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ORIGINAL ARTICLE

Western diet in the perinatal period promotes dysautonomia in the offspring of adult rats

R. Vidal-Santos[1], F. N. Macedo[1], M. N. S. Santana[1], V. U. De Melo[1], J. L. de Brito Alves[4], M. R. V. Santos[1], L. C. Brito[2], E. Nascimento[3], J. H. Costa-Silva[4] and V. J. Santana-Filho[1]

[1]*Department of Physiology, Federal University of Sergipe, São Cristovão, Brazil*
[2]*Department of Nutrition, Federal University of Sergipe, São Cristovão, Brazil*
[3]*Department of Nutrition, Federal University of Pernambuco, Recife, Brazil*
[4]*Department of Physical Education and Sport Sciences, Academic Center of Vitória (CAV), Federal University of Pernambuco, Vitória do Santo Antão, Brazil*

The present study investigated the impact of a western diet during gestation and lactation on the anthropometry, serum biochemical, blood pressure and cardiovascular autonomic control on the offspring. Male Wistar rats were divided into two groups according to their mother's diet received: control group (C: 18% calories of lipids) and westernized group (W: 32% calories of lipids). After weaning both groups received standard diet. On the 60th day of life, blood samples were collected for the analysis of fasting glucose and lipidogram. Cardiovascular parameters were measured on the same period. Autonomic nervous system modulation was evaluated by spectrum analysis of heart rate (HR) and systolic arterial pressure (SAP). The W increased glycemia (123 ± 2 *v.* 155 ± 2 mg/dl), low-density lipoprotein (15 ± 1 *v.* 31 ± 2 mg/dl), triglycerides (49 ± 1 *v.* 85 ± 2 mg/dl), total cholesterol (75 ± 2 *v.* 86 ± 2 mg/dl), and decreased high-density lipoprotein (50 ± 4 *v.* 38 ± 3 mg/dl), as well as increased body mass (209 ± 4 *v.* 229 ± 6 g) than C. Furthermore, the W showed higher SAP (130 ± 4 *v.* 157 ± 2 mmHg), HR (357 ± 10 *v.* 428 ± 14 bpm), sympathetic modulation to vessels (2.3 ± 0.56 *v.* 6 ± 0.84 $mmHg^2$) and LF/HF ratio (0.15 ± 0.01 *v.* 0.7 ± 0.2) than C. These findings suggest that a western diet during pregnancy and lactation leads to overweight associated with autonomic misbalance and hypertension in adulthood.

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Key words: autonomic control, hypertension, offspring, westernized diet

Introduction

Western diet (WD) is characterized by high levels of saturated fats, sodium, simple sugars and low levels of fiber. The consumption of this diet is rising worldwide, mainly in western countries.[1,2] WD has produced nutritional and epidemiological effects, leading to development of chronic non-communicable diseases such as hypertension, diabetes mellitus and obesity.[3–5] Studies in rodents have been used to understand the effects and mechanisms elicited by this kind of diet in physiological systems.[5–11]

Recently, it has been proposed that adverse events (e.g. nutritional manipulation of diet) experienced *in utero* or during perinatal life (i.e. gestation, lactation and early infancy) could be a trigger factor for the development of arterial hypertension and metabolic diseases in later life.[12,13] It has been suggested that cardiovascular disorders, such as hypertension, observed in obesity may be linked to the development of heart and vessels autonomic imbalance, reduced arterial baroreflex sensitivity and increased activity of the sympathetic nervous system.[14–18] In addition, it was proposed that in response to an adverse intrauterine environment, the fetus could adapt its physiological development to maximize immediate chances of survival. These adaptations include resetting metabolic rate, remodeling endocrine systems and downregulating growth, likely showing an altered birth phenotype.[19]

Conversely, nutritional factors during the perinatal period, such as feeding, fasting or nutrient composition can modulate rhythmicity and clock gene expression. Previous reports showed that high-fat diet causes three main changes in circadian rhythms in mices and rats: lengthened period, blunted feeding rhythm and alterations in the expression of circadian clock genes.[20]

We hypothesize that the ratio and quality of nutrients, such as fat type and amount of simple carbohydrate, provided at critical periods in physiological development promotes metabolic alterations and cardiovascular disorders. To test the hypothesis, we examined whether WD promotes hypertension through cardiovascular autonomic control impairment, and biochemical alterations in juvenile offspring.

Methods

All procedures were reviewed and approved by the Ethics Committee for Animal Research (CEPA) of the Federal University of Sergipe and followed the Guidelines of the National Council for the Control of Animal Research (CONCEA) and International Principles for Biomedical Research

*Address for correspondence: R. V. dos Santos, Department of Physiology, Federal University of Sergipe, Frei Paulo St. 445, apt 303, Building Pegasus, Aracaju/SE 49052-270, Brazil.
(Email robervanvidal@hotmail.com)

Involving Animals (Protocol 12/2012). All efforts were made to minimize animal suffering and reduce the number of animals used.

