2nd INTERNATIONAL SYMPOSIUM of DOHaD and STRESS:
METABOLISM, EXERCISE, STRESS and BEHAVIOR

In the last decades, a group of diseases has gained importance in human health, which are called, non-communicable diseases (NCD), among them its highlighted cardiovascular disease, diabetes and cancer. Recently, World Health Organization has estimated that this group of diseases has been doing more than 41 millions of victims every year, being between the main causes of death worldwide. The explanation that those diseases are exclusively caused by an inadequate lifestyle it's not sufficient to explain the rapid growth in the prevalence worldwide. A series of epidemiologic and experimental studies has shown evidences that these diseases may be caused by stressor events suffered by the subject during critical phases of his development (pre-conception, lactation, infancy and adolescence), programming his organism to the development of cardiometabolic diseases during adult life, being able to affect next generations.

In this sense, the DOHaD (Developmental Origins of Health and Disease) concept, search to clarify what are the susceptible phases to the programming of the organism, as well what are the insults that can initiate this phenom. The 2nd International Symposium of DOHaD and Stress (2ndISDS) approached the DOHaD concept, applied in differente themes, such as: metabolism, exercise, behavior and reproduction.

The 2ndISDS promoted the interaction and change of experiences between researchers, professor and students of graduation and post-graduation that act in different areas (Biological Sciences, Biomedicine, Medicine, Biotechnology, Physical education, Nutrition, among others). The first edition of ISDS occurred in 2017 at Buenos Aires, Argentina, being it second edition made in the State University of Maringá, bringing together Brazilian lecturers from UNICAMP, USP, UFRGS, and researchers from Argentina, Mexico and USA worldwide recognized for their works regarding the themes of the symposium.

There was participation of 80 congressmen, distributed between researchers, professors, post-graduation and graduation students from different universities. The congressmen had the opportunity to present works approaching the themes of the symposium and discuss them with internationally renowned researchers. Thus, the 2ndISDS 2018 had come to Brazil with the mission of spread the DOHaD concept and integrate the academic society around discussions that bring advances to the researches in favor of health and life, in all his phases of development.

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ABSTRACTS

REPRODUCTION

LOW PROTEIN DIET DURING THE LACTATION INDUCES PERMANENT DAMAGE IN RAT MALE REPRODUCTIVE SYSTEM WHICH WAS NOT EXACERBATE BY HIGH FAT DIET DURING ADULTHOOD

Gessica Dutra Gonçalves[1], Josana Klagenberg[1], Henrique Rodrigues Vieira[1], Isabela Peixoto Matins[1], Lucas Paulo Jacinto Saavedra[1], Maria Natália Chimirri Peres[1], Carina Previate[1], Monique Suellen da Silva Marcon[1], Sandra da Silva Silveira[1], Ana Maria Praxedes de Moraes[1], Glaura Scantamburlo Alves Fernandes[2], Paulo Cesar de Freitas Mathias[1].

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Background: The fetal malnutrition was related with alterations in the hypothalamic cells culminating in adults more susceptible to hormonal changes and diseases such as obesity. The male reproductive system is dependent of the fat tissue as well as the correct function of hypothalamic system. Some studies have been showing the relation between male reproductive disorders and different diets during developmental critical windows. Our aim was to evaluate if the second hit by high fat diet (HF) at adulthood can exacerbate the male reproductive system disorders after a fetal programming by low protein diet. **Methods:** Mothers were fed with a low-protein diet (LP; 4% protein) or a normal-protein diet (NP; 23% protein) during the first 2 weeks of lactation, after this time rats offspring from NP and LP mothers received a normal-protein diet until 60 days old. From 60 days old to 90 days old, half of animals from both groups (NP and LP) were fed an HF diet at 35% fat (LP/HF or NP/HF), while the other half received a NF diet at 7% fat (LP/NF or NP/NF). At 90 days of age, the animals were anesthetized, weighed and submitted to euthanasia. The blood was collected for lipid profile analysis, insulin and protein total dosage. The quality of the gamete was assessed by motility and reproductive organs were dissected and the weights were determined. **Results:** Sperm motility and insulin dosage were statistically similar in all groups, although both groups LP demonstrated a reduction of approximately 17% and 43% in the sperm motility and insulin dosage, respectively. LP/NF augment the triglycerides, while the analysis of cholesterol total, LDL, VLDL and HDL had not difference among the groups as well as the protein total dosage. Body weights were decreased in the animals LP/NF. The LP animals submitted to HF or NF during adulthood showed a reduction in the testicles and epididymis weight compared with NP groups. The NP/HF increased the vas deferens weight. **Conclusion:** The male reproduction presented an adaptation against damages caused by HF diet at adulthood, since few alterations was observed in the groups NP/HF and LP/HF, however the LP diet induced a permanent damage in the weights of the reproductive organs in LP/NF and LP/HF, it demonstrates the importance of lactational period for male reproduction health, but more studies are necessary to complete our understanding about this subject.

Key-words: Low Protein Diet, Hight Fat Diet, Reproduction.

Financial Support: CNPq, CAPES.

POSTNATAL METABOLIC PROGRAMMING INDUCES OBESITY AND REPRODUCTIVE CHANGES IN FEMALE RATS

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Background/Aims: Maternal obesity, environmental influences, postnatal and susceptibility are risk factors for the development of metabolic syndrome and childhood obesity. Postnatal (PN) early overfeeding by small litters (SL) leads pups to overnutrition and is a risk factor for metabolic and reproductive disorders. We aimed to investigate the effects of postnatal early overfeeding on metabolic and reproductive parameters in female rats. **Methods**: After postnatal 3-day (PN3), the female Wistar rats (F0) were divided in two groups: normal litter (NL, 9 pups) and small litter (SL, 3 pups) throughout lactation period. After weaning (PN21) female offspring (F1) were fed control diet *ad libitum*. At PN25, we verified the onset of puberty by observing the complete vaginal opening of the females. The frequency of the estrous cycle was determined by checking the phases of the cycle, obtained by vaginal lavage and fresh visualization under a light microscope with 10x and 40x objective, in PN50 to PN71. The sexual behavior the females was performed in the PN71 to PN80 in the proestrus phase with a video camera analyzing the behavioral parameters of proceptivity and receptivity. After a 12-hour fast, the females were anesthetized, collected blood samples and euthanized for tissues collections. The retroperitoneal, perigonadal and periuterine fats were extracted and weighed to provide estimates of the tissue accumulation of animal fat. The cesarean was performed in post gestational 19-day (PG19) for fetal viability (FV) analysis, counting of corpus luteum (CL), implantation (IS) and reabsorption (RS) sites. All procedures were approved by the ethics committee of UFG (Protocol 043/17). **Results**: The female offspring of F1 developed obesity, presented changes in lipid and glycemic profile, entered puberty earlier than the NL group, presented irregular estrous cyclicity and were less proceptive and receptive in sexual behavior ($p<0.05$). There were no changes in FV, IS and RS. However, females SL presented smaller numbers of CL in relation to NL females. **Conclusion**: Early postnatal overfeeding causes obesity, metabolic and reproductive changes in female rats.

Key-words: Small litter, Obesity, Reproduction.

Financial Support: FAPEG; CAPES and CNPq.

IN UTERO AND LACTATIONAL EXPOSURE TO TRICLOCARBAN INDUCES SEXUAL BEHAVIOR ALTERATIONS IN MALE RAT OFFSPRING

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Background: Triclocarban (TCC) is an antimicrobial compound widely used, since the 1960s, in personal care products. It is commonly found in soaps, toothpaste, and shampoo. This agent is incompletely removed by wastewater treatment and represents an environmental contaminant. Recent studies shown that TCC has been associated with some endocrine disruptions. In vitro, TCC demonstrated a potent androgen-augmenting activity. In this sense, we studied if TCC exposures during critical period of development (gestation and lactation) could lead to some adverse health outcomes, based on the concept of the Developmental Origins of Health and Disease. Therefore, the purpose of this study was to evaluate if TCC exposure during peri and post-natal period could adversely affect the pubertal onset, sexual behavior and reproductive organs weight in adulthood. **Methods:** Pregnant female *Wistar* rats were divided into four groups (n=8-11/group): Control (CTR); TCC 0.3 mg/kg (TCC 0.3); TCC 1.5 mg/kg (TCC 1.5); TCC 3.0 mg/kg (TCC 3.0). The females were treated daily by oral gavage from gestational day (GD) 0 to lactational day (LD) 21. The male pups (F1 generation) were weaned on post-natal day (PND) 21 and used for the study, no litter-mates were used for the same group. The preputial separation was observed (from PND 45) and the sexual behavior was evaluated at PND 90. At PND 120 all animals were weighted, euthanized and the following organs collected and weighted: testis, epididymis, prostate, seminal vesicle. Data were compared by ANOVA; or Kruskal- Wallis; and the copulatory/ejaculatory index by Fisher's exact test ($*p \leq 0.05$). (CEUA/UEL: 130.2016.24). **Results:** There were no alterations in the day of preputial separation and reproductive organs weight. However, it was observed a decrease in the number of animals that ejaculated at TCC 3,0 group (CTR: 100% [8/8]; TCC 0,3: 77,78% [7/9]; TCC 1,5: 60% [6/10]; TCC 3,0: 50%* [4/8]), when compared to the CTR group. **Conclusion:** The present study reveals that peri and post-natal treatment with TCC could impair the sexual behavior, which could be related to the hormonal profile during the hypothalamic sexual differentiation that occurs on GD 17/18 and remaining until PND 10.

Key-words: sexual behavior, antimicrobial, endocrine disrupter.

Financial Support: Fundação Araucária, Capes.

β-ESTRADIOL 17-VALERATE ACTING AS A POSSIBLE ENDOCRINE DISRUPTOR IN *ASTYANAX ALTIPARANAE*.

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

Key-words: Endocrine disruptors, Fishes, Gonads.

Acknowledgements: CAPES/UEM.

Financial Support: CAPES/UEM.

PTEROSTILBENE RESTORES THE EFFECTS CAUSED BY THE SUCROSE DIET IN THE TESTIS OF WISTAR RATS

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Background: In the last decades sugars consumption has been associated with increasing prevalence of metabolic diseases. Soft drinks and sugar-sweetened beverages are a leading source of added sugar in the world. Today about 18%–25% energy comes from simple sugars. Interestingly, the growing report of infertility and the increasing incidence of metabolic diseases are associated with changes in dietary pattern and behavior. Pterostilbene is an antioxidant component of blueberries. Multiple studies have demonstrated the antioxidant activity of pterostilbene in both *in vitro* and *in vivo* models illustrating both preventative and therapeutic benefits. However, few studies investigated the benefits of pterostilbene in male reproductive system and whether it improves fertility in a sugar-enriched diet model. In this study, we investigated the effect of sucrose diet on body weight, reproductive organ weights and spermatogenesis kinetics in rats. **Methods:** Male Wistar rats (60 days old) were obtained from the Central Animal House of Universidade Estadual de Maringá (UEM). Rats were acclimated to their new environment for 7 days. Then, for 150 days, 12 animals received filtered water and commercial chow *ad libitum* and the other 12 animals received commercial chow and water plus sucrose 40% *ad libitum*. Next, the animals were distributed into four groups: Control group; Control + Pterostilbene (40mg/kg) by gavage for 45 consecutive days; Sucrose (40% supplementation in water) for more 45 days; Sucrose + Pterostilbene (40mg/kg) by gavage and sucrose (40% supplementation in water) for more 45 days. After this period, euthanasia was performed and organs were removed and weighed for further analysis. Spermatogenesis kinetics was performed by histology and counting by the optic microscope. **Results:** The weight of the testis (1.43 ± 0.05) in the group treated with sucrose was lower when compared with the control group (1.63 ± 0.11). The group that received sucrose + Pterostilbene (1.60 ± 0.12) was similar to the control. Sucrose group had a percentage increase of phase I-VI in spermatogenesis. Thus, the sucrose appears to influence testis of Wistar rats decreasing the weight and phase I-VI in spermatogenesis. **Conclusion:** However, more studies will be done to investigate the role of sucrose in male fertility.

