed with tumor development. A local inflammatory reaction causes increase in ascites volume and number of tumor cells that induces the weight gain observed. Local inflammation also increases peritoneal vascular permeability, producing the hemorrhagic aspect of ascites. Although cell number increases, tumor viability decreases due to loss of nutritional intake and widespread animal cachexia. Ehrlich Tumor in its ascites form does not causes splenomegaly, which can be explained by dilution of toxic products and low levels of necrotic material absorption. **Conclusions:** Therefore, with these characteristics, Ehrlich Ascites Tumor become a good model to study lymphatic metastasis, and investigate antineoplastic, anti-angiogenic and anti-inflammatory drugs.

**Keywords:** Cancer, inflammation, animal models.

**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa e Desenvolvimento Científico do Maranhão (FAPEMA).

## EXP47 - Morphological evaluation and Nitric Oxide production by macrophages cultured with tumor cell lines.

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**Background/Aims:** Immune cells participate in tumor microenvironment, creating a coadaptation process with tumor cells. Among immune cells that infiltrate tumor, macrophages has achieved increasing importance and complexity, once

they are involved in chronic inflammation and seems to be associated to tumor progression and metastasis. This work aims to analyze morphological characteristics of macrophages cultured with supernatant obtained from cell cultures of MCF-7 e SKBR-3, and evaluate the Nitric Oxide (NO) production. **Methods:** Experiments to evaluate morphology and activation of macrophages were performed with different stimuli: Dexamethasone (DEX), Lipopolysaccharide from Escherichia coli (LPS), used as negative and positive controls, respectively, and/or supernatant from tumor cells culture (SOB). Stimuli were performed at different time, according to the groups (G1: DEX; G2: LPS+SOB (1h after LPS); G3: LPS+SOB simultaneously; G4: SOB+LPS (1h after SOB); G5: LPS). Morphology was analyzed by count of activated cell on fluorescence microscope, and quantification of NO was performed by Griess method. **Results:** Results indicated that G2 group have the highest frequency of activated cells (MCF-7: 88%; SKBR-3: 74%) when compared to other groups. NO production was higher in G2 than G5 group when treated with supernatant from MCF-7; whereas the G4 group had the highest production in macrophages treated with supernatant from SKBR-3. **Conclusions:** According to results shown, it can be inferred that macrophages exhibits a specific and differentiated response, related to control and tumor co-culture groups. Data indicate that macrophages treated with MCF-7 co-culture acquired a M1 polarization, equaling to LPS group, whereas macrophages treated with SKBR-3 co-culture acquired a M2 polarization.

**Keywords:** RAW 264.7, Cancer, MacrophageActivation.
**Financial Support:** Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa e Desenvolvimento Científico do Maranhão (FAPEMA).

## EXP48 - Hydroethanolic Extract of Syzygiumcumini Leaves Improve Non-alcoholic Fatty Liver Disease in MSG-obese Mice by a Joint Action on Insulin resistance and Endoplasmic Reticulum Stress

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The endoplasmic reticulum stress (ER stress) favors the maintenance of non-alcoholic fatty liver disease (NAFLD). The hydroethanolic extract of S. cumini leaves (HESc) improve NAFLD in monosodium glutamate (MSG)-obese rats. The aim was to investigate the effects of HESc on markers of lipid metabolism and ER stress in the NAFLD from obese mice. MSG-obese mice were treated with HESc (Obese+HESc) for 4 weeks, as well as other MSG-obese and lean mice received saline. The body weight, food intake and Lee index (LI) were evaluated. In the end, insulin tolerant test was realized. The serum, white adipose tissue (WAT) and liver were collected during the sacrifice of animals. The serum was used to measure the glucose (GL), triglycerides (TG), cholesterol, free fatty acids and insulin. With insulin was calculated the HOMAIR. The WAT was weighed and lipolytic activity evaluated. The liver used to quantification of the lipids and markers (qPCR) of synthesis (SREBP1c, PPARs, FAS, SCD1 and DGAT2) and exportation (APOB, PDI and MTTP) of TG. Genes of ER stress (ATF6, IRE1α, PERK, NRF2 and CHOP) also were quantitated. There were statistic differences among the groups (n=6) when $p<0.05$ (ANOVA). HESc reduced the body weight (12%), LI (6%) and WAT (20%). The GL, TG and insulin levels diminished in 38%, 37% and 29%, respectively. HESc improve the insulin sensitivity by reduction of HOMAIR (56%) and increase of kITT (87%). The lipolytic activity of Obese+HESc was increased. The liver total fat (29%) and TG (22%) have reduced. The HESc also decrease expression of PPARγ (35%), SREBP1c (52%), PPARα (56%), FAS (63%), DGAT2 (50%), ApoB (50%), MTTP (45%), PERK (66%) and NRF2 (50%). Therefore, the HESc can be ameliorating the NAFLD in MSG-obese mice by improve the insulin resistance and downregulate of the PERK expression, an important sensor of ER stress.

**Keywords:** Syzygiumcumini; NAFLD; insulin resistance; endoplasmic reticulum stress.
**Financial Support:** FAPEMA, UFMA and CNPq.

## EXP49 - Intrauterine Growth Restriction Is Associated with Increased Impulsivity and Altered Dopaminergic Signaling in Prefrontal Cortex.

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Intrauterine growth restriction (IUGR) is associated with adverse metabolic and behavioral outcomes during life course. Preliminary results show that 3-year-old IUGR girls present lesser ability to delay for food reward. Since impulsiveness is associated with alterations on feeding behavior, becomes important to investigate the relationship between IUGR and impulsivity. Here we investigated impulsive behavior in an animal model of IUGR and evaluated alterations on neural signaling associated with impulsivity. Pregnant dams received ad libitum food (AdLib) or were 50% food restricted (FR) from pregnancy days 10-21, producing control and low-birthweight newborn offspring respectively. Pups were nursed by control dams, generating AdLib/AdLib and FR/AdLib groups (pregnancy/lactation). All pups received ad libitum feed after weaning. In adult life, females were trained in a T-maze to choose between a small-but-immediate and a large-but-delayed reward. Animals were compared for their ability to tolerate a delay and still preferring the large reward, an operational measure of impulsive-related behavior. Tyrosine hydroxylase (TH) and dopamine receptors levels were evaluated in prefrontal cortex of newborn and adult animals. Along the sessions without delay, both groups choose more the arm giving access to large reward (AdLib/AdLib =86,2%; FR/AdLib = 82,2%). When introducing a 30 s delay, restricted animals showed a greater reduction in the percentage of choice of the large-but-delayed reward (AdLib/

AdLib =48,4%, FR/ AdLib = 18,8%; p<0,05). At birth, FR pups had an increase of 94% (p<0,05) in pTH/TH ratio (compared with control). Adult FR/AdLib animals showed an increase of 160% (p<0,05) in Dopamine D2 receptor levels in the medial portion of PFC. Since impulsivity has been associated with overfeeding, these small energy imbalances across life span could explain, at least in part, the increased risk of IUGR individuals to develop metabolic diseases in later life. Furthermore, an abnormal dopaminergic signaling since birth may underlie these behavioral alterations.