Diets

Control and WDs were made at the Laboratory of Experimental Nutrition – Department of Nutrition, Federal University of Pernambuco according to the American Institute of Nutrition – (AIN-93)[21] and Survey Familiar Budget (IBGE/Brazil, SFB 2002/2003), as previously described.[22] The control diet (kcal%) contained 19% protein, 18% lipid (26% saturated, 12% monosaturated, 62% polyunsaturated fatty acid), 63% carbohydrate, thereby providing 3.6 kcal/g; on the other hand, WD (kcal%) contained 20% protein, 32% lipid (68% saturated, 16% monounsaturated, 16% polyunsaturated fatty acid) and 49% carbohydrate, thereby providing 4.2 kcal/g, as previously described.[13]

Animals

All animals were obtained from the Animal Care Facility of the Federal University of Sergipe and maintained under controlled light/dark cycle (12/12 h), room temperature (23 ± 2°C) with free access to food and water. A total of 12 females (~200 g) and six males (~300 g) Wistar rats were mated overnight (proportion of two females: one male per cage). In the morning after presence of spermatozoid on the vaginal smear was considered a marker of day 0 of pregnancy. Pregnant rats were transferred to individual cages and WD (total energy, 32% derived from of fat and 19% from sample sugar) was provided pregnant rats ($n = 6$) during gestation and lactation (perinatal period). Control group of pregnant rats ($n = 6$) received a control diet (total energy, 18% from fat and 11% from sample sugar). Newborns were sexed and weighed on postnatal day (PND) 1. At the same period we made the standardized adjustment to eight pups per litter. All animals were weaned at PND 21. After weaning the offspring were divided into two groups according to the diet received westernized diet dams (W) and control diet dams (C). The offspring was housed in a collective cage and received standard chow *ad libitum* (63% carbohydrate, 26% protein and 11% lipids) Labina®; Purina Agriband, Sao Paulo, Brazil. The C and W experimental groups were formed with two male pups chosen randomly from each litter (C, $n = 12$ from six dams; W, $n = 12$ from six dams). One animal from each litter were chosen for cardiovascular recordings or biochemical analyses.

All the experimental procedures were performed only in males rats. Furthermore, female animals were excluded of study. Ovarian hormones have a protective cardiovascular effect and the phase of estrous cycle may cause a different physiological response. Future studies will be carried out in order to standardize the cardiovascular effects according to the cycle.

Ponderal gain and measurement of food intake

Male pups were weighed once weekly beginning from PND 1 until PND 60 with the 500 digital electronic scales (BS 3000A 500 TDS instrumental tecnológica LTDA, Paraná, Brazil). The specific rate of weight gain was calculated employing the formula of specific rate of weight gain = [(weight on day 60 – weight on day 1)/(weight on day 1 × total number of days)].[23] On day 60, animals were housed individually for 10 days in a metabolic cage. The first 4 days were designed for adaptation to the cage. Next, the animals daily food consumption was determined by the difference between the amount of food provided (50 g) at the onset of the light cycle and the amount of food remaining 24 h later.

Measurements of arterial blood pressure

The cardiovascular evaluation was made in one group of animals on PND 60. Initially animals were anesthetized with thiopental sodium (50 mg/kg, i.p.) and implanted with a polyethylene catheter (PE-10/PE-50; Intramedic, Becton Dickinson and Company, Sparks, MD, USA) into the femoral artery. The catheter was tunneled into the back of the rats and exteriorized in the nape. After 24 h, the catheter was connected to a pressure transducer (FE221, Bridge Amp; ADInstruments, Bella Vista, NSW, Australia) coupled to a pre-amplifier (Powerlab 8/35; ADInstruments).

Blood pressure was recorded in conscious rats for 30 min (2 kHz; Powerlab 8/35; ADInstruments) and processed using computer software (LabChart 7 Pro; ADInstruments) that identifies inflection points on signals and generates beat-by-beat time series with SAP, diastolic arterial pressure (DAP), mean arterial pressure (MAP) and HR.

Cardiovascular autonomic evaluation

The baroreflex sensitivity (BRS) was measured in the time domain by the sequence method.[24] Series beat-to-beat were analyzed by software CardioSeries v2.4 (http://sites.google.com/site/cardioseries). Sequences of at least 4 heart beats with increased SAP followed by PI lengthening or subsequent decrease of SAP with PI shortening with correlation greater than 0.85 were identified as baroreflex sequence. The slope of the linear regression between SAP and PI was considered as a measure of BRS.