Key-words: Sucrose, male fertility, spermatogenesis.

HYPERHOMOCYSTEINEMIA IMPAIRS THE MALE REPRODUCTIVE SYSTEM OF MICE

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Background: Homocysteine is an amino acid (Hcy) formed from methionine demethylation. This amino acid interacts for two metabolic pathways: remethylation and transsulfuration. Imbalance in these pathways may cause elevation in plasma concentrations of Hcy characterizing hyperhomocysteinemia (HHcy). Currently, HHcy has been correlated with deficient sperm function by induction the formation of reactive oxygen species, damage to DNA and lipid peroxidation. However, a better understanding is needed about the effect of HHcy directly on the male genital system organs. **Methods:** Two different experimental times (30 and 60 days) were used. Swiss mice weighing 20 grams were distributed in 4 experimental groups: mice in C30 and HHcy30 (treatment 30 days, n=7 per group), C60 and HHcy60 (treatment 60 days, n=6 per group), kept in individual cages received food and water *ad libitum*. The HHcy groups received 1g/Kg/day of dl-Homocysteine thiolactone in water for the HHcy induction. After the treatment the animals were anesthetized (isoflurane) and euthanized by decapitation. Spermatozoa from deferent ducts were used to evaluation of sperm morphology and motility. Testicles and epididymis were used to calculate the daily sperm production and sperm transit time through the epididymis and evaluation of myeloperoxidase (MPO) and N-acetylglucosaminidase (NAG) activity. Statistical analysis was performed by the GraphPad Prisma® program, using the t-test to identify differences between groups (significant when $p<0.05$). **Results:** According to sperm motility analysis, only the HHcy60 animal group show an increase in the percentage of immobile spermatozoa compared to their control group ($p=0.0095$). However, there were no differences between groups in relation to number of morphologically abnormal spermatozoa, daily sperm production and sperm transit time. The MPO analysis showed no increase in neutrophil migration to the testicular and epididymal tissue, however the NAG analysis indicated increase of monocyte migration only in the testicular tissue of the HHcy60 group compared to the control group ($p = 0.0083$). **Conclusion:** HHcy-induction in Swiss mice for 60 days impairs the sperm motility and increase migration of monocytes to the testicular tissue are associated with male reproductive damage.

Key-words: Hyperhomocysteinemia, Reproductive System, Spermatozoa.

Financial Support: CAPES.

CONSUMPTION OF FRUCTOSE REDUCES THE WEIGHTS OF THE REPRODUCTIVE ORGANS AND SPERM MOTILITY OF WISTAR RATS

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Background: The consumption of sugars has increased the last three decades and is partly responsible for the increase of obesity, metabolic syndrome and diabetes. Some studies show positive correlations between intake of sweeteners and male reproductive system. The consumption of fructose has increased considerably during the past years. Fructose commonly is found in foods and beverages as a natural component (fruits) or as an added ingredient. Increase in consumption of foods with high amount of fructose is considered as one of the main factors responsible for progression to metabolic syndrome, but there is still little evidence about fructose influence in male fertility. In this study, we investigated the effect of fructose diet on body weight, reproductive organ weights and sperm motility in rats. **Methods**: Male Wistar rats (25 days old) were obtained from the Central Animal House, State University of Maringá. Rats were acclimated to their new environment for 5 days. The animals were distributed into two groups: Control and Fructose group that received 20% fructose supplementation in water for 30 days (PN90-PN120). Euthanasia was performed at 120 days of age. The organs were removed and weighed for further analysis. Sperm motility was performed by washing the vas deferens and counting by the optic microscope. **Results:** The weight of the testis (1.44 ± 0.12), epididymis (0.48 ± 0.05), vas deferens (0.08 ± 0.01) and prostate (0.30 ± 0.06) in the group treated with fructose 20% was lower when compared with the control group: testis (1.58 ± 0.12), epididymis (0.61 ± 0.04), vas deferens (0.12 ± 0.01) and prostate (0.39 ± 0.06), respectively. Animals that received fructose had a decrease in the number of sperm motility (56.80 ± 8.66) when compared to control group (70.11 ± 11.36). **Conclusion:** Therefore, the fructose diet impairs the male reproductive system of Wistar rats.

Key-words: Fructose diet, male fertility, sperm motility.

Financial Support: CAPES.

EARLY APPLICATION OF METFORMIN PREVENTS THE SPERM DAMAGE INDUCED BY HIGH-FAT DIET INTAKES IN ADULTHOOD.

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Background: Nowadays, among the health problem, obesity has been highlighted. The rate increased in all phases of life during the last decade. Patients with obesity commonly show another issues, such as type II diabetes and reproductive damages. The drug metformin has been widely used in patients with type II diabetes to control glucose levels in the blood. However, recent researches reported the drug may be use to promote another benefits, like health span and longevity. The aim of this study is evaluate whether the response of Metformin in the early life at 90 days old may modulate normal function of testis and prevents later insults in the male reproductive. **Methods:** Rat Wistar pups were divided in two groups, Saline (S), that received saline solution 0.9%, and Metformin (M), that received 100mg/kg body weight (bw)/day, both the vehicle were applied via an intraperitoneal injection from the first to the 12 days old. At 60 days old, S group and M group were subdivided in a normal fat diet (4.5% of fat; NF), SNF and MNF, high-fat diet (35% of fat; HF), SHF and MHF, up to 90 days old. **Results:** The absolute testes weight was equal in all groups. Relative weight of testis of groups SHF and MHF decreased compared with SNF. The seminiferous tubules diameters were reduced in all groups compared with SNF. The seminiferous epithelium height decreased in the MNF and MHF groups in relation to SNF groups. The histopathological analysis and spermatogenic kinetics in the testes did not change in all groups. The number of abnormal sperm and isolated head was increased in the SHF group compared to others groups. Head without characteristic curvature reduced in the M groups when compared with S groups. **Conclusion:** Early life metformin treatment was able to program the function of testicle with changes in the morphological structure of seminiferous epithelium and also ameliorated the sperm morphology. Also, the early application of metformin may be prevent injures of high fat diet intake. However, more studies are necessary to better understand these modifications.

Key-words: Reproductive programs, Metformin, Lactation.

Financial Support: CAPES.

PULMONARY EMPHYSEMA MODIFIES THE OXIDATIVE BALANCE, TESTOSTERONE LEVELS AND LEYDIG AND SERTOLI NUMBERS IN THE TESTICLE IN *MESOCRICETUS AUTRATUS*

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Background: The Chronic Obstructive Pulmonary Disease (COPD) has been characterized by remodeling of airways and pulmonary parenchyma and inflammation; these factors change the pulmonary physiology. The COPD is related to increased oxidative stress in patients. There are studies that show the association of some chronic diseases with male infertility, such as obesity, hypertension and type II diabetes. The aim of this study is to investigate the relation between pulmonary emphysema and the male reproductive system in the *Mesocricetus auratus.* **Methods:** For it, 35 male rats, which weighing between 90 – 130g, were separated in two groups: The control group (C) and emphysema group (E). The animals of the group C received the instillation of saline solution (0.3 mL/ 100 g of body weight) and the E group with instillation of papain (40 mg / 100 g of body weight). After 60 days, the plasma, right testicle and epididymis were collected to oxidative stress, to histological analyses the left testicle was collected. **Results:** Leydig and Sertoli cells numbers were decreased in E group. The Leydig cell showed bigger volume and area of nucleo than C group, which can reflect in more plasma testosterone concentration in the blood of group E. There was also an alteration in the chemiluminescence of testis and epididymis (caput and cauda) in group E, demonstrating an increase in lipid peroxidation and a reduction of the antioxidant potential of the radical in the cauda epididymis and reduction of glutathione in the caput epididymis. **Conclusion:** The pulmonary emphysema impaired testosterone levels and affected the oxidative stress balance in testicle and epidydimis. Therefore, these alterations may be involved in the reduction of Sertoli and Leydig cells numbers, leading to an unbalance among the normal function of the male reproductive system. However, more studies are necessary to better understand these modifications.

Key-words: Testosterone, emphysema, testicle.

Financial Support: CAPES.

EVALUATION OF THE SIMULTANEOUS MATERNAL EXPOSURE TO PARABEN AND PHTHALATE EFFECTS ON THE OFFSPRING SEXUAL DEVELOPMENT

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Background: Parabens and phthalates are widely used in industry and are frequently found as contaminants in human tissues and biological fluids. Studies have shown that these chemicals are considered endocrine disruptors, able to alter the homeostasis of the reproductive system. Knowing that the exposure to several substances present in the environment may occur simultaneously throughout lifespan and contribute to reproductive dysfunctions, specially in critical periods of development as intrauterine and post-natal periods, the present study aimed to assess the toxic effects of the simultaneous exposure to parabens and phthalates on the sexual development of rats. **Methods:** pregnant *Wistar* rats were allocated into six experimental groups: gavage control (GC , n=6) which received corn oil (vehicle) - orally - gavage; subcutaneous control (SG, n=6) received vehicle subcutaneously; gavage + subcutaneous control (SGC, n=5) was exposed to vehicle orally and subcutaneously; Butyl paraben (BP, n=7) treated with 100mg/kg subcutaneously; Di-(2-ethylhexyl) phthalate (DEHP, n=5) exposed to 500mg/kg orally (gavage); and BP+DEHP (n=8), exposed to 100mg/kg of BP (subcutaneously) and 500mg/kg of DEHP (gavage) simultaneously. The doses of BP and DEHP represent the LOAEL for reproductive parameters. The exposure period was between gestational day 12 until the end of lactation (post-natal day –PND 21). Maternal body weight was assessed on alternate days for evaluation of toxicity. In the offspring, the following parameters were studied: number of live pups, body weight and relative anogenital distance on PND1, number of nipples on PND13 and, beginning on PND30, the puberty onset (preputial separation on male pups and vaginal opening and first estrus on female pups). **Results:** Results showed the simultaneous exposure to BP and DEHP did not alter the maternal body weight evolution, neither the number of live pups. Male offspring from BP+DEHP group presented reduced body weight on PND1 when compared to SGC and BP groups. The other evaluated parameters were similar among experimental groups. **Conclusion:** We may conclude, based on presented results, that BP and DEHP were not able to significantly alter the sexual development of the offspring, when administered alone or in combination.

Key-words: pregnancy, paraben, phthalate, offspring, development.