**Keywords:** IUGR, Impulsivity, Dopamine, Prefrontal cortex.
**Financial Support:** CAPES, CNPq, FIPE/HCPA.

## EXP50 - Oral insulin treatment improves metabolic dysfunction in high fat diet-induced obesity rat

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**Background/Aim:** The gut has shown to have a pivotal role on the pathophysiology of metabolic disease. Digestion of food, mainly in distal intestinal segments promotes enterohormones (incretins) secretion that directly influence insulin metabolism. Additionally, incretin based drugs became the mainstay of diabetes treatment. In diabetic rats, oral insulin has potential to change intestinal epithelium behavior, function and morphologically. Even not being absorbed this macromolecule promotes positive effects on laboratorial metabolic disease parameters and decreases intestinal hypertrophy of diabetes. This study aims to test whether oral insulin can influence metabolic parameters and intestinal weight (duodenum, proximal jejunum and distal ileum) in obese non-diabetic rats. **Methods:** Twelve weeks old Wistar rats were divided in 3 groups: Control group (CTRL) submitted to standard chow (low fat and normal carbohydrates); high fat and lower carbohydrate diet group (HFD) and HFD plus daily oral 20U regular insulin gavage (HFD+INS). Weight and food consumption were weekly obtained. After six weeks, fasting blood samples were collected for glucose, triglycerides and insulin dosage. After euthanasia visceral fat pad was isolated and weighted. **Results:** Rat treated with high fat diet had significant more body weight and less intestinal weight than CTRL (p<0,05). Oral insulin decreased body weight gain (p<0,0001), fasting glucose and triglycerides serum levels (p<0,05) and promoted a trend of increasing intestinal weight in jejunum that turned significant in distal ileum (P<0,05). HOMA-IR was not different between HFD and HFD+INS, however HOMA-beta was significantly higher (p<0,05) in animal submitted to oral insulin gavage. Visceral fat was 10% lower in HFD+INS than HFD but the difference was not significant. **Conclusion:** In non-diabetic obese rats, oral insulin treatment improves metabolic malfunction associated to rescue beta-cell activity.

**Keywords:** Oral insulin, intestine, diabetes, obesity, metabolism, pancreatic beta-cell.

## EXP51 - Metformin Improves Transcription Of Insulin Mediators, In An Insulin Resistance Model Caused By Prenatal Hyperandrogenization.

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Insulin Resistance (InR) isone of the main contributing factors to metabolic comorbidities found in women with Polycystic Ovary Syndrome (PCOS). Insulin sensitizer drugssuch as metformin (Met) improveI nR as well as reproductiveab normalities in PCOS. Here, we tested the effects of prenatal hyperandrogenism (PH) onthe insulin signaling pathway and the effects of Mettreatment during adult life. Pregnant rats were prenatally hyperandrogenized (HA). A Control group was obtained by vehicle injection. Offspring were euthanized at adulthood (N=80). Fromday 70 to 90 of age, 20 rats of each group were treate dorally daily with 50 mg/kg of Met (HAM). We evaluated serum insulin and glucos elevels and HOMA-IR index. Gene expression of thei nsulin receptor (IR), insulin substrate 1 and 2 (IRS-1, IRS-2) and glucos etransporters (GLUT2 and GLUT4) were measure dbyqPCR in hepatic and ovariantissue. Serum insulin, glucos elevels and HOMA-IR index were higher in HA group vs Control. Metrestored the levels to those of the Control group (p<0.01). mRNAlevels of IR in boththeliver and ovarywerelower in HA group vs Control Metincreased IR levelsonly in theliver (HAM group, p<0.01). Gene expression of hepatic GLUT2 and IRS-1 (in bothtissues) waslower in HA group vs Control, and Metrestored levels to Control values (p<0.01). Ovarianm RNA levels of GLUT4 in HA and HAM groups were low erthan in the Control group (p<0.01). IRS-2 expression was lower in HA and HAM groups vs Control in both tissues (p<0.01). PH inducedanIn Rstate, which was reversed with Met. Hepatic and ovarian tissues show eddecreased gene expression of insulin sign alingmediato rscausedby PH. The liverwas more sensitive to the treatment with Metthan the ovary, restoringal most totally the gene expression of insulin path way mediators.

**Keywords:** Insulin Resistance; prenatal hyperandrogenism; metformin; polycystic ovary syndrome
**Financial Support:** This study was supported by Agencia Nacional de Promoción Científica y Tecnológica (Grant 577/2012 and Grant 689/2013). G.A.A. and M.F.H. are supported by a doctoral fellowship awarded by CONICET and A.B.M. is a Principal Researcher from CONICET.

## EXP52 - Maternal intake of chia during lactation programs for higher adiposity without oxidative damage at adulthood.

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**Background/ Aims:** Chia seed (Salvia hispanica L) is a rich source of protein, dietary fiber, omega-3 and antioxidant compounds which leads to some health benefits. However, there is no study about the effects of chia consumption during lactation on the offspring development. Thus, we aimed to evaluate the effects of maternal chia flour intake during lactation on body composition, glucose homeostasis, lipid profile and oxidative balance in male and female progeny rats at weaning and adulthood. **Methods:** At birth, 23 lactating Wistar rats were divided into: control (C=11), with free access to a diet containing 17% protein, 51% carbohydrate, 10% lipid and 5% fiber (cellulose); Chia flour (CHIA=12), with free access to a diet containing 17% protein (14.3% casein and 2.7% chia seed), 56% carbohydrate, 10% lipid (5.5% soybean oil and 4.5% chia seed) and 5% fiber (exclusive chia seed). **Results:** At weaning (PN21) no important changes were observed. At adulthood (PN180), male CHIA offspring showed higher total body fat, visceral and subcutaneous fat mass, with lower total T3. Female CHIA offspring showed higher total and visceral fat mass, but lower subcutaneous fat mass, and hypertriglyceridemia. At PN180, despite the higher adiposity in both genders, no changes were observed in redox balance and glucose homeostasis, which suggest that Chia compounds may prevent these metabolic dysfunctions usually associated with higher adiposity. **Conclusion:** Thus, mothers should limit the intake of chia during lactation to avoid obesity in their progeny in adult life.

**Keywords:** Chia, Salvia hispanica L., lactation, body composition, rats.
**Financial Support:** CAPES, CNPq, FAPERJ and UERJ.

## EXP53 - Effects of glucocorticoids use on glucose metabolism in rats: Comparative study between dexamethasone and prednisone

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**Background:** Synthetic glucocorticoids (GCs) induce several adverse effects when administered in high doses and/or prolonged, as alterations in glucose and lipid metabolism, especially hypertriglyceridemia. Aim: Verify the metabolic alterations caused by sub chronic treatment with prednisone in rats and compare them with gifts acute model induced by dexamethasone effects. **Methods:** Wistar rats of 90 days were treated with dexamethasone (D5) (1 mg/kg, i.p.) for 5 consecutive days and, its controls (C5) with saline, and rats of 60 days old were treated with prednisone (80 mg/kg, orally) for 15 days (P15) and 30 days (P30) consecutive and their respective controls (C15 and C30) received vehicle solution. **Results:** The D5 rats decreased body weight (12.3%) and lower weight of the retroperitoneal fat (38%), increased serum fasting glucose (12%) and fed (30%), insulin (80%) and triglycerides (339%) ($p < 0.05$). Total fat and triglycerides liver were 29% and 52% higher in rats D5, compared to the C5 rats ($p < 0.05$). The P15 rats had increased weight 61% less, reduction of retroperitoneal fat (29%) and increased plasma triglyceride concentrations (60%) compared to the C15 rats ($p < 0.05$). As long as P30 rats had increased weight 44% less, reduction of retroperitoneal fat (25%) and increased serum triglycerides (78%) and liver total fat (26%) compared to the C30 rats ($p < 0,05$). In vivo tests revealed the presence of impaired glucose tolerance (oGTT) in rats D5 and P30, and reduced insulin sensitivity (ipITT, HOMA, TYG) in D5 animals ($p < 0.05$). Ex vivo test showed greater sensitivity in the pancreatic islets only in D5 rats. **Conclusion:** the sub chronic administration of prednisone promoted finer metabolic changes in glucose homeostasis, compared to acute administration of dexamethasone, thus suggesting the preferential use of prednisone when it is intended to minimize the adverse metabolic effects associated with the use of GCs.

**Keywords:** Dexamethasone, prednisone, glucose homeostasis, insulin sensitivity, hypertriglyceridemia.
**Financial Support:** CAPES, FAPEMA and CNPq.

## EXP54 - Adult Offspring Undernourished in utero Present Reduced Lung Inflammatory Response and High Levels of Corticosterone.