Cardiac autonomic balance was evaluated by frequency domain. The PI and SAP variability analysis were performed using the same software previously described. Series beat-to-beat were obtained by pulsatile arterial pressure and converted into points every 100 ms using cubic spline interpolation (10 Hz). The interpolated series were divided into half overlapping sequential sets of 512 data points (51.2 s). Before calculation of the spectral power density, the segments were visually inspected and the non-stationary data were not taken into consideration. The spectrum was calculated from the fast Fourier transformation algorithm direct and Hanning window

was used to attenuate side effects. The spectrum is composed of bands of low frequency (LF; 0.2–0.75 Hz) and high frequency (HF; 0.75–3 Hz), the results were showed in normalized units, by calculating the percentage of the LF and HF variability with respect to the total power after subtracting the power of the very low frequency component (frequencies < 0.20 Hz), namely low frequency/high frequency (LF/HF) ratio.

The LF/HF ratio from pulse interval represents sympathovagal balance. LF and HF components mean cardiac sympathetic and parasympathetic activity. LF from systolic arterial pressure (LFsys) represents sympathetic vascular modulation.[25]

Serum biochemical measurements

At the day 60 of life all animals were submitted to 12 h of fasting overnight. After pups were anesthetized with ketamine (80 mg/kg) and xylazine (10 mg/kg), and blood samples (~1 ml) were collected by plexus retro-orbital disruption. Biochemical analyses were carried out in accordance with the procedures detailed by the manufacturer (DOLES, Goiânia, GO, Brazil). Serum levels of glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-c), and triglycerides were obtained by spectrophotometer Genesys 10 s UV-Vis (Thermo Scientific™, Amarillo, TX, USA), absorbance was based on the values given in each kit. Levels of low-density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c) were obtained by Friedwald calculations.[26]

Insulin tolerance test (ITT)

For the ITT, six animals were used in each group with 60 days of age. Animals were previously fasted for 6 h and then injected with human regular insulin (0.75 U/kg i.p., insunorm R, 100 UI/ml). Blood samples were collected from tail vein at 0, 20, 40, 60 and 90 min for glycemia measurement.[27]

Statistical analysis

Data are expressed as mean ± standard errors mean (S.E.M.). Comparisons between and within the groups were assessed by unpaired and paired Student's *t*-tests, respectively. To evaluate biochemical parameters, average intake and serum glucose post injection of insulin was used the repeated measures two-way ANOVA. To determine the differences in comparisons, a Student's two-tailed *t*-test was used. The trapezoidal rule was used to determine the area under the curve (AUC). Differences were considered statistically significant when $P < 0.05$. All the analyses were performed by the statistical program Graphpad Prism 5 (GraphPad Software Inc., La Jolla, CA, USA).

Results

W had higher birth weight than C (6.1 ± 0.1 *v.* 5.3 ± 0.06 g, $P < 0.05$) (Fig. 1a). High body weight in the W group was maintained at 30 (73 ± 2.05 *v.* 48 ± 1.58 g, $P < 0.05$) and 60 days (224 ± 6.09 *v.* 185 ± 6.1 g, $P < 0.05$) of age. The specific rate of weight gain (0.66 ± 0.02 *v.* 0.56 ± 0.02 g, $P < 0.05$) (Fig. 1b) from lactation to adulthood was higher in the W group.

Intake of a standard chow diet was monitored in male offspring from the two maternal dietary groups at 64 PND (Fig. 2). The data presented show that consumption of feed in the W group (26 ± 1 *v.* 21 ± 1 g, $P < 0.05$) was greater compared with the C group.

The W group presented higher glycemia and LDL starting on PND 30, with increased total cholesterol, triglycerides (TAG), very low density lipoprotein (VLDL) and decreased high-density lipoprotein (HDL) on PND 60 when compared with the C group, as shown in Table 1.

As shown in (Fig. 3a) the W group exhibited higher serum glucose after intraperitoneal insulin injection 20 (96 ± 5.3 *v.* 66 ± 5 mg/dl, $P < 0.05$), 40 (73 ± 4 *v.* 46 ± 3.7 mg/dl, $P < 0.05$) and 60 min (58 ± 1.4 *v.* 43.8 ± 2.4 mg/dl, $P < 0.05$). Figure 3b presents the AUC 90 min after injection of insulin (6650 ± 252 *v.* 5260 ± 226 mg/dl × 90 min, $P < 0.05$).

Representative tracings of pulsatile arterial pressure, SAP, DAP and HR of male pups at 60 days of age are given in Fig. 4. Table 2 presents hemodynamic parameters at 60 days of age: the W group exhibited tachycardia (428 ± 14 *v.* 357 ± 19 bpm, $P < 0.05$), increased MAP (130 ± 3 *v.* 117 ± 1 mmHg, $P < 0.05$), DAP (111 ± 1 *v.* 98 ± 2 mmHg, $P < 0.05$) and SAP (157 ± 2 *v.* 130 ± 4 mmHg, $P < 0.05$) compared with the C group.