EXERCISE

SOLEUS MUSCLE CAPILLARY AND NUCLEI BY FIBER RATIO OF OOPHORECTOMIZED RATS AND SUBMITTED TO VIBRATORY PLATFORM TREATMENT

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Background. Nowadays, the use of mechanical vibrations is growing as a prevention for disorders caused in muscle tissue, for example, by the transformations caused in the body with the menopause. Therefore, this study aims to evaluate the effects of oophorectomy and its vibratory platform treatment on the capillaries and peripheral nuclei of the soleus muscle of female rats. **Methods.** A total of 72 female *Wistar* rats were used and randomized into the Pseudoophorectomy (PG) and Oophorectomy (OG) groups. After 60 postoperative days, the animals were submitted to therapeutic interventions and divided into eight subgroups: animals that did not undergo any treatment and were euthanized after four (GP4 and GO4) and eight (GP8 and GO8) weeks, and animals treated during the same periods (GPT4, GOT4, GPT8 and GOT8) weeks. The treatment consisted of the use of vibratory platform, 60 hertz frequency for 10 minutes, three times a week. At the end of the experimental periods the animals were euthanized and the soleus muscle was collected, the left antimer was frozen in liquid nitrogen and submitted to cross sections (7 μm thick) in a cryostat chamber and stained with Hematoxylin-Eosin. This material was photodocumented and used to measure the ratio of nuclei and capillary/fiber through 10 microscopic fields (40x objective). Data were analyzed regarding normality and analysis of the three-way variance, and significance level of 5%. **Results.** In the results of the capillary/fiber ratio, there were no significant differences between any of the sample groups. For the nuclei/fiber ratio, GP4 and GO4 had higher means in relation to GPT4 and GOT4 and, when time was compared, the ratio was higher in four weeks than in eight. **Conclusion**. In this way, it is concluded that the treatment with the use of the vibratory platform leads to a reduction of the number of cores per fiber, being more evident in the period of four weeks.
Key-words: Hormonal Deprivation, Whole Body Vibration, Skeletal Muscle.

Acknowledgements: A CAPES pelo apoio financeiro ao grupo de pesquisa.

WHOLE-BODY VIBRATION EFFECTS UNDER LIPOPEROXIDATION AND ANTIOXIDANT HEPATIC SYSTEM OF OBESE RATS

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Background: The Oxidative stress, imbalance between reactive oxygen species production and antioxidant protection, is characteristic in obese individuals. Considering the prevalence of obesity associated diseases and damage caused by oxidative stress, there is a search for alternative treatment forms one of them is the whole-body vibration (WBV). The study aimed to evaluate the WBV effects on obese rats antioxidant system by monosodium glutamate (MSG). **Methods:** Male offspring of 10 female rats were divided in two groups during the neonatal period (1st - 5th day), whose animals received subcutaneous injections of MSG (Ob), or equimolar saline solution (Ct). After weaning (21), pups were randomized again resulting in four subgroups (n = 10): Ob-Ct and Ct-Ct: no treatment; Ob-P and Ct-P which were treated over an eight weeks period with a vibratory platform (60 Hz frequency) three times a week for 10 minutes. At euthanasia, about 100 mg of the liver medial lobe was removed and macerated in Tris buffer solution (pH = 7.4) and then, centrifuged. Supernatant was used for protein quantification, enzyme superoxide dismutase (SOD) dosing, and lipoperoxidation reaction (LPO) analysis by malondialdehyde byproduct absorbance means. **Results:** The groups submitted to MSG showed higher hepatic protein concentration regarding to the ones exposed only to saline solution ($p = 0.03$). When the groups classified according to the use of the platform were evaluated, the means were similar ($p = 0.98$) and there was no significant interaction between the factors ($p = 0.093$). The frequency of lipoperoxidation reaction was higher in obese animals compared to the other groups ($p < 0.01$) and considering the statistical interaction among the factors, the Ob-P groups showed this activity more pronounced ($p = 0, 03$), since the mean was significantly higher. On the other hand, the activity of the SOD enzyme was similar among all groups, and there was no observed effect between the isolated factors (MSG $p = 0.08$, Platform $p = 0.09$) nor the interaction between them ($p = 0,44$). **Conclusion:** The obesity model increased the amount of liver protein as well as tissue lipoperoxidation, which was accentuated by WBV and, there was no change in the activity of the antioxidant enzyme SOD.

Key-words: oxidative stress, whole-body vibration, obesity.

Acknowledgements: To the Postgraduate Program in Biosciences and Health and to the Western Paraná State University for the opportunity of this study development, to CAPES, for the scholarship granting and to Fundação Araucária for the financial assistance.

SOLEUS MUSCLE MORPHOLOGY OF FEMALE OOPHORECTOMIZED RATS AND SUBMITTED TO TWO PERIODS VIBRATORY PLATFORM TREATMENT

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Background. Menopause is a stage where transformations occur in the body which may result in skeletal muscles alterations. To mitigate this fact, mechanical stimuli have been used as treatment. Thus, this study aims to evaluate the morphological effects of the vibratory platform treatment in different periods in the soleus muscle of oophorectomized rats. **Methods.** A total of 72 female *Wistar* rats were used and randomized into the Pseudoophorectomy (PG) and Oophorectomy (OG) groups, and subdivided (n=9) into untreated and euthanized animals after four (PG4 and OG4) and eight (PG8 and OG8) weeks and animals treated for four (TPG4 and TOG4) and eight (TPG 8 and TOG8) weeks. The treatment consisted of the use of vibratory platform, 60 hertz frequency for 10 minutes, three times a week. At the end of the experimental periods the animals were euthanized and the soleus muscle was collected, the left antimer was frozen in liquid nitrogen and submitted to cross sections (7 μm thick) in a cryostat chamber and stained with Hematoxylin-Eosin. This material was photodocumented and used for general morphological analysis of the tissue through 10 microscopic fields (objective of 40x). Data were analized regarding normality and analysis of the three-way variance, and significance level of 5%. **Results.** The soleus muscle of the groups GP4 and GP8 presented well preserved morphology, with its fibers in polygonal format and homogeneous, arranged in fascicles, besides its nuclei located in the periphery of the fibers. In TPG4 and TPG8 groups, the morphological characteristics were similar, however, they presented larger diameter of their fibers, demonstrating muscular hypertrophy caused by the vibratory platform treatment. In the GO4 and GO8 groups, there were no significant tissue changes, however, compared to the GOT4, GOT8, GP4 and GP8 groups, the muscle fibers were smaller, indicating hypotrophy. On the other hand, the GOT4 and GOT8 groups presented muscle fiber size similar to that of the GP4 and GP8 groups, which may suggest treatment efficacy in the reversal of the hypotrophy process. **Conclusion.** Herewith we conclude that the hormonal deprivation leads to muscular hypotrophy in the animals submitted to oophorectomy, and this process can be reverted with vibratory platform use, which leads to hypertrophy.

Key-words: Hormonal Deprivation, Whole Body Vibration, Skeletal Muscle.

Acknowledgements: A CAPES pelo apoio financeiro ao grupo de pesquisa.

BODY AND METABOLIC PARAMETERS OF OBESE RATS SUBMITTED TO WHOLE-BODY VIBRATION

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Background: Obesity is a multifactorial pathology that can be a risk factor for associated diseases. Among the searches for prevention and treatment alternatives the whole-body vibration (WBV) modality has been highlighted, however, little is known about its real effects. Therefore, this study aims to evaluate the vibratory platform action on body parameters and metabolism of obese Wistar rats by monosodium glutamate (MSG). **Methods:** Male offspring of 10 female rats were randomized into two groups, whose animals received subcutaneous MSG injections (Ob) during the first five days of life, or equimolar saline solution (Ct). At weaning (21 days) the pups were subdivided into four subgroups (n = 10): Ob-Ct and Ct-Ct: without treatment; Ob-P and Ct-P were treated with vibratory platform (60 Hz frequency) three times a week for 10 minutes over a total period of eight weeks. After that, we measured the body weight (BW), nasoanal length (NAL), Lee index (LI) and performed euthanasia by anesthetic overdose. Retroperitoneal (RF) and perigonadal (PF) fats were weighed and plasma collected for triglyceride (TG) and cholesterol (COL) dosages. **Results:** The BW and NAL were significantly higher in the Ct-Ct and Ct-P groups ($p < 0.01$) than the other groups. However, WBV treatment didn't influence ($p = 0.52$, $p = 0.12$) and there was no interaction between factors ($p = 0.92$, $p = 0.95$). As for LI, the obese groups had averages higher than the others ($p = 0.02$) and non-significant interaction ($p = 0.75$). RF and PF had higher mean values in the obese groups ($p < 0.01$), but the treatment did not reverse these values ($p = 0.66$), as there was no interaction between the factors ($p = 0.56$). The MSG increased TG ($p < 0.01$) and the WBV treatment was able to raise this parameter, since Ob-P presented more TG than Ob-Ct ($p = 0.01$) with interaction between the factors ($p = 0.03$). Unlikely, COL was elevated only in the Ob-Ct and Ob-P groups ($p = 0.01$), similar between the treated and non-treated groups ($p = 0.67$) and without significant interaction ($p = 0.43$). **Conclusion:** MSG was effective to induce obesity, once increased fat deposits, LI, TG and COL and the treatment influenced only plasma TG. The smaller NAL and BW are characteristic of this model.

Key-words: monosodium glutamate, obesity, whole-body vibration.

Acknowledgements: To the Postgraduate Program in Biosciences and Health and to the Western Paraná State University for the opportunity of this study development, to CAPES, for the scholarship granting and to Fundação Araucária for the financial assistance.

MORPHOLOGICAL ALTERATIONS AND PRINCIPALS COMPONENTS ANALYSIS OF VIBRATORY PLATAFORM APPLICATION AS TREATMENT FOR MUSCULAR ATROPHY

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Background: When skeletal muscle is submitted to prolonged disuse, it can lead to morphological changes that are not always easily reversed. Commonly employed for treatment in lesions or diseases in the musculoskeletal system, segmental immobilization is capable to cause this kind of alterations, and many rehabilitation protocols are used in an attempt to revert the functional damage caused by immobilization. Recently, Vibratory Platform with a whole body vibration is being used in association with experimental muscular disuse models with the aim of trying to understand these tissue responses. **Methods:** For this study 32 male *Wistar* rats were used, randomized in 4 groups: Control Group (GC), Immobilized Group (GI), Association of the Immobilization and Free Remobilization Group (GL) and Association of the Immobilization and Vibratory Platform. The immobilization protocol consisted by plaster bandage application in posterior member right antimer, in maximum elongation position of the tibialis anterior muscle. The free remobilization consisted of orthosis followed by 15 days of release, and the remobilization by Vibratory Platform consisted in animals exposition during 10 minutes, 5 days a week, for 15 days. **Results:** The GC, GL and GP tibialis anterior muscles presented normal morphological characteristics, with predominantly polygonal fibers, arranged in fascicles, with peripheral nuclei. However, in GL and GP were observed centralized nuclei, inflammatory infiltrate and greater connective tissue deposition in the endomysium and perimysium. GI Animals presented several important morphological alterations, such as amorphous and atrophic fibers, partitions and cytoplasmic deposits, high occurrence of central nuclei, degeneration sings and necrosis. In the connective tissue was observed a large amount of disorganized fibroblast in addition to the presence of inflammatory infiltrate. In Principal Components Analysis was observed that the area variance values lead the response pattern followed by the nuclei variance number. **Conclusions:** The association of Whole Body Vibration using the Vibratory Platform proved being effective as treatment in the muscular alterations analyzed, and it could be applied mainly to individuals with functional restrictions in high impact exercises development.

Key-words: Disuse, Musculoskeletal System, Whole Body Vibration.

Acknowledgements: Fundação Araucária pelo apoio financeiro ao grupo de pesquisa.

Financial Support: Programa de Iniciação Cientifica Unioeste.