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**Introduction:** The offspring of undernourished dams present reduced lung inflammatory response, and increased levels of corticosterone. In the present study we investigated the influence of corticosterone in the lower lung inflammatory response observed in these animals. **Materials and Methods:** Intrauterine nourished (NR) and undernourished (UR) (50 % food restriction) male rats, adrenalectomized, were replaced with corticosterone (i.p. 3 mg/kg/day) or saline for seven consecutive days. Then, the acute lung injury induced by LPS intranasal instillation (750 mg/200mL) was evaluated: the bronchoalveolar lavage fluid was collected and cellular infiltration into lung tissue was analyzed. Lungs were harvested for: measurement of cytokines (multiplex), PGE2 (ELISA), and evaluation of glucocorticoid receptor and COX-2 expression (western Blotting). The hormone corticosterone was quantified in serum (multiplex). **Results:** The results obtained by total and differencial cells in fluid lavage bronchoalveolar showed an increase in the neutrophil infiltration into lung after reducing of corticosterone through adrenalectomy in UR. The proteic expression of COX-2 was reduced in UR stimulated with LPS (0.5 ± 1.2x10-8 a.u.), however, after surgery and inflammatory stimulus the

expression was increased (1.1 ± 1.2x10-7 a.u.). The same occured to production of PGE2 which increased in UR stimulated (67.6 %). There was no difference between NR and UR under stimulus in IL-1β and IL-6 release, whereas TNF-α was increased in UR which received LPS (69.8 %). The expression levels of glucocorticoids receptors were reduced in UR (0.46 ± 0.01a.u.), however, after adrenalectomy and replacement with corticosterone, expression levels were recovered (1.10 ± 0.06 a.u.). The levels of corticosterone increased after inflammatory stimulus in NR (203.0 ± 42.4 ng/ml), whereas UR showed high levels of corticosterone and these levels were not altered after inflammatory stimulus (170.0 ± 24.1 pg/ml). **Conclusion:** High levels of corticosterone present in intrauterine undernourished rats are related to reduced lung inflammatory response.

**Keywords:** Undernourishment, Inflammation, Corticosterone
**Financial Support:** FAPESP-2012/51104-8, 2010/01404-0, CNPq and CAPES.

## EXP55 - Intrauterine growth trajectories modify the epigenetic programming of NOS3 gene in human umbilical artery endothelium.

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**Introduction:** The association of low and excessive fetal weight with cardiovascular risk are in the central interest of DOHaD. We have previously showed that umbilical artery endothelium (HUAEC) from intrauterine growth restricted (IUGR) fetuses show deficient endothelium-dependent relaxation, high NOS3 expression and low NOS activity. Aim: Due to the key role of endothelium in the umbilical cord vascular function we have studied markers of endothelial epigenetic heterogeneity in HUAEC from IUGR, control and large for gestational age (LGA) fetuses. **Methods:** In HUAEC from IUGR, control and LGA fetuses the expression of eNOS, Arg2, NOX4, GPX1, SOD1, Nrf2 and HO1 was determined under normoxia (8% O2), hypoxia (2% O2) and oxidative stress (OxS). The methylation % (pyrosecuencing) of the promoter of these genes as well as histone modifications (H3 & H4) was determined by ChIP. Knockdown of DNMT1 was performed to study methylation-dependent changes in NOS3 and Arg2. **Results:** In IUGR-derived HUAEC there is an increase in the basal expression of eNOS. The mRNA of Arg2 and eNOS are induced by hypoxia in AGA-HUAEC but no change is observed in IUGR or LGA-HUAEC. No changes were observed with OxS. NOS3 showed significant decrease in methylation at its promoter region (-352 from the TSS) and increased methylation in two HRE elements in the distal promoter (~5000 bp from the TSS) in IUGR and LGA along with open chromatin hallmarks (H3K9 Ac, H4K12 Ac) in the proximal NOS3 promoter. DNMT1-knockdown modified the expression of eNOS in IUGR and LGA compared to AGA, and this was associated to changes in methylation in CpG -352 in the NOS3 gene promoter. **Conclusion:** In summary both extreme phenotypes (IUGR and LGA) show changes in some key endothelial genes. These changes are associated to epigenetic marks of vascular programming in fetuses in both extremes of the growth curve.

**Keywords:** NOS3, methylation, IUGR, LGA, HUAEC.
**Financial Support:** Funded by Fondecyt #1120928, 1130801, 1141195 CONICYT, Chile.

## EXP56 - xperimental Model of Cerebral Palsy and Perinatal Undernutrition Promotes Damage on Masticatory Function in Rats.

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**Background/aims:** Children with Cerebral Palsy (CP) generally present multiples orofacial dysfunctions. In this context, chewing causes feeding difficulties, in which could promote undernutrition in these children. The nutrition in early life has a significant role of development of Central Nervous System as well as motor function, important factors for a successfully chew. Thus, the present study aims evaluate the motor parameters of the masticatory function in rats submitted to model of cerebral palsy associated with protein undernutrition. **Methods:** This study was approved by ethics committee of animal use of Federal University of Pernambuco – UFPE (protocol number: 23076.025165/2014-10) and performed in Department of Nutrition in UFPE. 40 male Wistar newborn rats were distributed in 4 groups: control nourished (NC,n=10), control undernourished (UC,n=10), cerebral palsy nourished (NCP,n=10) and cerebral palsy undernourished (UCP,n=10). The animals of NCP and UCP groups were subjected an experimental model of CP, that consists in association of neonatal anoxia (P0 and P1) and sensorimotor restriction of hind paws (P2 until P29). During the breastfeeding period, the dams received one of two experimental diets: normal (17%casein) or low protein diet (8% casein). On P21, puppies were filmed individually, and were evaluated the masticatory parameters (incision and rhythmic chewing period, number of chewing cycles and chewing frequency). The results were showed in mean and standard mean error. In statistical analysis were made ANOVA two-way and Bonferroni´s test (P<0,05). Results: The NCP group spent more time in the incision period (2,76 ± 0,359), and had a lower frequency of chewing (3,29 ± 0,167), and number of masticatory cycles (4,81 ± 0,635), when compared with NC. In addition, the UCP group also decreased chewing frequency (2,71 ± 0,123), compared to NCP group (3,29 ± 0,167). **Final considerations:** Perinatal undernutrition exacerbates the damages on chewing function in young rats with cerebral palsy.

**Keywords:** Cerebral Palsy, Undernutrition, Masticatory function, Chewing.
**Financial Support:** FACEPE.

## EXP57 - High-Fat Diet Intake During Puberty Induces Obesity and Liver Steatosis in Male Rats at Adulthood.

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**Background/Aims:** Adolescence is a critical developmental period characterized by physical, hormonal and psychological changes. This stage of life is evidenced by changes in the neuroendocrine systems, mainly hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary– gonads (HPG) axis. Thus, the present study aimed to evaluate whether high-fat diet intake during puberty provoke obesity and metabolic disorders, such as liver steatosis in adulthood. **Methods:** Male Wistar rats aged 30-day-old were divided into two groups: control (CO), fed with standard rodent chow and a group treated with a high-fat diet (HFD). The HFD treatment was from 30 to 60-day-old; after, from 60 to 120-day-old CO and HFD were fed with standard rodent chow. At 120-day-old some animals, from both groups, were submitted to glucose and insulin tolerance tests (ivGTT and ipITT). Other batch of animals, from both groups, were euthanized for blood and tissue samples collection for further analysis. **Results:** HFD animals shows overweight (+10%, p<0.05) and hyperphagia (+12%, p<0.05). Adipose tissue of HFD animals was increased significantly, inguinal (+75%, p<0.05), retroperitoneal (+40%, p<0.05) and periepididymal (+27%, p<0,05). HFD group showed hyperglycemia during the ivGTT (+56%, p<0.05) and reduction in glucose decay rate (Kitt) during the ipITT test (-56%, p<0.05), characterizing insulin resistance. On the other hand, HFD animals shows increased pancreatic β-cell mass (+70%, p <0.001) and pancreatic islet area (+57%, p <0.001) when compared to control animals. Furthermore, HFD animals shows severe liver steatosis observed by morphological analysis, which was 10-fold higher than the control animals (p<0.0001). **Conclusions:** We conclude that high-fat diet intake during puberty induces obesity, insulin resistance and liver steatosis in male rats at adulthood.

**Keywords:** High-fat Diet, Obesity, Liver Steatosis, Adolescence, Metabolic programming.
**Financial Support:** Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes).

## EXP58 - Topical treatment with insulin on cell proliferation index and revascularization on the wound healing skin in pre-diabetic MSG-rats.

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**Introduction:** Diabetes is accompanied by delayed wound healing and insufficient granulation tissue formation, possibly because of a defect in fibroblast function, the insulin hormone can promove cell division and growth through its mitogenic effects Aim: Was to evaluate the effectiveness of gel based containing insulin in the healing of excisional skin wounds in insulin-resistent rats (MSG-model). **Method:** Male Wistar rats, 50 days were used, two parallel demarcations were made with the aid of a 1 cm2 metal delimiter, after excision, the wounds on the right side, the control, were treated with the base gel and those on the left side were treated with insulin gel. After periods of 4, 7, 10 and 14 days, the animals were sacrificed, two hours before death, the animals were injected vincristine sulfate intravenously, a blocker of the mitotic spindle, for study of cell proliferation. The skin with the wounds was removed, fixed and stained with hematoxylin and eosin (HE), used for study of the proliferation of the epidermis and evaluation of revascularization. **Results:** After seven days, the insulin treated wounds showed a significant increase in the proliferative activity. Only after 10 days of treatment in control animals it was found a peak in the keratinocyte's proliferation, although not statistically different from animals treated with insulin. At 14 days, it can be seen that in both groups cell proliferation was reduced. An increased vessel's number was re-established after 7 days compared to animals treated with insulin. In those treated with insulin, after 7 days should occur where a proliferative peak found a certain resistance in restoring the number of vessels. **Conclusion:** MSG animals treated with insulin, proliferative stimulus was similar to control animals during the first four days of treatment and the insulin had an inversely proportional angiogenesis modulating action to normal animals.

**Keywords:** MSG-model, diabetes, insulin, cell proliferation, revascularization.
**Financial Support:** CNPq and CAPES.

## EXP59 - Gestational Protein Restriction Increases Cardiac Connexin 43 mRNA Levels in Male Adult Rat Offspring.

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**Background:** The dietary limitation during pregnancy influences the growth and development of the fetus and offspring and their health into adult life. The mechanisms underlying the adverse effects of gestational protein restriction (GPR) in the development of the offspring hearts are not well understood. The aim of this study was to evaluate the effects

of GPR on cardiac structure and function in male rat offspring at day 60 after birth (d60). **Methods:** Pregnant Wistar rats were fed a normal-protein (NP, 17% casein) or low-protein (LP, 6% casein) diet. Blood pressure (BP) values from 60-day-old male offspring were measured by an indirect tail-cuff method using an electro sphygmomanometer. Hearts (d60) were collected for assessment of connexin 43 (Cx43) mRNA expression and morphological and morphometric analysis. **Results:** LP offspring showed no difference in body weight, although they were born lighter than NP offspring. BP levels were significantly higher in the LP group. We observed a significant increase in the area occupied by collagen fibers, a decrease in the number of cardiomyocytes by 104µm2, and an increase in cardiomyocyte area associated with an increased Cx43 expression. **Conclusion:** GPR changes myocardial levels of Cx43 mRNA in male young adult rats, suggesting a compensatory mechanism for a fibrotic process promoted by an increase in BP and amount of collagen fibers.

**Keywords:** Metabolism, Gestational Protein Restriction, Development, Heart, connexin 43.

**Financial Support:** Supported by HermínioOmetto Foundation (FHO-UNIARARAS).

## EXP60 - Gestational Food Restriction Affects Myocardial Organization in Heart Offspring at 21th Day of Gestation.

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**Background:** The dietary limitation during pregnancy influences the growth and development of the fetus and offspring and their health into adult life. The mechanisms underlying the adverse effects of gestational food restriction in the development of the offspring hearts are unclear. The aim of this study was to evaluate the effects of gestational food restriction on cardiac structure and function in rat offspring at 21th day of gestation (21dG). **Methods:** Pregnant rats were divided into 3 groups: normal protein (NP, 17% casein, n = 6), low-protein (LP, 6% casein, n=6) and restricted group fed 50% of the diet consumed by NP group (R, n = 6). After anestesia, at 21dG, hearts of puppies were collected for morphological and morphometric analysis. **Results:** LP and R offspring were born lighter than NP offspring. Heart mass (g) were significantly higher in the NP group. We observed in the LP and the R groups a significant increase in the area occupied by collagen fibers, a decrease in the number of cardiomyocytes by 104µm2, and a decrease in cardiomyocyte area. **Conclusion:** Gestational food restriction affects myocardium organization in heart offspring at 21dG.

**Keywords:** Metabolism, gestational food restriction, development, heart, collagen.

**Financial Support:** Supported by HermínioOmetto Foundation (FHO-UNIARARAS).

## EXP61 - Evaluation of The Effect of Sterebins Extracted Stevia rebaudiana on Insulin Release Triggered by Different Concentrations of Glucose.

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**Background/Aims:** Recent studies have shown that the Stevia rebaudiana plant, besides being an important source of non-caloric sweeteners, contains substances with antidiabetic properties. Among the molecules with possible effect on glucose homeostasis are the sterebins (Stn), terpenoids isolated from the systematic cleansing of the extract from the leaves of stevia. These substances negatively influence the composition of the sensory profile of stevia sweeteners, even present at level of 0.05%, and its effect on insulin may be associated with presence of residual bitter. The aim of this work was to evaluate the effect of Stn on insulin release triggered by different concentrations of glucose. **Method:** To study the acute effects of Stn on insulin production and secretion, islets of Langerhans were isolated from adult Wistar rats maintained with free access to food (regular rat chow diet) and tap water, and incubated in the presence of different concentrations of glucose (5.6 and 16.7mM) in the presence of Stn (1 nM, 1 ?M and 1 mM). We use Stn extracted from the leaves of Stevia rebaudiana of the Center for Studies in Natural Products (NEPRON - DBQ - UEM). The supernatants from the incubations were collected and stored for posterior insulin measurements using a radioimmunoassay method. **Results:** The Stn increased the release of insulin in basal glucose concentration and in presence of 16.7 mM of glucose concentration in dose of 1 mM, showing a dose effect response. **Conclusion:** Stn extracted from Stevia rebaudiana leaves have effects on insulin secretion by increasing the release of this hormone by isolated islets in high glucose levels, and may be an option for treatment of diabetes mellitus.

**Keywords:** Stevia rebaudiana, Sterebins, Insulin.

**Financial Support:** CNPq.

## EXP62 - Influence of Maternal Exposure to Metformin in Sperm Parameters of Male Rat Pups.

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The "Developmental Origins of Health and Disease" (DOHaD) theory hypothesizes that environmental insults, as maternal exposure to drugs, during early development, can affect their sensitivity to, or risk of developing, disease later in life. Metformin (MET) is prescribed in the therapeutic management of type 2 diabetes mellitus and gestational. Although MET crosses the placenta and has been detected in the umbilical cord at the same concentrations as in the maternal venous,

it is considered a safe drug throughout gestation. However, it was shown that maternal exposure to MET increases sex hormone binding globulin levels in newborn babies, which could interfere with the biological effects of androgens and estradiol, and suggesting an increase in risk factors for low sperm counts and development of testicular cancer in adulthood. Thus, the aim of the present study was investigate if maternal exposure to MET could interfere with sperm parameters of male offspring. Wistar female rats were treated with MET 293mg/kg/day or water (control group CTRG) by gavage from gestational day (GD) 0 to the GD21 (METG). At postnatal day 110, the male pups were euthanized and the reproductive organs were removed and weighted. The vas deferens content was collected to perform sperm parameters: motility, viability, concentration and morphology. The testis and epididymis were homogenized for sperm counting. Data±SEM were compared by Student´s t-test (*p<0.05) (CEUA/UEL-6996.2015.02).The reproductive organs weight, as well as sperm concentration were similar between groups. Treatment did not altered the sperm parameters, such as, daily sperm production [CTRG:19.70±0.65; METG:21.49±3.14, n=6] or abnormal sperm morphology (%) [CTRG:20.61±1.38, n=9; METG:17.26±2.31, n=11]. These results suggest that maternal exposure to metformin seems to be safe on the reproductive development of the male rat pups. However, there is a necessity of more researches about the effects of maternal exposure to MET during critical periods of development.