EFFECTS OF EXPERIMENTAL IMMOBILIZATION AND WHOLE BODY VIBRATION ASSOCIATION IN TIBIALIS ANTERIOR MUSCLE MORPHOMETRIC PARAMETERS

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Background: The segment immobilization is commonly used as treatment in cases of musculoskeletal system lesions but, prolonged member disuse may cause muscle changes, and the atrophy has being the most frequently alteration founded. Many rehabilitation protocols are used to revert the damage caused by therapeutic restriction, the whole body vibration has been used as one of these physiotherapeutic treatments. Experimental models that seek muscular characteristics evaluation are fundamental to better understanding and application of this kind of protocols. **Methods:** For this study were used 32 male *Wistar*, sepated randomly in 4 groups: 1) Control Group (GC), 2) Immobilized Group (GI), 3) Association of the Immobilization and Free Remobilization Group (GL) and 4) Association of the Immobilization and Vibratory Platform. The immobilization consisted by the application of plaster bandage posterior member right antimer, in maximum elongation of the tibialis anterior muscle. The free remobilization consisted of withdrawal orthosis followed by 15 days of release, and the Vibratory Platform remobilization consisted in 10 minutes, 5 days a week, during 15 days. **Results:** As regards muscle nuclei number there the GL showed a higher total nuclei count when compared other groups ($F=22.595$; $p<0.001$), GL ,GP and GC presented similar means, what shows that the free remobilization and the vibratory platform were capable to normalize de damage caused by immobilization and the same was observed in the higher ($F=28.807$; $p<0.001$) and smaller ($F=23.255$; $p<0.001$) diameter. About the nuclei number there was a significant increase in GL total nuclei count when compared to the others. GC and GP presented similar means, while GI had the smallest mean between groups ($F=31.828$; $p>0.001$). However, in the central nuclei showed percentual comparison GI showed the highest nuclei centralization percentual, followed by GL, GC and GP, respectively ($F=1314.2$; $p>0.001$). The relation between total nuclei by fiber, GL mean was higher when compared to GC and GP, and all groups present higher means than GI ($F=29.504$; $p>0.001$). **Conclusions:** The Whole Body Vibration using Vibratory Platform proved be effective as treatment in the muscular alterations analyzed, and could be applied mainly to individuals with functional restrictions in development of high impact exercises.

Key-words: Atrophy, Skeletal Muscle, Remobilization.

Acknowledgements: Fundação Araucária pelo apoio financeiro ao grupo de pesquisa.

Financial Support: Programa de Iniciação Cientifica Unioeste.

METABOLISM

AZURE A AFFECTS ENERGY METABOLISM IN HEPATIC MITOCHONDRIA IN THE PRESENCE AND ABSENCE OF PHOTOACTIVATION

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Background: Azure A is a drug that has the property of interacting with light and generate reactive oxygen species such as singlet oxygen, species that are capable of altering the oxidative metabolism of cells. This effect is known as photodynamic effect and is used in the treatment of diseases such as cancer. Therefore, the purpose of the study was to evaluate the energetic metabolism of the liver by measuring the activity of the respiratory chain by observing the oxygen consumption in liver isolated mitochondria of rats. **Methods:** The intact mitochondria were obtained by differential centrifugation from liver of male Wistar rats at approximately 57 days of age. The measurement of oxygen consumption was determined by polarography using a Clark type electrode. The light source was a red light emitting diode system, and the mitochondria were incubated in polarography medium for 10 minutes, with and without illumination, prior to the start of the experiment in a polarography system. The drug concentration used was 10μM and succinate was used as substrate. **Results:** Azure A caused a stimulus (+ 151.58%) in the oxygen consumption on state II of mitochondrial respiration, but when illuminated the drug caused an inhibition in the oxygen consumption (- 59, 83%). In state III, without light, the drug caused a decrease in oxygen consumption (- 3.13%), and this effect was more significant than illuminated (- 87.59%). In state IV, the behavior was similar to state II, there was a stimulus (+ 195.85%) in the absence of illumination and an inhibition (- 62.98%) in the presence of light. Respiratory control (CR) showed a decrease caused by the drug both in the absence of light (- 68.08%) and presence (- 100%). The ADP/O ratio showed the same tendency, decay in the absence of light (- 90.93%) and in the presence of light (- 100%).
Conclusion: The Azure A showed an effect on energy metabolism of the liver, both in the presence of light, showing an inhibitory effect on oxygen consumption in the respiratory chain, and in the absence of light, where the decoupling effect is observed in state II and IV. Therefore, mitochondria are a target for this drug action and this should be considered for its eventual use in the treatment of diseases.

Key-words: energy metabolism, photoactivation, liver.

METHYLENE BLUE IMPAIRS THE MITOCHONDRIAL OXIDATIVE METABOLISM

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Background: Photodynamic therapy is a useful clinical technique used to treat pathologies such as cancer. It consists in using photosensitive molecules that, when exposed to light, are capable of generating reactive oxygen species, inducing cell death. Mitochondrion is considered a potential target for differentphotosensitizers. However, much lesser is known about the effects of such molecules on mitochondrial energy metabolism. hus, our objective was to evaluate the effects of the known photosensitizermethylene blue on some parameters of hepatic mitochondrial energy metabolism. **Methods:**Male Wistar rats weighing between 180 and 220 g were used. Liver mitochondria were isolatedand preincubated for 10 minin the presence or absence of methylene blue [5 and 40 μM, irradiated (658 nm, 3 mW/cm^2) or not].The oxygen consumption was monitored in the presence of 10 mM succinate.The respiratory control (RC) and ADP/O ratios were calculatedaccording to standard procedures.**Results:** In non-irradiated condition, states II and IVrespiration were increased at the concentrations of 5μM(+97.56%) and 40μM(+49.70%) of methylene blue. When irradiated, however, the stimuli were transformed into inhibitions: -54.43% and -66.46% at 5 and 40 μM methylene blue, respectively. The photosensitizer also inhibited the respiratory activity during state III respiration (-43.59% at 5 μM and -63.18% at 40 μM), being this effect more pronounced under irradiated conditions (-87.03% at 5 μM and -91.32% at 40 μM).The RC wasreduced and eventually abolished, depending on the concentration and photoactivation condition. In the absence of photoactivation, methylene blue reduced significantly the ADP/O ratio already at the concentration of 5 μM (-73.70%). In all other situations, the ADP/O ratio could no longer be determined.**Conclusion:**Methylene blue exerted harmful effects on the mitochondrial energy metabolism, probably affecting the biosynthesis of ATP.These effects were potentialized when it was irradiated by light. Such effects are probably important regarding cancer cell death. However, it should be used cautiously once it has presented accentuated action on mitochondriaunder dark conditions.This could be correlated with the occurrence of collateral effects, especially when methylene is systemically administrated.

Key-words: Methylene blue, Photodynamic Therapy, Photosensitizers, Mitochondrion, Energy Metabolism.

Financial Support: This study was supported by grants from the National Council for Scientific and Technological Development (CNPq), Araucária Foundation (FA) and Coordination for the Improvement of Higher Education Personnel (CAPES).

THE CAFETERIA DIET INDUCES OXIDATIVE STRESS IN WHITE ADIPOSE TISSUES OF MICE

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Background: Obesity caused by unbalanced diets is associated with oxidative stress, but the adipose tissue role in the pathogenesis of this disease is still being established. The overproduction of reactive oxygen species (ROS) and the incapacity of antioxidant systems, promote a harmful environment favorable to alterations in biomolecules. The aim of this study was to evaluate the levels of some enzymatic and non-enzymatic markers of oxidative stress in two different white adipose tissues (WATs) in cafeteria diet-induced obesity in mice. **Methods:** Swiss male and female mice were divided into four groups: male control (MC), male cafeteria (MCaf), female control (FC) and female cafeteria (FCaf). The animals were fed *ad libitum* with standard chow or cafeteria-diet and, after 14 weeks, the gonadal (gWAT) and inguinal (iWAT) adipose tissues were properly excised and used in the measurements. **Results:** The activity of glucose 6-phosphate dehydrogenase (G6PD) in gWAT was higher in MCaf (+112%) and FCaf (+45%), compared to control. Similarly, increases in the acivity of this enzyme were observed in iWAT of MCaf (+216) and FCaf (+29%). G6PD is an important regulator of redox potential and its increase may be linked to oxidative stress. The cafeteria diet also elevated the levels of lipid peroxidation in gWAT of MCaf (+25%) and FCaf (+25%), and in iWAT of FCaf (25%). These findings are probably a consequence of increased ROS production, especially in females. Additionally, the cafeteria diet induced a significant increase in the percentage of protein thiol groups (─SH) in gWAT of MCaf (+177%) and FCaf (+315%) and in iWAT of MCaf (+173%) and FCaf (+89%). In both tissues, the ─SH levels were higher in the obese females compared to males. The oxidative state of ─SH groups regulates several protein functions, being the protein thiols increase probably a consequence of the increased activity of thioredoxin reductase, a crucial enzyme that reduces a variety of proteins containing thiol groups as a response to enhanced ROS production. **Conclusion:** The overload of nutrients may alter the cellular redox environment in white adipose tissues, damaging lipids. Protein ─SH groups are known as strong antioxidants and their increases could possibly be a response to the continuous production of ROS which need thiols for detoxification.

Key-words: oxidative stress, adipose tissue, obesity.

METHYLGLYOXAL TREATMENT IN MOTHERS DURING LACTATION LEADS TO OFFSPRING LOW INSULIN LEVES EARLY IN LIFE

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Background: Advanced Glycation End products (AGEs) and it precursors consumption is related to metabolic alterations associated to diabetes, such as β-cell dysfunction and insulin resistance. Environmental disturbances in the perinatal life lead offspring to metabolic dysfunction. Thereby, we hypothesized that maternal treatment with methylglyoxal (MG), an AGE precursor, during the suckling phase, may impair offspring glucose homeostasis. **Methods**: Pregnant Wistar rats were kept in standard conditions until natural delivering. All animals had free access to standard chow and water through all the experimental period. Delivery was considered day 0, in day 1 rats litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups: Control (CO), whose mothers received saline 0,9% by gavage (1mL/kg), and Methylglyoxal (MG), treated daily by gavage with methylglyoxal (60mg/kg). Treatment starts at day 1 after birth and halt at the end of lactation. Offsprings were euthanized by quick decapitation at day 7, 14 and 21. Blood and tissue samples were collected for further analysis. **Results:** No differences were observed in body weight gain among groups; however, MG offspring showed increased adiposity as evidenced by elevated mass in perigonadal and mesenteric fat pad ($p<0,05$) at day 21. Interestingly, MG pups showed decreased insulin levels at day 14 ($p<0,05$) and 21 ($p<0,0001$). Despite a high tendency to increased glucose levels at day 21 ($p=0,0528$), no statistical difference was observed in this parameter.
Conclusions: The present research shows for the first time that maternal intake of MG during lactation leads to offspring impaired insulin levels and increased adiposity, which may predispose these animals to the development of type 2 diabetes later in life.

Key-words: Methylglyoxal; Insulin; Lactation.

Acknowledgements: We would like to thank Maroly Alves Pinto and other.
technicians for their assistance.

Financial Support: CNPq / CAPES.

ADRENODEMEDULATION DISTURB LONG-TERM CARDIOMETABOLISM

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Background: Obesity and its comorbidities (high blood pressure, hyperglicemia and dyslipidaemia) characterise the cardiometabolic syndrome, which is an important risk factor for cardiovascular death. The sympathetic nervous system has an important role in the regulation of blood pressure and glucose levels. In this context, we hypothesize that adrenalectomy may contribute to long-term control of cardiometabolic parameters. **Methods**: Sixty days-old Wistar male rats were exposed to bilateral adrenodemedulation. Blood pressure, fat pad deposition (retroperitoneal and mesenteric) and intravenous glucose tolerance test was evaluated in 120 days-old animals. **Results:** Adrenalectomy increased the body fat deposition in 51% for retroperitoneal fat pad and in 64% for mesenteric fat pad, characterizing obesity. Blood pressure was reduced in 12% ($p<0.001$), and the area under the curve of glycemia was reduced in 8.4% ($p<0.01$) in adrenalectomized animals. **Conclusion:** The present data suggest that adrenalectomy may be an efficient strategy to control the cardiometabolic parameters, however the fat deposition resulting of adrenalectomy is still deleterious.