**Keywords:** Sperm counting, sperm morphology, sperm motility, sperm viability, sperm concentration.
**Financial Support:** CAPES.

## EXP63 - In vivo and in vitro genotoxic characterization of bendamustine using human blood cells and an Aspergillus nidulans diploid strain.

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Bendamustine is an anticancer drug with alkylating properties and widely used to treat haematological malignancies. Since the nitrogen mustard family alkylators induce DNA damages and have been associated with an elevated risk of second malignancy, current study evaluates the cytotoxic, mutagenic and recombinogenic effects of bendamustine using respectively the mitotic index assay, the in vitro mammalian cell micronucleus test (Mnvit) and the chromosome aberration (CA) test in human peripheral lymphocytes, and the in vivo homozygotization assay in Aspergillus nidulans, which detects the loss of heterozygosity (LOH) due to somatic recombination. Bendamustine (6 µg/ml, 9 µg/ml and 12 µg/ml) induced a statistically significant concentration-related increase in the frequencies of micronuclei and a significant reduction in the cytokinesis block proliferation indices (CBPI) when compared to negative control. In the CA test, bendamustine at the three tested concentrations significantly increased the frequencies of structural aberrations when compared to the negative control. The A. nidulans diploids obtained after bendamustine treatment (6 µg/ml, 12 µg/ml and 24 µg/ml) produced, after haploidization, homozygotization indices (HI) higher than 2.0 and significantly different from the negative control. Although the cytotoxic and genotoxic activities of bendamustine described in current assay may be regarded as a benefit to the bendamustine anticancer action, these same activities point to the need to submit patients who received chemotherapy with bendamustine to ongoing physical investigation for the detection of potential late sequelae of the chemotherapeutic treatment, since second malignancies are severe long-term consequences of cytotoxic therapies in patients cured of the primary disorder.

**Keywords:** Alkylating agents, cytotoxicity, in vitro mammalian cells micronucleus test, chromosome aberrations test, mitotic recombination
**Financial Support:** CAPES.

## EXP64 - Comfort food" intake is use as a self medication to reverse anxiety in female rats submitted to early life stress.

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**Background/Aims:** Variations in maternal care in rats can program the function of the hypothalamic–pituitary–adrenal (HPA) axis persistently; pups raised by low maternal care mothers are more anxious and secrete more corticosterone in response to stress in adulthood. In our research group, we demonstrated that early life stress (ELS) affects maternal care and increases offspring anxiety, "comfort food" intake and exacerbates the HPA response to an acute stress. It is suggested that increased corticosterone levels modulate the altered feeding behavior observed in this model. The objective of this research was to investigate the effect of chronic "comfort-food" exposure on the anxiety-related behaviors in animals exposed to ELS and the neuroendocrine response to acute stress. **Methods:** By the second day of life litters of Wistar rats were subjected to reduced nesting material protocol (Early–Life Stress) or standard care (Controls). Maternal care was assessed from days 2-9. In adulthood, females from both groups received ad libitum comfort food diet and regular diet on their homecage for 5 weeks. The following experiments were performed: 1) anxiety was assessed using the novelty-suppressed feeding test (NSFT), 2) the neuroendocrine stress response to 20 minutes restraint stress was verified by measuring plasma corticosterone levels at baseline and immediately, 20, 40, and 70 min. following the stress exposure. **Results:** ELS dams demonstrated lower maternal care (licking and grooming score-LG) compared to controls dams. After the chronic comfort food exposure, ELS group showed levels of corticosterone comparable to controls in response to restraint stress and the previously reported differences in anxiety novelty-suppressed feeding test (NSFT test) were reverted after chronic "comfort food" exposure. **Conclusion:** "comfort food" intake by ELS female rats ameliorated anxiety symptoms and reverted the HPA hyperresponsivity to acute stress.

**Keywords:** Trauma, Anxiety , cortisol
**Financial Support:** BrazilianNationalCouncil for Technologic alandScientificDevelopment (CNPq), CAPES and Fundo de Incentivo à Pesquisa e Eventos do Hospital de Clínicas de Porto Alegre (FIPE/HCPA).

## EXP65 - Paternal obesity affect glucose metabolism in female offspring.

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**Background/Aims:** Although programming of offspring metabolic function is well established in the context of maternal obesity, impacts of paternal obesity has not been well established. This study aim investigates the contribution of paternal obesity status on female offspring glucose dysfunction. **Methods:** Male C57BL/6 mice were divided in 2 groups: high fat diet (HF; 60%kcal fat, n=5) and standard chow (SC, 5%kcal fat, n=5), and fed their respective diets for 10 weeks ad libitum. Males were mated with chow fed female C57BL/6 mice. At birth, the litter size was standardized to 6 pups per dam in both groups: HF Offspring and SC Offspring. The offspring were weaned at postnatal day (P)21, and at P60 were subjected to an intraperitoneal glucose tolerance test (ipGTT) and euthanized to collected pancreatic islets and fat pad stores to evaluated insulin secretion and adiposity respectively. **Results:** HF fathers showed increased body weight (BW), mesenteric and gonadal fat and were hyperglycemic compared to control fathers. In female offspring born to obese fathers, fasting insulin was 49.3% higher compared to chow fed fathers ($p< 0.03$). Although fasting glucose was 6.2% higher in HF offspring this difference did not reach statistical significance ($p< 0.20$), however, HOMA IR was 56.3% higher in HF offspring compared to SC offpring ($p< 0.003$). Female offspring of obese fathers displayed higher glucose levels during ipGTT, where the area under the curve was 33.7% higher compared to SC offspring ($p< 0.001$). In cultured islets, insulin stimulated glucose release was similar between groups. Offspring body weight, food intake and fat pad weights were not different between groups. **Conclusion:** Paternal obesity provoke imbalance of fasting glucose and insulin levels, and led female offspring to glucose intolerance, but this does not appear to be associated with changes glucose stimulated insulin release. Future studies will investigate peripheral insulin sensitivity.

**Keywords:** Paternal obesity, pregnancy, glucose dysfunction
**Financial Support:** Brazilian Federal Financial Agencies: CNPq and Dept of Biochemistry and Biomedical sciences, Ob/Gyn, and Pediatrics MacMaster University- Canada.

## EXP66 - Mobile Phones Radiation During Intrauterine Period Programs Rats for Higher Serum Estradiol in Early Pregnancy.

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**Background/Aim:** Radiation emitted by cell phones decreases the number of ovarian follicles in rats offspring exposed during pregnancy, but the effects on the reproductive capacity and reproductive hormones are still unknown. Thus, we aimed to evaluate the reproductive capacity and reproductive hormones in pregnant rats which was exposed to radiation emitted by mobile phone during intrauterine period. **Methods:** Approval by the CEEA/UFJF (Protocol number 98/2012). Wistar female rats in the 1st day after intercourse were randomized into two groups: exposed to radiation (n=10) and non exposed to radiation (n=10). The exposure took place from 1st to 20th day of pregnancy through phone calls of 25 seconds every 2 minutes for 12h. At birth, litters were weighed and standardized. On the 90th day of life, female from each litter was mated with male fertility previously proven, considering a maximum of three estral cycle of cohabitation. Euthanasia proceeded on the 15th day of pregnancy. After laparotomy, the ovaries were removed and weighed and the number of corpora lutea were counted. Maternal and reproductive variables analyzed: presence of clinical signs of toxicity; proportion of implants, pre and post-implantation losses per group; average weight of fetuses/litter; placentas/litter and external fetal malformations. In serum were measured 17 β-estradiol and progesterone. Statistics: Student's t test ($\alpha$=0.05). **Results:** Females were mated in proposed time. No changes were observed in maternal and reproductive variables analyzed. However, the exposed group showed higher concentration of 17 β-estradiol (+18.73%) in serum, but without changes in serum progesterone when compared to the control group. **Conclusion:** Radiation emitted by mobile phones increase serum estrogen in female pregnant rats that was exposure to radiation during intrauterine period, suggesting a programmer effect on breeding females.

**Keywords:** Mobile phones, programming, radiation, reproductive toxicity, sex hormone.
**Financial Support:** CAPES, UFJF and CNPq.