Key-words: cardiometabolic programming, sympathetic nervous system, blood pressure.

FECAL MICROBIOTA TRANSPLANTATION DURING LACTATION PROTECTS PANCREATIC ISLET FUNCTION IN OBESE FEMALE RATS AT ADULTHOOD

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Background: Intestinal microbiota is involved in many physiological processes. Recently, it has been implied that the microbiota is involved in obesity onset. The first contact happens during early life but the effects of microbiota in metabolic programming at adulthood are still not understood. The aim of this work was to evaluate the transplantation of fecal microbiota during lactation to female offspring rats from lean and obese mothers. **Methods and Results**: NL and SL males and females (parents), from different litters, were mated, NL male vs NL female; SL male vs SL female. At birth, the litter was standardized in the 3rd day of life to NL or SL. From the 10th until the 25th day of life the offspring received gavage of a solution containing the diluted feces of the opposite dam. Four experimental groups were created: normal litter offspring saline (NLS), normal litter offspring fecal microbiota (NLM), small litter offspring saline (SLS), small litter offspring microbiota (SLM). Fecal microbiota transplantation caused decreased body weight gain during life and increased fat deposition in SLM animals. Early life obesity caused glucose intolerance in SLS and SLM groups, fecal microbiota transplantation protected against insulin resistance. All groups had increased secretory response of insulin in 5.6 and 8.3 mmol/L of glucose, fecal microbiota transplantation lowered this value in 16.7 mmol/L of glucose in NLM and SLM. Fecal microbiota transplantation lead to decreased cholinergic insulinotropic response. NLM animals showed increased adrenergic insulinostatic response, SLM animals showed an opposite response. **Conclusions**: Fecal microbiota transplantation caused protection against pancreatic islet dysfunction caused by obesity in early life.

Key-words: small litter, metabolic programming, microbiota.

REGULATION OF GLUCOSE AND INSULIN LEVELS BY AUTONOMIC NERVOUS SYSTEM IN OBESE MSG RATS.

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Background: The obese rodents may be obtained from different techniques, such as high-fat diet or monossodium glutamate (MSG) application in the early life. The MSG rats are characterized with a disruption in the fine balance between energy intake and consumption of energy stores. There are characteristics of high parasympathetic activities in this model. These factors change the autonomic nervous system (ANS) activity, which is involved the metabolic dysfunction . The aim of this study is knows how the ANS unbalance can change the insulin secretion and blood glucose in MSG adults rats. **Methods**: The animals were submitted to subcutaneous injections of MSG and equimolar saline solution during during the first 5 days after birth with MSG [4mg /g body weight (wt)/day]. At 90 days old, the Lee index ([body weight (g)$^{1/3}$/nasal-anal length (cm) x 1000] was obtained from 24 adult rats, treated or not with MSG. Pancreatic islets were isolated by collagenase technique. Subsequently other animals were used to observe the effect of parasympathetic and sympathetic neurotransmitters agonists intravenous glucose tolerance test. **Results**: MSG-treated rats showed significant increase (8%) on the Lee index when compared to untreated animals. Exogenous acetylcholine (Ach) decreased glycemia and increased insulinemia of control rats. However, no changes were observed in MSG-rats. Treatments with an agonist alpha 2- adrenergic receptor, oxymetazoline (Oxy) caused decrease in insulinemia and increase in glycemia in both groups. Furthermore, the effect was pronounced in MSG-rats. Isolated pancreatics islets from obese-MSG rats show increased glucose insulinotropic effect; however, they presented low insulinotropic response to a cholinergic receptor agonist carbachol (Cch) and pronounced insulin secretion inhibition by epinephrine (Epi) when compared to controls. **Conclusions:** The results show that obese hypothalamic-MSG rats show imbalances in glycemic homeostasis, which is related to alterations in the autonomic nervous system.

Key-words: Insulin Secretion; Obesity; Autonomic Nervous System.

Acknowledgements: Optional.

Financial Support: CAPES.

EFFECTS OF EUGENOL ON THE MITOCHONDRIAL RESPIRATORY CHAIN

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Background: Eugenol (4-allyl-2-methoxyphenol) is the main component of the essential oil of many aromatic plants, including clove and is known to have antioxidant, analgesic and neuroprotective properties. Studies have reported that eugenol inhibits rat liver mitochondrial respiration and may cause oxidative phosphorylation to be dissociated by interfering with the transfer of electrons in the respiratory chain, suggesting that it has an effect on NADH and Coenzyme Q. Effects in mitochondria are not yet fully understood. Therefore, the objective of this study was to verify the effects of eugenol on oxygen consumption and correlated parameters, such as respiratory control (RC) in mitochondria isolated from the liver of Wistar rats (200-250g), in a fasting of 18 hours. **Methods:** Succinate was used as the substrate for respiration and eugenol was tested at concentrations ranging from 1 to 5000 μM. Oxygen consumption was measured polarographically using a platinum electrode protected with a teflon membrane. **Results:** A tendency was observed to increase mitochondrial respiration rate in states II and IV and decrease of respiratory chain III state from concentrations above 2500 μM. These phenomena directly affected respiratory control, decreasing RC in 25%. **Conclusion:** These results allow us to conclude that eugenol actually interferes with mitochondrial respiration, alternating electron transport in complexes II, III and IV, thus dissipating the mitochondrial membrane potential.

Key-words: Essential oil, mitochondria, respiratory chain.

EARLY METFORMIN TREATMENT PROTECTED ADULT RAT OFFSPRING FOR INSULIN RESISTANCE

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Background: Metformin is worldwide the most used drug for the treatment of type 2 diabetes and metabolic diseases. Perinatal phases are known as window to program adulthood metabolism. Therefore, the aim of this study was verified whether metformin treatment during lactation could attenuate later metabolic dysfunction caused by obesity induced by high fat diet exposition in adulthood. **Methods:** At Wistar rat birth, all litters were adjusted to 9 pups for each dam and divided in two experimental groups. Saline (S) pups received a 0,9% saline solution in the first to the twelfth day of life via an intraperitoneal injection, while the other group received metformin (M) (100mg/kg body weight (bw)/day) in the same period of life. At sixty days of age, offspring from S and M groups were fed with a normal fat diet (4.5% of fat; NF) or high-fat diet (35% of fat; HF) until ninety day-olds. Thus, the four experimental groups used were: S-NF: saline offspring with NF, M-NF: metformin offspring with NF, S-HF: saline offspring with HF, and M-HF: metformin offspring with HF. **Results:** The early metformin treatment did not change bw and food intake in rats with 60 days old. High-fat diet consumption at adulthood resulted in increased bw in both groups, S-HF and M-HF; although they had a lower food intake compared to groups NF. The S-HF animals presented a higher final weight compared to S-NF. The fat pad mass was higher in the rats were fed with HF. Fasting glycemia was higher in M-HF rats compared to M-NF rats, although the treatment with metformin normalized fasting insulinemia and Homa-IR. **Conclusions:** Metformin treatment in early life not prevent weight gain and the increase of fat pad mass caused by a high-fat diet in adulthood, however, this treatment protected the animals for insulin resistance.

Key-words: Metformin, high-fat diet, insulin resistance.

POSTNATAL EARLY METHYLGLYOXAL EXPOSURE INDUCES OXIDATIVE STRESS AND INFLAMMATORY STATE LEADING TO METABOLIC DYSFUNCTION IN ADULT RAT OFFSPRING

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Background - Methylglyoxal (MG) is a precursor for the generation of endogenous AGEs that are commonly found in the processed foods and infant formulas due to the industrial processing applied in their production. Postnatal (PN) early nutritional disorders are critical for the developmental origins of health and disease. This study aimed to investigate the effects of early MG exposure in progeny programming for metabolic dysfunction later in life. **Methods** - At delivery (PN1), the animals were divided into two groups: control group (CO), treated with saline and methylglyoxal group (MG), treated with MG (20 mg/kg of BW i.p.) during the first two weeks of the lactation period. Throughout the experimental period, food intake and body weight were evaluated daily. We evaluated the weight of organs and main fat stores well as metabolic parameters as glucose homeostasis, insulin resistance and lipid profile, oxidative stress and inflammation CO and MG offspring at adulthood (PN90). **Results** - At PN90, MG treatment decreased body weight ($p<0.05$), adipose tissue ($p<0.05$ and $p<0.0001$) and liver and kidney mass ($p<0.01$ and $p<0.05$). Differentially, MG increased food intake ($p<0.001$), blood fructosamine ($p<0.01$), insulin levels ($p<0.01$) and HOMA-IR ($p<0.05$), evidencing insulin resistance. Besides, MG animals presented dyslipidemia, oxidative stress and inflammation in liver, kidney and pancreas. **Conclusion** - In conclusion, postnatal early MG exposure induces oxidative stress and inflammatory state leading to metabolic syndrome in adult rat offspring and increased risk of cardiovascular disease. Such results support the hypothesis that lactation is an important period for health or disease programming.

Key-words: Metabolic programming; Diabetes; AGEs; Methylglyoxal; Dyslipidemia; Lactation.

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

HISTOPATHOLOGICAL ALTERATIONS IN GILL OF *ASTYANAX ALTIPARANAE* (PISCES, CHARACIDAE) EXPOSED TO EXPOSED TO AGROCHEMICAL DORMEX®

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Background: Studies on environmental impacts caused by herbicides, using fish as bioindicators, have contributed greatly to the knowledge of the biological effects of these agents on these organisms which indirectly can affect human health by the contamination of water. Herbicides as to growth regulators has been used to break dormancy in fruit plants, among which we highlight the Dormex®, a compound based in hydrogen cyanamide H_2CN_2 widely used used in agriculture due to its high efficiency. However, it is highly toxic and hazardous to the workers exposed to this substance. **Methods:** Thus, the present study aimed to evaluate the biological responses of *Astyanax altiparanae* when exposed to the Dormex® solution, through histological analysis of gills. Forty specimens of *A. altiparanae* obtained from commercial establishments were divided into 10 groups (4 fish / aquarium containing 10L of water): one control group containing only dechlorinated water and nine containing Dormex® at concentrations of 0.05 ml, 0.1 ml and 0.5 ml, for 24, 48 and 72 hours for each tratament. After period of exposure, animals were euthanized and gills were fixed and submitted to histological cuts. **Results:** The groups exposed to Dormex® caused a significant increase in tissue resulting in lamellar hyperplasia and fusion in the gills, independent of the concentration and time of exposure to the treatments, when compared to the control group in which the gills had their preserved structures there. There was a gradual increase in lesion severity as a function of concentrations/times according to the mean values analyzed (M.C.V). **Conclusion:** The histological changes presented by the gills coincided with reports in the literature as a significant biological response to fish in contaminated environments thus, alerting to the toxicity of this agrochemical.

Key-words: agrochemicals, hyperplasia, lamellar fusion.

Acknowledgments: CAPES - PPG/ PBA/ State University of Maringá (UEM).