## EXP67 - Fetal programming by protein restriction leads to reduction of early neurogenesis in CA3 and dentate gyrus of hippocampus.

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**Background:** Nutritional changes in different intensities and ontogenic periods in prenatal life considerably modify the developmental and cells differentiation of key organ tissues. The brain is extremely sensitive to adverse intrauterine environment promoting fetal programming associated to impaired neuronal myelination, reduction of dendritic spines and inhibition of proliferation of neural precursor cells. Aims: Here, we investigate the effects of intrauterine exposure to protein restriction on hippocampal neurogenesis in LP offspring compared to age-matched control group. Methods: Pregnant rats received normal (NP – 17% protein) or low protein (LP – 6% protein) diet during pregnancy. After birth, was measured

birthweight of animals and the body mass on the 14th day of life; the rats were sacrificed and the brains collected for analysis by immunohistochemistry for doublecortin (DCX). **Results:** The current study shows a significant reduction in birthweight in animals LP group. Regarding DCX, we observed a significant decreased expression in CA3 (10%) and dentate gyrus (63%) of LP hippocampus offspring. **Conclusions:** How DCX is highly expressed in neuronal precursor cells and being also important on dendrites development, we might conclude that both neuroprogenitor cells and dendritic arborization development are reduced in the hippocampus of LP group rats as consequence of decreased expression of DCX in CA3 and DG hippocampal regions.

**Keywords:** Fetal Programming, neurogenesis, protein restriction, hippocampus

**Financial Support:** Fapesp: 2013/20539-1 and 2013/12486-5.

## EXP68 - Air pollution as component of metabolic programming.

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**Background/Aims:** DOHaD as concept can be a trigger to cause cardiometabolic diseases spreading fast worldwide. Imbalanced nutrition and physical inactivity during early life has been appointed as a component to cause metabolic dysfunction later in life. Urban agglomeration, as well as in the country, brings contaminants spread into food, clothes, constructions, buildings, houses, electronic devices, ground, radiations and air; which is dangerous to health. After two decades of DOHaD concept some studies have been suggested that environmental contaminants stressing early life can also programming cardiometabolic diseases in adulthood. After all, we can suggest that nutritional abundance combine with air pollution can programming to metabolic dysfunction when offspring turn to adult life. **Methods:** To test the hypothesis we used early overnutrition rat model and air particulate matter (PM<10) were collected in an urban area of Cotonou, Benin (West Africa). The PM<10 solution was prepared with corn oil, and throughout pregnancy and lactation, dams were exposed by oral rote via gavage with 50µg PM<10 per day. After deliverance from dams treated with oil (control-CT) or treated with air particulate matter (PM group) had corrected the litters to 3 pups; given two groups: controls CT-SL and PM-SL. Mothersandoffspringreceived normal commercialchow. All adult offspring with 90 days-old received a high fat diet (HFD) for 30 days. It was taken food intake, body weight gain (bw), fat tissue accretion, glycemia and insulinemia during all protocol. Leaver samples were collected to measure enzyme activities involved with oxidative stress. **Results:** Adult offspring, from mothers treated with PM, eating HFD presented accelerate bw, disruption in glycemic and lipid controls, insulin resistance and degeneration of oxidative stress system, regarding adult offspring that were raised by mothers PM-untreated. Conclusion: Air pollution combined with nutritional abundance during early life malprograms metabolism in adulthood.

**Keywords:** Air pollution, early overnutrition, DOHaD, metabolic dysfunction, oxidative stress

**Financial Support:** CNPq, CAPES.

## EXP69 - Intrauterine Growth Restriction Leads to Endothelial Dysfunction – Possible Involvement of Circulating Endothelial Progenitor Cells.

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**Objective:** The present study aimed to evaluate the effects of intrauterine nutrient restriction (IUGR) on vascular reactivity and endothelial progenitor cells proprieties (EPCs) in adult offspring. **Methods:** Pregnant Wistar Rats received Ad libitum or 50% of Ad libitum diet throughout gestation. At birth, pups were weighted. Adult male offspring from both groups (age range: 19-20 weeks) were euthanized thoracic aorta were excised. Vascular reactivity were evaluated by cumulative concentration-response curves to Acetylcholine (ACh: 10-9M-3X10-5M) and to Sodium Nitroprusside (SNP: 10-9M-10-6M) in thoracic aorta rings. Protein expression of eNOS phosphorylated in serine1177 by western blotting, and Nitric oxide concentration by NO Analyzer were investigated in thoracic aorta. Circulating EPCs number were characterized as CD34+VEGFR2+ cells by flow cytometer, and its functional capacity was assessed in vitro by the colony-forming unit assays. Results are show as mean ± EPM, unpaired test t student were used. (CEUA: 63880). **Results:** Body weight at birth was reduced in restricted offspring (Control: 7.01±0.34g vs. Restricted: 4.3±0.08g). Restricted group exhibited reduction in vasodilatation via ACh (Control: 92.18±2.7% vs. Restricted: 65.04±4.4%), but normal response to NPS (Control: 98.45±2.38% vs Restricted: 93.97±2.64%) in aorta rings. The protein expression of eNOS phosphorylated was similar between groups (Control: 1.16±0.05 vs. Restricted: 1.05±0.01), whereas decrease in NO concentration were observed (Control: 426.2±63.03µM/mg vs Restricted: 217.8±18.22 µM/mg). In addition, we found that circulating EPCs number was not altered by IUGR (Control: 0.008±0.0019% vs. Restricted: 0.007± 0.0009%), but the number of colony-forming unit was reduced (Control: 7.75±0.97 vs. Restricted: 3.80±0.82). **Conclusion:** IUGR-induced endothelial dysfunction, in part due to reduction in NO concentration. Furthermore, given the role of EPCs on vascular repair, the deleterious effects induced by IUGR on EPCs function may have a potential role in the maintenance and/or establishment of endothelial dysfunction in adult male rats submitted to IUGR.

**Keywords:** Intrauterine growth restriction, endothelial progenitor cells, nitric oxide.

**Financial Support:** FAPESP.

# EXP70 - Moderate Exercise Training Prevent Tumor Rat Growth and Cachexia.

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**Background/Aims:** Cancer disrupts metabolism causing cachexia and driving mostly energy reserves to tumor growth. Insulin secretion and insulin tissue sensitivity are decreased in human and rodent who suffer with tumor cancer. Aerobic exercise training has been observed that improved metabolism associated to amelioration of insulin function. The aim of this study was to evaluate the tumor growth (TG) and cachexia (CAC) in Walker-256 tumor bearing rats submitted to the moderate intensity treadmill training (MITT). **Methods:** Male rats with 30 and 70 days old performed MITT (Trained Control= TC) during 16 weeks, 3 days/week, 44 min/day, 55% to 65% VO2max. A group was kept inactive (Sedentary Control= SC). Thereafter, one batch of animals from TC and SC groups were grafted with Walker-256 tumor cells (Trained Walker= TW and Sedentary Walker= SW, respectively). Glucose tolerance (IP GTT) and insulin resistance (IP ITT) intraperitoneal tests were performed. After 14 days of transplantation the rats were euthanized. Body weight (BW), visceral fat pad (VFP), TG and CAC were evaluated. **Results:** Young and adult TC compared to SC rats showed the end of the training an increase in VO2max of 37.8% and 24.7%, respectively. KITT was 10% higher in TC compared to SC and 26.2% higher in TW compared to TC-young-rats. TW-adult-rats showed 19% lower glucose tolerance compared to SW. BW and VFP were reduced by 7,1% and 38,7% in TW-young-rats and 3,3% and 18,4% in TW-adult-rats, respectively. The CAC was 18% lower in both TW-young and TW-adult-rats and TG was reduced 34% in TW-young-rats and 19% in TW-adult-rats compared to SW. **Conclusion:** Moderate exercise training is able to prevent growth of Walker rat carcinoma 256. This inhibition is associated to cachexia and metabolic improvement. These effects are more pronounced when exercise started at adolescence.

**Keywords:** Aerobic exercise, rats, cachexia, insulin sensitivity, metabolism, Walker Carcinoma 256.

**Financial Support:** CNPq and CAPES.

# 5TH INTERNATIONAL SYMPOSIUM ON METABOLIC PROGRAMMING AND STRESS AND THE 2ND MEETING OF IBERO-AMERICAN DOHAD CHAPTER

# FULL CONFERENCES

## FC01 - Mitochondria, the Flexible.

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We will discuss how mitochondrial form and function are altered in caloric restriction, a dietary intervention that enhances lifespan and healthspan. Caloric restriction protects the brain against excitotoxic stimuli by increasing Ca2+ uptake in mitochondrial. Caloric restriction also regulates insulin release by modulating islet mitochondrial dynamics. Finally, mitochondrial morphological changes are central for the differentiation of stem cells. Overall, our results show that mitochondrial form and function are intimately interconnected, and present central regulatory roles in energy metabolism.

**Keywords:** Caloric restriction, mitochondria, energy metabolism

## FC02 - Translating DOHaD concept into epidemiological world.

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One of the challenges of translating DOHaD concept into epidemiological world is to find statistical models suitable for testing DOHaD hypothesis. DOHaD hypothesis are complex, involve longitudinal relationships and deal with many variables at once. Statistical models are a simplification of reality. How can you simplify the complexities of DOHaD hypothesis? In this presentation we will highlight some models that are useful in translating DOHaD concept into epidemiological world. There are two main options: exploratory and explanatory models. But first and foremost one needs to begin with theory. The theoretical model is usually depicted graphically because it is easier to show the complex relationships between variables in a graph. One of the best ways to test exploratory ideas is by structural equation modeling (SEM). In SEM measurement error can be reduced by constructing latent variables, direct and indirect effects can be estimated in multiple regression models that are estimated simultaneously. An example of SEM to test several hypothesis of factors associated with an “asthmatic phenotype” will be shown. In explanatory models, first a directed acyclic graph (DAG) with its testable implications is drawn. The DAGs codify qualitative hypothesis about the causal processes that generate the data. With the help of a DAG, by using the back door criterion, it is possible to identify a minimum set of variables to adjust for confounding, avoid collider bias and unnecessary adjustments. The last step is then to estimate the target quantity using models more appropriate to make causal inference under the counterfactual perspective. For this purpose marginal structural models using inverse probability (IP) weighting, propensity score models, g-estimation or targeted maximum likelihood estimation are used. An example of a DAG made in the DAGitty program and estimation of the target quantity in a marginal structural model using IP weighting will be shown.

**Keywords:** Epidemiology, structural equation modeling, counterfactuals, directed acyclic graph, causal inference.

## FC03 - Maternal obesity and the intersection with microbiota: what are the pathways?

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Since the advent of the Developmental Origins of Health and Disease (DOHaD) hypothesis, many models have consistently shown that the early life environment plays a central role in offspring disease risk. Recent studies have identified new connections between the mother and its developing fetus through the maternal intestinal microbiome, suggestive of novel links between the maternal-fetal unit and new avenues of investigation into postnatal metabolic development and function. Although still controversial, it has been suggested that the developing fetal gut may be colonized before birth. Bacteria associated with the maternal gut have been isolated from meconium, fetal membranes and cord blood of healthy neonates. Experiments in mice support the notion that the fetus may be exposed to maternal gut-derived bacteria which may prime fetal gut development. There is currently no direct evidence of a fetal-microbial interaction in the context of maternal obesity - although maternal obesity results in offspring that have metabolic defects associated with intestinal dysbiosis, inflammation, and altered immune responses. Studies have shown that maternal microbial priming of neonatal intestinal development likely occurs during lactation through breast milk, and that bacterial populations are modifiable by diet and obesity. Whether early life exposure to maternal microbial/inflammatory triggers in the context of maternal obesity impairs offspring development and predisposes to postnatal obesity, is unclear, but is an exciting new avenue of obesity related programming research.

**Keywords:** Maternal obesity, microbiome, fetal gut development, inflammation.
**Financial Support:** Canada Research Chairs Programme, Canadian Institutes for Health Research , NSERC.

## FC04 - The ABC of DOHaD concept.

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The concept of developmental programming is now well established as a result of human epidemiological studies such as those of offspring of the Dutch Hunger Winter and animal models. A compelling body of carefully controlled animal studies in several species has shown that decreased and increased fetal nutrition can program function in multiple offspring organ systems and predispose to chronic diseases and premature aging. Developmental Programming can be defined as **Responses to challenges to developing organisms during a critical time window in fetal and neonatal life that can alter the trajectory of development and predispose to conditions which emerge later.** Programming can also alter the rate of aging, both beneficially and adversely. A metaphor that can be used is that if the automobile is built with substandard materials and functional parts it will not travel for as fast, as far or as long. To understand developmental programming it is necessary to determine 1) the exact nature of the challenges to the fetus and newborn, 2) the precise changes in phenotype produced and 3) cellular and molecular gene-environment mechanisms involved.

**Keywords:** Deveplomental programming, overnutrition, undernutrition.

## FC05 - The Missing Link between Metabolic and Cardiovascular Disease

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The past three decades has seen an unprecedented increase in metabolic and cardiovascular disease, which many attribute, at least in part, to the obesity epidemic. The pathophysiological processes that drive metabolic and cardiovascular disease as a result of excessive caloric intake are becoming clearer. Recent studies demonstrate that alterations in neuroendocrine mechanisms may occur when adipocytes become activated or when their capacity to store lipid is exceeded. Although a myriad of peptides and hormones are involved in the signalling systems that maintain energy homeostasis, recent studies provide convergent lines of evidence that leptinergic, and insulinergic signalling are key. Peripherally generated leptin and insulin acting at central loci modulate outflow of sympathetic and parasympathetic neural activity to target orangs in the periphery, creating a control loop which links the cardiovascular and metabolic systems. An understanding of these control mechanisms may provide opportunities to develop novel treatment modalities for diseases that the World Health Organization predicts as being amongst the greatest risks to human health across the globe.

**Keywords:** Cardiovascular disease, metabolic, caloric intake

## FC06 - Deconstructing Hypothalamic Dysfunction in Obesity.

*LICIO A. VELLOSO.*
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Selected subpopulations of hypothalamic neurons play important roles in the regulation of whole body energy homeostasis. Studies have shown that the saturated fats present in large amounts in western diets can activate an inflammatory response in the hypothalamus, affecting the capacity of such neurons to respond appropriately to satiety and adipostatic signals. In the first part of this conference the mechanisms behind saturated fatty acid-induced hypothalamic dysfunction will be presented. Next, studies that have identified mechanisms that mediate some of the anti-inflammatory actions of unsaturated fatty acids in the hypothalamus will be presented on the context of their preventive and therapeutic potential in obesity.

**Keywords:** Obesity, diabetes, hypothalamus, leptin, inflammation.
**Financial Support:** Sao Paulo research Foundation (FAPESP).

## FC07 - DOHaD Concept at Epigenetic Era.

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Metabolic diseases contribute a massive burden to healthcare throughout the world. The development of disease later in life has been linked to exposure to an adverse intrauterine environment, as observed in offspring of pregnancies complicated by intrauterine growth restriction (IUGR), obesity, or diabetes. The period from conception to birth is a time of rapid growth, cellular replication and differentiation, and functional maturation of organ systems. These processes are very sensitive to alterations in nutrient availability and an abnormal intrauterine metabolic milieu can have long-lasting effects on the offspring. Perhaps the best example of how nutrient availability during pregnancy affects longterm health and disease in the offspring is exemplified by the Dutch Hunger Winter. This period of famine occurred in the western part of The Netherlands during the winter of 1944–45 and the period of famine was clearly defined, and official food rations were documented. Extensive health care and birth weight registries still exist for this population which have allowed numerous studies to be performed which have clearly shown that prenatal exposure to famine is associated with the later development of diseases such as obesity, diabetes, and cardiovascular disease. David Barker and Nicholas Hales coined the term “fetal origins of adult disease” based on their studies demonstrating a relationship between low birth weight and the later development of cardiovascular disease and impaired glucose tolerance. This

concept has been broadened to include nutritional excess and or diabetes during pregnancy. Multiple studies in diverse populations throughout the world have demonstrated a significant correlation between low birth weight, maternal obesity, or maternal diabetes, and the later development of chronic diseases such as type 2 diabetes and or obesity. Both human and animal studies demonstrate intergenerational transmission of the maternal or paternal phenotype, suggesting the possibility that an epigenetic mechanism is mediating these effects.
**Keywords:** Epigenetics, Intrauterine growth restriction (IUGR), Developmental origins of health and disease (DOHaD).