CIRCADIAN CYCLE RUPTURE IN PREGNANCY DOES NOT SCHEDULE METABOLIC DYSFUNCTIONS IN ADULT RATS

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Backgroud: Over time, organisms has developed a rhythmicity of physiological and behavioral processes related to environmental changes, like the light-dark cycle, determining a circadian cycle. Mammals have the suprachiasmatic nucleus, a central coordinator located in the hypothalamus, in which occurs the coordination of the cycle through a feedback loop of clock genes that determine the rhythmicity of the peripheral tissues. During gestation, the rhythmicity arising from the mother is synchronized with the fetus, which is maintained after birth. Nowadays, however, due to the modern lifestyle, there have been noticed changes in the circadian cycle of pregnant women, expressing a desynchronization with the fetus. This fact may result in future cardiometabolic diseases. Therefore, our goal was to assess if the rupture of the circadian cycle during pregnancy caused metabolic dysfunctions in female offspring during adulthood. **Methods:** Female Wistar rats after pregnancy were separated into 2 groups: LD group (light-dark, normal cycle) and LL group (constantly exposed to light, 200 lx), both pregnancies were kept in a specific rack to study the circadian rhythms. At birth, all animals returned to the standard light-dark cycle and kept under controlled temperatures (23 ± 2 ° C). The litters were standardized: eight rats per mother. After 21 days, the animals were weaned. Weight and maternal food intake were recorded every 12 hours. The glycemic and lipid profile of milk and fat stores were also evaluated. In the female offspring, the evolution of body weight, fat stores, lipid profile and glycemic homeostasis were analyzed at 90 days of life. Data were expressed as average ± standard error of the average and analyzed by Student's t test. **Results:** The feeding behavior of the pregnant rats was altered, indicating a desynchronization of the maternal circadian cycle of the light-dark phase. LL animals in adulthood showed no change in glucose tolerance, fasting insulinemia and body fat stores. However, a small increase in weight at 90 days of life (2.74%) and decrease in total cholesterol (23.95%) was observed. **Conclusion:** Exposure to constant light during pregnancy does not promote significant metabolic changes in adult rats. We suggest a possible resistance of the mother and/or fetus to a maternal dysynchrony of circadian cycle.

Key-words: Pregnancy, Circadian, Metabolism.

Financial Support: CNPq/CAPES.

METABOLIC MODIFICATIONS OUTCOME IN OBESITY AND SEX-SPECIFIC CARDIAC IMPAIRMENT IN YOUNG MALE RAT OFFSPRING BY MATERNAL POSTNATAL EARLY OVERFEEDING

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Background/Aims*:*Postnatal early overfeeding, by small litter (SL), is a risk factor for metabolic disorders. These animals develop overweight, hyperphagia and hypertension when adults. Besides, obesity is associated with reproductive disruption. We aimed to investigate the effects of maternal postnatal early overfeeding on metabolic and cardiac parameters in male and female rat offspring of second generation (F2). **Methods:** At delivery (P1), female Wistar rats (F0) were divided in two groups: normal litter (NL, 9 pups) and small litter (SL, 3 pups) throughout lactation period. At weaning (P21) female offspring (F1) were fed standard chow during remainder of the study and weighed daily. At adulthood (P70), female offspring were mated. During pregnancy and lactation dams (F1) fed standard chow. At P45, their offspring (F2) were fasted overnight, euthanized following anaesthesia and fat, liver, pancreas, kidney, heart and blood samples collected. All procedures were approved by the ethics committee of UFG (Protocol 043/17). **Results:** Female and male F2 SL offspring developing obesity, showing increased milk intake during suckling period and food intake after weaning in relation to F2 NL offspring ($p<0.05$). In addition, male F2 SL offspring showed heart hypertrophy as evidenced by increased ventricular mass index induced by pressure overload ($p<0.05$). **Conclusion:** Maternal postnatal early overfeeding causes obesity and metabolic impairments in female and male F2 rat offspring. However, only male F2 SL offspringshowed cardiac dysfunction.

Keywords: Small litter, Obesity, Cardiovascular.

Financial Supporting: FAPEG; CAPES and CNPq.

DIETARY INSULTS DURING ADOLESCENCE PROGRAM THE METABOLISM IN ADULTHOOD

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Background: Perinatal life has been extensively investigated as a susceptible window for programming to disease. Recently, other phases, as pre-conception, also have been considered, however little is known about the adolescence. Considering the hormonal explosion and plasticity observed during adolescence, we hypothesised that this life phase may also represent a period of susceptibility for program health dysfunction in adulthood. **Methods:** Thirty days old Wistar rats were exposed to low protein diet (5% of casein), or high fat diet during thirty days. Control animals received commercial diet. Food intake was evaluated three times a week and body weight evaluated once a week. Al the other parameters were evaluated at 120 days of life. Blood pressure was evaluated by direct canulation of the femoral artery; short term variability of blood pressure and heart rate estimated cardiovascular autonomic nervous system; glycemia and insulinemia was measured during intravenous glucose tolerance test; pancreas and reproductive organs structure was evaluated by imunohitochemistry. **Results:** Protein-restriction or high fat diet exposure during adolescence induced increase in food intake, body weight gain, fat tissue accumulation and blood pressure at adulthood. Glucose metabolism and autonomic nervous system was disrupted in adult diets-exposed animals and beta cells structure and function were also altered. Reproduction function is also susceptible of programing by dietary insult. Adolescent Wistar rats exposed to high fat diet showed long-term increase in the number of abnormal seminiferous tubule and reduction in seminiferous epithelium height and seminiferous tubular diameter. **Conclusion:** These changes points to the adolescence as a phase of susceptibility to dietary insults and program of cardiometabolic and reproductive dysfunction at adulthood, which may depend on tissue and autonomic nervous system alterations.

Key-words: adolescence, dietary insults, cardiometabolic syndrome.

Financial Support: Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPQ; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Capes; Consejo Nacional de Ciencia y Tecnología (CONACyT), México and Programa Latinoamericano para la Investigación en Salud Sexual y Reproductiva (PLISSER).

EFFECTS OF FRUCTOSE CONSUMPTION AT ADULTHOOD WERE NOT EXACERBATED BY RITALIN TREATMENT AT ADOLESCENCE

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Background: Metabolic syndrome is characterized by obesity, dyslipidemia, hyperglycemia and cardiovascular diseases. In addition to sedentary lifestyle, the consumption of hypercaloric diet has been considered as one of the causes for the metabolic syndrome. Fructose consumption increased in the past decade, mainly due to the use of high fructose corn syrup (HFCS). At adolescence, Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common behavioral disorders and Ritalin (methylphenidate) is a psychostimulant used in the treatment. We evaluated whether Ritalin treatment at adolescence can exacerbate the effects of fructose consumption on biometrical parameters and glucose metabolism of adult male rats. **Methods:** From weaning, male Wistar rats received Ritalin by gavage (Rit; 1 mg/kg/day) for 30 days, whereas control rats received saline (Sal; NaCl 0.9%) in the same volume. From 51 to 80 days-old both groups were untreated. At 81 days-old animals, a batch of control and Ritalin animals received water and another batch received Fructose (10%) in the water until 110 days-old. At this age, intravenous glucose tolerance test (ivGTT) was performed, body weight was assessedand fat tissue stores were removed. **Results**: Rit-W showed no difference in body weight and increased periepididymal ($P<0.05$) fat tissue accumulation compared to Sal-W group. Fructose supplementation (Sal-F) induced increased periepididymal($P<0.01$) and mesenteric ($P<0.05$)fat tissue accumulation, compared with Sal-W group. We observed no difference in final body weight among Sal-F and Rit-F groups. In the same way, periepididymal, retroperitoneal and mesenteric fat pads presented no difference between Sal-F and Rit-F animals. All groups presented equal glucose tolerance, as showed by ivGTT. **Conclusions:** Ritalin treatment at adolescence does not exacerbate the effect of fructose consumption in adulthood.

Key-words: Ritalin, fructose, adolescence.

GLYPHOSATE ALTERS HEPATIC METABOLISM IN ADULT OFFSPRING HIGH-FAT DIET-FED MICE

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Background: Glyphosate leavings have high risk to liver functions by altering levels of triglycerides (TG) and cholesterol (CHOL) and inhibiting liver fatty acid oxidation enzymes. The aim of this work was to evaluate the effects of maternal exposure to glyphosate in hepatic lipid metabolism on adult mice offspring high-fat diet-fed. **Methods**: The pregnant female mice were divided in control group (CTL, n=7) or glyphosate group (GF, n=9), which received water with 0.5% of GF (Roundup Original DI®). At 60th postnatal day, the first generation of male offspring was divided in: CTL-LF-F1 (n=12), CTL-HF-F1 (n=9), GF-LF-F1 (n=8) and GF-HF-F1 (n=5) group. Male offspring received LF or high-fat (HF) diet for 90 days and the euthanasia occurred at 150 days. **Results:** At 150 days, GF-HF-F1 had body weight 21% lower than CTL-HF-F1, but similar to GF-LF-F1. The GF increased liver weight in GF-LF-F1 when compared to
CTL-LF-F1 and in GF-HF-F1 to compare to CTL-HF-F1. Liver total lipids content and triglycerides (TG) were 32% lower in GF-HF-F1 when compared to CTL-HF-F1, without influencing the liver cholesterol (CHOL) content. The HF diet increased the liver total lipids content (21%), CHOL (49%) and TG (42%) in CTL-HF-F1 when compared to CTL-LF-F1. The liver of CTL-HF-F1 and GF-HF-F1 presented steatosis (score 3 and 1, respectively) and fibrosis. All the treatment groups had lobular inflammation. Our study shows that glyphosate exposure in pregnancy and lactation period prevented body weight increasing in adult male offspring mice with high-fat diet-fed due to possible herbicide effects, or its metabolites, at their neuronal center, possibly in hypothalamus. Treatment with high doses of glyphosate cause alteration in >60 distinct lipid species including several neutral lipids and increased fat storage and CHOL esters in mouse liver. **Conclusion:** We show that maternal exposure in low doses increased the liver weight, CHOL and TG content in male offspring that receives LF diet. However, when offered HF diet to these mice, we observed a reduction in their liver weight, liver total lipids content and TG, without influencing CHOL content. The HF diet was not effective to elevate the lipids levels, due to previous alteration in these pathways caused by glyphosate exposure. These alterations can be observed in lower steatosis grade and presences of fibrosis and inflammation on their liver.

Key-words: Roundup, liver, metabolism.

MATERNAL METFORMIN TREATMENT DURING LACTATION DOES NOT CAUSE CHANGES IN ADULT RAT OFFSPRING METABOLISM

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Background: Metformin is a widely used drug in the treatment of type 2 diabetes. This antidiabetic is becoming an attractive drug to treated and prevent others metabolic diseases, as well as cancer. It has been shown that insults during early life phases, such as pregnancy and lactation induce serious health risks later in life. There are evidences that metformin can attenuating/blocking early programming-metabolic dysfunction; however, data are scarce regarding any damage caused by metformin early treatment in normal individuals, without any metabolic programming. So, the aim of this study was verified whether metformin a safe preventive treatment to block metabolic dysfunction programming. **Methods:** At birth, all litters were adjusted to 9 Wistar rat pups for each dam and divided in two experimental groups. Saline mothers (SM) that received by gavage 0,9% saline solution, while the other mothers group received metformin (MM), 250mg/kg body weight/day, during all lactation period. At weaning, the metabolic and biochemical parameters of dams and their male offspring at 90 days old were evaluated. **Results**: Although, the food intake was reduced in the MM group dams; metformin treatment did not change body weight, food intake, Lee index, fat pad mass store and fasting glycemia in dams and their male offspring. **Conclusions:** The results suggest that metformin treatment can be used during the perinatal period, as a safe preventive maneuver against metabolic dysfunction programming.