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**01** All the manuscripts will be published in English. The journal accepts original articles, preliminary notes, case reports, review articles, updates and letters to editor. There a topic dedicate to internal medicine linking endocrinology and medical clinic. The journal strongly encourages on line submissions of manuscripts. Those should be accompanied by a title, keywords and an abstract in English for the purposes of international registration. Abstracts in other languages may also be attached.

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# 5th International Symposium on Metabolic Programming and Stress
# &
# 2nd Meeting of Ibero-American DOHaD Chapter

São Luís (MA) - Brazil | 2nd - 4th November 2016

## Final Scientific Program

**November 2nd**

14:00 – 17:00 h: **DOHaD School: Expanding Horizons**

**Chair: Prof. Kesia Palma-Rigo, PhD** *State University of Maringá – Brazil.*

*The ABC of DOHaD Concept*

**Prof. Elena Zambrano**, PhD *Inst. Nac. de Ciencias Médicas y Nutrición "Salvador Zubirán" – Mexico*

*Translating DOHaD concept into epidemiological world*

**Prof. Antonio Augusto Moura da Silva**, MD PhD *Universidade Federal do Maranhão - Brazil*

*Setting up your own DOHaD research line… and life!*

**Prof. Deborah Sloboda**, MD PhD *McMaster University - Canada*

18:00 – 18:30 h: **Opening Ceremony**

18:30 – 20:00h: **"Prof. David Baker Golden Conference"** *DOHaD Concept at Epigenetic Era*

**Prof. Rebecca Simmons**, MD PhD *University of Pennsylvania – USA*

20:00 – 22:00 h: **Catirina's Welcoming Reception**

**November 3rd**

14:00 – 15:30 h: **Session 1:** *Nutritional patterns and metabolic programming*

**Chair: Prof. Egberto Moura, PhD** *State University of Rio de Janeiro - Brazil*

**Main Talk: *Mitochondria, the flexible.***

**Prof. Alicia Kowaltowski**, MD PhD *Universidade de São Paulo – Brazil.*

**Short talk: Gestational protein restriction is related to differential modulation of key developmental regulators in the CA1, CA3 and dentate gyrus of the dorsal hippocampus.**

***Agnes da Silva Lopes Oliveira***, *State University of Campinas - Brazil.*

**Short talk: Early and sustained exposure to high-sucrose diet triggers hippocampal impairments related to oxidative and endoplasmic reticulum stresses in adult rats.**

***Bruno Araújo Serra Pinto***, *Federal University of Maranhão - Brazil*.

**Short talk: High-Fat Diet modulates the Expression of HIF-1 in Hypothalamus: Impact on POMC Expression.**

***Joana Margarida Gaspar,*** *State University of Campinas – Brazil.*

15:30 – 17:00 h: **Session 2:** *Gut Microbiota and metabolic programming*

**Chair: Prof. Alex Rafacho, PhD** *Federal University of Santa Catarina - Brazil*

**Main talk: Maternal obesity intersection with microbiota: What are the pathways?**

**Prof. Deborah Sloboda**, PhD *McMaster University – Canada*

**Short Talk: Early Fecal Microbiota Transplantation: Programming of Pancreatic Islet Function.**

***Audrei Pavanello,*** *State University of Maringá – Brazil.*

**Short Talk: Roux-en-Y Gastric Bypass improves glucose tolerance on male rats fed a cafeteria diet and their offspring.**

***Mariana Carla Mendes***, *State University of Campinas - Brazil.*

**Short talk: Maternal Obesity Leads to Negative Outcomes on Male Offspring Metabolism: Effects of Maternal Metformin Intervention.**

***Gabriela Lira Léon***, *Inst. Nac. de Ciencias Médicas y Nutrición "Salvador Zubirán" – Mexico*



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17:00 – 18:30 h: **Poster Session & Coffee Break**

18:30 – 20:00 h: **Session 3:** *Metabolic Programming and neurocardiovascular outcomes*

**Chair: Prof. Elaine Vieira, PhD.** *Catholic University of Brasília - Brazil*

**Main talk: Metabolic and cardiovascular dysfunctions: The lost chain.**
**Prof. James Andrew Armitage,** PhD. *Monash University - Autralia*

**Short Talk: Intrauterine growth restriction persistently changes the degree of reward to the sweet food - study of dopaminergic pathway.**
***Daniela Pereira Laureano,*** *Federal University of Rio Grande do Sul – Brazil.*

**Short Talk: Maternal overnutrition induces sex-dependent endocannabinoid system dysfunction and oxidative stress in rat offspring liver at adulthood.**
***Rosiane Aparecida Miranda****, Federal University of Rio de Janeiro - Brazil.*

**Short talk: Soy isoflavone treatment in early postnatally overfed Rats affect metabolism and autonomic nervous system.**
***Sandra Silveira****, State University of Maringá – Brazil.*

**November 4th**

10:00 – 12:00 h: **Extraordinary Assembly of the Directive Committee of Ibero-American DOHaD Chapter**

14:00 – 15:30 h: **Session 4:** *Maternal metabolic disturbances and offspring metabolic outcomes*

**Chair: Prof. Elena Zambrano, PhD** *Inst. Nac. de Cienc. Méd. y Nutrición "Salvador Zubirán" – Mexico*

**Main Talk: Long-term effects of maternal obesity and gestational diabetes on their offspring growth and development.**
**Prof. Cristina Campoy**, MD PhD *Universidad de Granada – Spain*

**Short Talk: Birth Weight is Associated with Lean Mass Compartment in Young Healthy Adults from Nutritionists' Health Study.**
***Angélica Marques Martins Valente,*** *Universidade de São Paulo – Brazil.*

**Short Talk: Unbalanced M1 and M2 responses in neonatal monocyte-derived macrophages from women with pre-gestational obesity.**
***Bernardo J. Krause,*** *Pontificia Universidad Católica de Chile – Chile.*

**Short talk: Eating Behavior in Fetal Growth Restricted Adolescents: Programming Goes Beyond Food preferences.**
***Roberta Dalle Molle****, Federal University of Rio Grande do Sul – Brazil.*

15:30 – 17:00 h: **Round Table:** *Birth cohorts and maternal nutrition in Latin America*

**Chair: Prof. Antonio Augusto Moura da Silva**, MD PhD *Universidade Federal do Maranhão – Brazil.*

**Prof. Francisco Mardones**, MD PhD *Pontifícia Universidad Católica – Chile*

**Prof. Heloísa Bettiol**, MD PhD *Universidade de São Paulo – Brazil*

**Short talk: Birth weight and blood pressure in two cohorts 15 years apart in Valparaiso Region, Chile**.
***Patricia Bustos****, University of Chile- Chile*.

**Short talk: Pre-pregnancy Nutritional Status, Gestational Weight Gain and Birth Weight in the BRISA Cohort.**
***Raina Jansen C. Propp Lima,*** *Fed. Inst. of Educ., Sci. and Tech. of Maranhão – Brazil.*

# 5th International Symposium on Metabolic Programming and Stress
# &
# 2nd Meeting of Ibero-American DOHaD Chapter

São Luís (MA) - Brazil | 2nd - 4th November 2016

17:00 – 18:30 h: **Poster Session & Coffee Break**

18:30 – 20:00 h: **"Take-home Conference"** *Deconstructing Hypothalamic Dysfunction in Obesity*
**Prof. Licio Velloso**, MD PhD *State University of Campinas - Brazil*

20:00 – 20:30 h: **Symposium Remarks and Closing Ceremony**
**Prof. Paulo Cezar de Freitas Mathias**, PhD *State University of Maringá - Brazil*

21:30 – 24:00 h: **Cacuriá's Dinner**

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