Key-words: Metformin, lactation, safe programming.

BAROREFLEX SENSITIVITY IS IMPAIRED IN POSTNATAL-OVERFED ADULT MALE WISTAR RATS

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Background: Metabolic syndrome is a worldwide pandemia. The prevalence of the metabolic syndrome, intimately associated with type 2 diabetes mellitus, hypertension or obesity, increases every year. Excessive visceral fat, insulin resistance, dyslipidemia and hypertension are components which may diagnose metabolic syndrome. Postnatal overfed rat and mice become obese and hypertensive in later stages of life. However, remain unclear the mechanisms involved in obesity-associated hypertension in the postnatal overfeeding model of metabolic syndrome. This study evaluates cardiovascular parameters in post-natal overfed adult male Wistar rats, such as blood pressure, heart rate and pressure reflexes. **Methods:** Pregnant female Wistar rats were divided into two groups: Normal Litter (NL, n = 5) and Small Litter (SL, n = 5). Three days after delivery (D3), normal litters were reduced to 9 pups and small litters was reduced to 3 pups. Only litters with more than 9 pups were used. At D21, all groups were weaned. Body weight, food and water intake of offspring were monitored weekly. Water and standard chow were provided *ad libitum*. At D119, after ketamine and xylazine anesthesia (70 and 7 mg/ kg BW, i.p.), catheters was implanted in right femoral artery and vein. At D120, blood pressure, heart rate, and cardiac electrical signals were monitored. Likewise, baroreflex (phenylephrine 1, 1.5 and 2 µg; Sodium Nitroprusside 10, 20 and 30 µg) and chemoreflex (Potassium cyanide 40 µg) tests were performed. All procedures were approved by the ethics committee of UFG (Protocol 043/17). **Results:** In baseline values, there was no difference in mean arterial pressure (MAP) (NL 117,06 ± 5,22 mmHg vs SL 127,38 ± 13,52 mmHg) and heart rate (HR) (NL 344,55 ± 29,63 bpm vs SL 384,97±47,62 bpm). In the baroreflex test, there was a decrease in the baroreflex index (BI) in SL animals compared to the NL group, but only in constriction response reflex (NL -2,01±0,18 bpm/mmHg vs SL -0,74±0,15 bpm/mmHg; p=0,0166). In the chemoreflex test, there was no difference in MAP and HR variations. **Conclusion:** Together, our results show that SL animals present impaired baroreflex sensitivity to increased pressure and tends to increase HR when they are submitted to hypoxia, suggesting favorable conditions for the installation of hypertension.

Key-words: Hypertension, Metabolic syndrome, Obesity.

Financial Support: CAPES, CNPQ and FAPEG.

CARDIOVASCULAR CHANGES IN OBESE RATS FED A HYPERSODIUM DIET DURING PUBERTY

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Background/Aims: Postnatal early overfeeding, by small litter (SL), is a risk factor for metabolic disorders. SL rats develop overweight, hyperphagia and hypertension when adults. Besides, high-salt diets are associated with obesity, oxidative stress and cardiac diseases. We aimed to investigate the effects of high-salt intake on cardiometabolic parameters in rats. **Methods:** At delivery, Wistar rats were divided in two groups: normal litter (NL, 9 pups) and small litter (SL, 3 pups) throughout lactation period. At 30-day-old, offspring were subdivided in two groups: normal litter + high-salt intake (NL+HS) and small litter + high-salt intake (SL+HS). High salt intake was from 30- to 60-days-old. Plethysmography was performed at 60, 90 and 120-days-old. At 120-day-old, glucose and insulin tolerance tests were performed, and offspring were euthanized for sample collection. Body weight and food intake were monitored throughout the experimental period. **Results:** SL and SL+HS offspring developing obese phenotype, showing insulin resistance and glucose intolerance during insulin and glucose tolerance tests in relation to NL and NL+HS offspring ($p<0.05$). In addition, SL and SL+HS offspring showed hypertension during the plethysmography ($p<0.05$). **Conclusion*:*** Postnatal early overfeeding causes obesity, hypertension and impairments in glucose homeostasis. Indeed, SL+HS animals showed similar impairments in cardiometabolic parameters. However, NL+HS animals showed only cardiovascular disruptions.

Key-words: Small litter, Obesity, High-salt intake.

Financial Support: FAPEG; CAPES and CNPq.

EFFECT OF STEVIOLBISIDE ON INSULIN SECRETION: AN ALTERNATIVE PATHWAY

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Background: Stevia leaves components, major glicosides, has been used as an artificial sweetener. One substance extract from Stevia, Steviolbioside (STB) shows a sweetness intensity 44 times than sucrose. However, STB have more intense bitter taste than other glycosides. STB in sweetener industry products may be the cause of always being bitter, especially those with lower purity. Some evidence confirms that the residual bitter taste characteristic of steviol glycosides may be the determining factor for the observed hypoglycemic effects, since sweeteners with this characteristic stimulate insulin secretion. The present study aimed to evaluate the possible effect of STB on the release of insulin from pancreatic islets of rats and the mechanisms involved. **Methods and Results:** To investigate how STB stimulates insulin secretion, different pathways of amplification or inhibition of insulin secretion have been evaluated. Islets of Langerhans were isolated from adult Wistar rats were incubated with different substances in the presence or in the absence of STB (1 μM) during 60 min. The supernatants from the incubations were collected and stored for posterior insulin measurements using a radioimmunoassay method. STB significantly stimulated insulin secretion (38%, $p < 0.05$) only at the highest glucose concentration (16.7 mM). Increasing extracellular KCl was observed approximately 120% increase in glucose-stimulate insulin secretion (GSIS); STB did not changed GSIS. The reduction caused by verapamil (-65%) was 10% lower in the islets incubated in the presence of STB ($p < 0.05$). STB did not altered the Forskolin effect in GSIS. It was observed that in 16.7 mM of glucose diazoxide reduced 50% GSIS ($p < 0.0001$); however, in presence of STB, this inhibition was not observed. **Conclusion:** STB, like other bitter-tasting molecules, activates GSIS only in high glucose concentration. Alternatively STB insulinotropic effect is related to the activation of pathways involved in the perception of taste, mostly bitter taste. These characteristics make STB a molecule with great therapeutic potential for the treatment of diabetes mellitus, especially in cases where the secretion of insulin does not respond to high levels of glucose.

Keywords: Steviolbioside, insulin secretion, bitter taste.

AUTONOMIC NERVOUS SYSTEM AND HYPOTHALAMUS-PITUITARY-ADRENAL IS DISRUPTED IN MSG-OBESE RATS.

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Background: Recent evidences suggest that, imbalanced autonomic nervous system (ANS) output and defects in the hypothalamic-pituitary-adrenal axis (HPA), allowing high glucocorticoids levels, is linked to obesity and cardiometabolic diseases onset. The HPA axis exert important catabolic peripheral effects and influence ANS mediated processes. Impaired negative feedback control /or reduced sensitivity to HPA axis feedback and altered ANS activity seems to be associated with the development and maintenance of obesity. In the present study, therefore, we examined the hypothesis that central HPA axis is dysregulated favoring ANS disbalance in obesity. **Methods:** We used monosodium L-glutamate (MSG)-induce rat obesity. Adult MSG-obese rat was treated with corticotrophin-releasing factor (CRF) and synthetic Dexamethasone (DEXA) given intracerebroventricular (ICV) injection for 3 days. Metabolic parameters, glucose homeostasis and ANS electrical activity was evaluated. **Results:** Adult MSG-obese rats presented fasting hyperinsulinemia, insulin resistance, glucose intolerance, hypercorticosteronemia, hyperleptinemia and ANS activity unbalanced. CRF ICV caused decrease in food intake. DEXA ICV injection induced, increase fasting insulin and glucose levels, associated to insulin resistance. As expected, central CRF caused decrease of parasympathetic and increase in sympathetic activity; while, DEXA induced opposite effects, in control rats. In contrast, MSG-rats appear to be unresponsive to the central injections, mostly in ANS electrical activity. **Conclusion:** Our study supports evidence that glucocorticoids participate, using HPA axis, as a signal to central nervous system-periphery communication, including changes in ANS activity and glucose levels; which allow maintaining metabolic homeostasis. Activity of the HPA axis is increased in MSG-obese rats; however, reduced sensitivity to HPA axis is observed after central DEXA or CRF infusion, which can be involved in obesity and metabolic syndrome onset.

Keywords: MSG-obese rats, glucocorticoids, autonomic nervous system.

Financial Support: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Fundação Araucária (FA).

BLOOD PRESSURE AT ADULTHOOD MAY BE MODULATE BY HIGH FAT DIET DURING ADOLESCENCE IN MALE RATS

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Background: There is a negative relationship between exposure to high fat diet (HFD) diet during the gestation and lactation periods and changes in blood pressure in adult life. It has also been suggested that adolescence is a susceptible phase for programming to metabolic syndrome. Thus, our hypothesis argues that HFD diet during adolescence can lead to increased blood pressure in adult life. **Methods:** Adolescent Wistar rats (30 to 60 day-old) were exposed to a high fat diet (HFD, 35% of fat). Control animals had access to normal commercial chow (NFD, 4.5% of fat). Blood pressure, heart rate and pulse pressure were verified at 120-day-old rats. Student t-test was used to compare groups. **Results:** At basal test, HFD animals showed increased systolic blood pressure (SBP) and mean blood pleasure (MBP) compared with control animals (SBP: 125.4 mmHg ±1.8 vs. 117 ± 1.9 mmHg, respectively, $p< 0.05$; MBP: 95.78 ±1.8 vs. 88.85 ± 1.6 mmHg, respectively, $p< 0.05$); Diastolic blood pressure (DBP) was similar (HFD: 73.29 ± 2.5 and NFD: 70 ± 2.5 mmHg, $p=0.3394$) between groups, as well as pulse pressure (52.08 ± 1.1 vs. 49.89 ± 2.4 mmHg, respectively, $p=0.3930$) and Heart Rate (HFD: 339.6 ± 10 and NFD: 339.5 ± 9 bpm, $p=0.9976$). Blood pressure decrease in response to hexamethonium injection (30mg/kg of Body Weight) was greater in HFD animals compared with control animals (ΔSBP -43.5 ±3.1 vs. -33.8 ± 3.1 mmHg; ΔMBP -37.9 ±3.3 vs. -27.8 ± 1.9 mmHg; ΔDBP -33.2 ±3.5 vs. -23.7 ± 1.1 mmHg respectively, $p< 0.05$). No difference between groups was observed in pulse pressure response (HFD: -10.2 ± 2.1 and NFD -9.4 ± 2.2 mmHg, $p=0.4$) and heart rate response (HFD: -5.9 ± 20.2 and NFD -3.3 ± 6.9 bpm, $p=0.2$) to hexamethonium. **Conclusions:** HFD exposition during adolescence programs to higher levels of systolic blood pressure and mean blood pressure later in life. In addition, the exacerbated blood pressure reduction in response to hexamethonium injection observed in HFD animals suggest that the increased blood pressure programed by HFD during adolescence may depends on sympathetic nervous system, which is an important predictor for cardiovascular death.

Key-words: Adolescence, metabolic disease, high-fat diet.

EARLY TREATMENT WITH CHOLINERGIC ANTAGONIST PREVENTS OBESITY IN ADULT MALE RATS

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Background: Obesity has become, over time, a worldwide public health problem. The DOHaD concept, through clinical and preclinical studies, suggests a strong association between environmental damages occurred in the fetal or perinatal life and the emergence of chronic diseases in adult life. The Central Nervous System is easily affected at critical stages of development, such as in lactation. Hyperinsulinemia in early life has been associated with an obese phenotype in adult life. In opposition, hypoinsulinemia in the perinatal phase is related to a lean phenotype. Cholinergic terminals activity into pancreatic beta-cell has been associated to those phenotype-early low-insulin levels. Our aim was to investigate whether the short-term treatment with a buscopan, could prevent obesity. **Methods and results:** After birth, male Wistar rats received intraperitoneal injection of scopolamine butylbromide, 0.5 mg/Kg body weight (bw)/day during the first 12 days of lactation (Treated Group; T) or saline 0.9% (Control Group; C). At 60-days-old, the offspring from both group consumed normal fat diet (NF) or high fat diet (HF:35% of fat) by next thirty days. At 90-days-old body weight, food intake, fat tissue accumulation, glucose tolerance, insulin tissue sensitivity and fasting glucose and insulin blood levels were evaluated. The lean phenotype was observed in rats of treated group. T group presented lower body weight than C group until 60-days-old (11%, $p<0,0001$) associated to a lower food intake (5%, $p<0,05$). At 90-days-old, T-HF group showed low body weight (14%, $p< 0,0001$) compared to C-HF. The T-HL animals presented increased fasting glycemia and insulinemia 23% ($p<0,05$) and 60% ($p<0,001$) lower than the C-HF group, respectively. The T-HF group had greater insulin sensitivity by the HOMA index, compared to C-HF control. T groups presented lower fat tissue accretion (T-NF 30%; T-HF 14%; respectively, $p< 0, 05$) compared to C-NF and C-HF respectively. During intraperitoneal glucose tolerant test, the T-HF animals presented lower glucose levels than C-HL animals ($p< 0,01$). **Conclusions:** Treatment with a cholinergic antagonist, during lactation protects the animals against metabolic dysfunction and obesity onset later in life; at least in part this resistance can be attributed to improvement of insulin action and secretion.

Key-words: Lactation, Hypoinsulinemia, Obesity.

Financial Support: CNPq/CAPES.

BEHAVIOR

ROLE OF IN UTERO EXPOSURE TO TRICLOCARBAN IN POLYMICROBIAL SEPSIS INDUCED BY CECAL LIGATION AND PUNCTURE.

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Background: Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Environmental pollutants can suppress innate immunity and increases the susceptibility to infection. Triclocarban (TCC) is an antimicrobial used in personal care products and it has been widely detected in wastewater around the world. The exposure of external environmental factors, like TCC, to a developing fetus may have very different consequences from the same exposure to an adult. However, the interrelationship between the maternal exposure to TCC and the outcome of sepsis remains uncertain. Therefore, in the present study we evaluated if maternal exposure to TCC could interfere with clinical signals of sepsis and in neutrophil migration to the infectious site of female offspring. **Methods:** Pregnant female Wistar rats were treated with TCC 0,3 mg/kg/day, 1,5 mg/kg/day, or 3 mg/kg/day by gavage from gestational day (GD) GD0 to GD21 and the control group (CTR) received corn oil (n=8-11/group). Pups were weaned at PND 21. The female offspring was used for this study, no litter-mates was used for the same group. Sepsis was induced by cecal ligation and puncture model (CLP) in the adult female offspring. A triple puncture was made using a 23-gauge needle to induce non-severe septic injury (CLP). The functional features of animals were evaluated 24 hours after sepsis induction and were scored as: alertness, mobility, piloerection, diarrhea, encrusted eyes, dirty nose and tail and neutrophil migration to the infection focus was determined 6 hours after sepsis induction (CEUA/UEL: 130.2016.24). **Results:** Our results demonstrate that maternal exposure to TCC reduces significantly the mobility (TCC 1,5 mg/kg/day and TCC 3 mg/kg/day) and alertness (TCC 3 mg/kg/day) of female offspring rat subjected to sepsis. Moreover, it was observed a tendency to reduction in the neutrophil recruitment to the focus of infection. **Conclusion:** Altogether, our results suggest that maternal exposure to TCC can worsens the prognosis of sepsis.

Key-words: Sepsis, neutrophils, maternal exposure, environmental pollutants, Triclocarban.

Financial Support: Fundação Araucária, Capes.

THE IMPACTS OF FOOD RESTRICTION DURING PUBERTY ON CARDIOMETABOLIC AND BEHAVIORAL PARAMETERS

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Background: Environmental and nutritional disorders during the perinatal period cause metabolic dysfunction in the progeny and impairs health, which is observable in the Small Litter experimental model. Therefore, severe caloric restriction has the potential of affecting several organic systems through the same epigenetic mechanisms, and its effects in metabolically programed animals need elucidation. The objective of this work was to determine whether the caloric restriction would impact small litter and normal litter animals equally if at all, and what that would entail on the obesity prognosis. **Methods:** At delivery, female Wistar rats (CEUA protocol 52/2017) were separated in small litter (3 pups) and normal litter (9 pups) groups, their offspring in turn were subjected to caloric restriction (50% restriction when compared to controls) or left with free access to chow during the puberty period (from 30 to 60 days). These animal
s were then subjected to non-anaesthetized recording for the evaluation of cardiovascular parameters, open field (OF) and elevated plus maze (EPM) tests for behavioral analysis, then glucose and insulin tolerance tests. In addition, their body weight and food intake were monitored throughout the experimental period. **Results:** SL and SLR offspring were overweight, developing obese phenotype, showing insulin resistance and glucose intolerance during insulin and glucose tolerance tests in relation to NL and NLR offspring ($p<0.05$). Differences in mean arterial pressure were also observed, when comparing small litter control animals with the rest of the groups ($p<0.05$). In addition, SL and SLR offspring showed a tendency for anxiety-like behavior during the OF and EPM tests ($p<0.05$). **Conclusion:** The present study showed that
early overnutrition caused obesity, anxiety-like behaviors and impairments in glucose homeostasis. Also, the animals subjected to food restriction showed no improvement in the behavioral tests, however the non-obese animals showed similar impairments in behavior. There was also a tendency for high blood pressure observed in the obese animals, and a tendency for the attenuation these levels in obese animals that were subjected to food restriction.

Key-words: Obesity, Cardiometabolic, Behaviour.

Financial Support: FAPEG; CAPES and CNPq.

EVALUATION OF THE EFFECTS OF MATERNAL TREATMENT TO TRICLOCARBAN ON REPRODUCTIVE BEHAVIOR IN FEMALE OFFSPRING RATS

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Background: Triclocarban (TCC) is an antibacterial agent widely used in daily personal care products. In addition to direct exposure, this compound has already been found in water resources and sludge, which can be used in agriculture as fertilizer. Studies have shown that exposure to TCC could lead adverse effects, once it acts as an endocrine disrupter (ED) altering the synthesis, secretion, transport, metabolism, binding or elimination of sex hormones in the reproductive system. Knowing the importance of these hormones in the development, maintenance and function of the reproductive system - and the ability of TCC to cross the blood-supply barrier - exposure to this compound early in life could impair the reproductive system of the offspring. The aim of this study was to evaluate the maternal behavior of rats treated with TCC during pregnancy and lactation and to evaluate the sexual and maternal behavior of their exposed female offspring. **Methods:** All procedures performed with the animals were approved by the Ethics Committee for the Use of Animals (CEUA: 130.2016.24).Pregnant rats were treated daily by gavage with TCC (0,3mg/kg/day; 1,5mg/kg/day and 3,0 mg/kg/day) or corn oil (C: control group) from gestational day 0 (DG 0) to lactational day 21 (DL 21). The maternal behavior was analyzed during the first 10 postnatal days (PND). Observations occurred at regular times each day during the light phase (10 a.m/1 p.m./4 p.m.) and dark phase (7 p.m.). The target maternal behaviors were:pup grooming, nest building, going outside of the nest, retrieving (carrying the pups and placing them in the nest), and nursing pups. After weaning, the dams were euthanized and one female from each litter was used for the sexual behavior test and maternal behavior test. The lordosis quotient (LQ: number of lordosis/ten mounts x 100) was calculated and the magnitude of the lordosis reflex were observed in ten mounts. The data were compared by ANOVA complemented with Bonferroni and lordosis reflex magnitude by Fisher's exact test. **Results:** TCC treatment during gestation and lactation did not altered the maternal and female offspring behavior (P and F1). Besides that, no difference was observed in sexual behavior: lordosis coefficient: C group: 92,50 ± 10,35 0,3 group: 96,66 ± 7,07 1,5 group: 92,22 ± 8,33 and 3,0 group: 98,00 ± 4,21.**Conclusion**: TCC treatment during gestation and lactation does not alter maternal behavior and exposure during these periods does not alter the sexual and maternal behavior of female offspring.

Key-words: Maternal behavior, sexual behavior, endocrine disruptor, Triclocarban.

Financial Support: Fundação Araucária, CAPES-UEL.

EFFECTS OF ROSUVASTATIN TREATMENT ON SHORT AND LONG-TERM MEMORY IN BALB/C MICE WITH *TOXOPLASMA GONDII*

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Background: The *Toxoplasma Gondii (T. Gondii)* infection have elevated prevalence in world population and may manifest with considerable severity in congenital transmission and in immunocompromised individuals, reaching the retina and the central nervous system. Studies in humans and rodents showed that *T. Gondii* infection may promote the emergence of psychiatric disorders, such as schizophrenia that can promote cognitive deficits. However, no there is study that evaluated Rosuvastatin treatment on the short and long-term memory in balb/c mice with *T. Gondii*infected.Thus, the aim of this work was evaluate the effect Rosuvastatin treatment on short and long-term memory in balb/c mice with *T. Gondii*in fected. **Methods:** For this, were used 48 balb/c mice with 21 days infecteds with 25-30 cyst of the strain ME-49 per gavage. After 40 days, the animals were Rosuvastatin treated in the dose of 40 mg/day at morning for 21 days, and control groups received sterile saline. Twenty-four hours after the last treatment, the animal were submitted to the Open Field (OF) per 5 minutes for habituation to apparatus. We evaluated the short and long-term memory by object recognition test in the OF. For this, four objects were use: object 1 and 1': square objects, object 2: cilindric object and object: 3 round. The animals explored objects 1 and 1' for 5 minutes, after the exploration the animals remained in their houses boxes for 10 minutes to then explore objects 1 and 2 for another 5 minutes for evaluate short-term memory. For evaluate long-term memory, twenty-four hours the object 2 was replaced by object 3 and the animals explored for 5 minutes. The OF arena, consisted in a circular arena with 30 cm of diameter and 30 cm of height. **Results:** In short-term memory, the infection decrease exploration of the new object ($F_{(1,44)}$=25.70,$p<0.0001$) this effect reverted with the rosuvastatin treatment ($F_{(1,44)}$=29.11,$p<0.0001$). The same effect was observed in long-term memory, where the infection decrease exploration of the new object($F_{(1,44)}$=26.34,$p<0.0001$) being this effect reverted with rosuvastatin treatment ($F_{(1,44)}$=49.81;$p<0.0001$). **Conclusion:** Therefore, our results showed that *T. Gondii*infection promote short and long-term memory injury, and that treatment with rosuvastatin has been able to revert such problems.

Key-words: *Toxoplasma Gondii,* Rosuvastatin, Psychiatric disorders, mice.

Acknowledgements: I would like to thank everyone at the Laboratory of Parasitology at the University and those involved in this research.

Financial Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)for providing Master scholarship.