W group showed increased strength of the LF band of the HR spectrum in the W group (34.5 ± 6.8 *v.* 12.3 ± 1.1 nu) and the weaker HF band (65.5 ± 6.8 *v.* 87.6 ± 1.1 nu) compared with the C group, resulting in an altered autonomic balance, described as LF/HF ratio (0.70 ± 0.22 *v.* 0.14 ± 0.02). To examine further alterations in sympathetic modulation, the LF band of the SAP spectrum (LFsys) was analyzed. The W group showed stronger LFsys (6.19 ± 0.8 *v.* 2.29 ± 0.56 $mmHg^2$). Finally, decreased BRS was observed in W (1.48 ± 0.19 *v.* 2.86 ± 0.63 ms/mmHg) in Fig. 5.

Discussion

The main finding of the present study was that the introduction of a WD in the perinatal period in the absence of obesity caused metabolic disruption such as hyperglycemia and dyslipidemia, at an early age. The study also found an imbalance in cardiovascular autonomic function in the heart and vessels. Together, these may contribute to the development of hypertension in these subjects.

Studies in humans have shown that obesity is highly correlated with cardiovascular disorders.[28–31] It is well known that a diet with a high content of lipids can lead to obesity.[32,33] The present study demonstrated that the WD implementation in pregnant dams results in high offspring body weight.

The control diet used in this study has a higher carbohydrate content compared with WD. However, western-style diet has almost twice as much sugar (sucrose) content than the control.

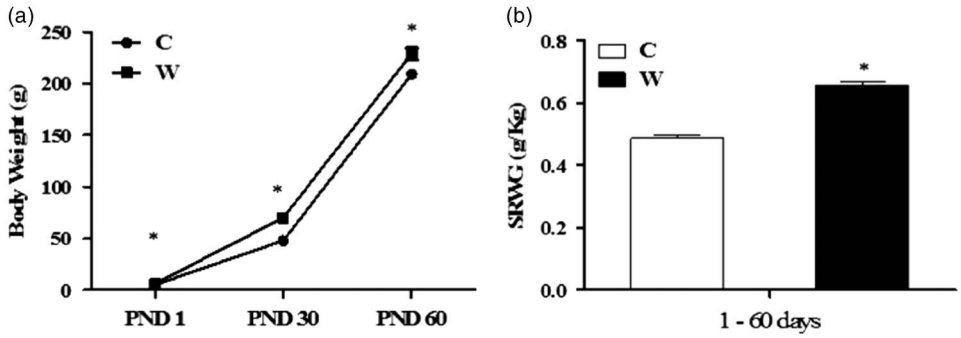

Fig. 1. (*a*) Postnatal body weight in relation to age and (*b*) specific rate of weight gain (g/kg) of male offspring until 60 days of age from dams submitted to control (C, $n = 10$) or westernized diet (W, $n = 10$) and from dams submitted to a control diet (18% of lipids) or a westernized diet (32% of lipids) during pregnancy and lactation. All pups were fed on a standard chow diet at weaning. Offspring in each litter was weighed on postnatal days 1, 30 and 60. Values are means, with their standard errors represented by vertical bars. *Mean values were significantly different from those of the W group at each age (1, 30 or 60 days) ($P = 0.05$; unpaired Student's *t*-test).

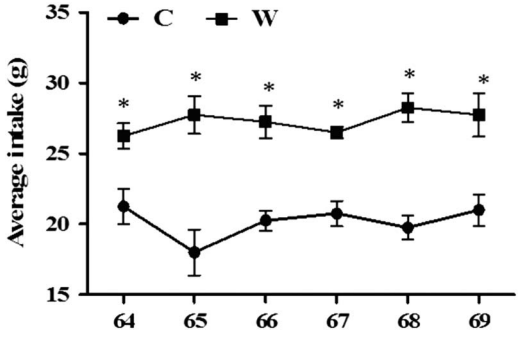

Fig. 2. Representative tracings of food intake in the male offspring from dams submitted to a control diet (18% of lipids) or a westernized diet (32% of lipids) during pregnancy and lactation. All pups were fed on a standard chow diet at weaning. Food intake was evaluated daily since day 64 to the postnatal day 69. Control (C, $n = 6$, 1 pup from each of six litters per group) and westernized diet (W, $n = 6$, one pup from each of six litters per group). The values are presented as means ± S.E.M. $P < 0.05$ using two-way ANOVA and Bonferroni's post-hoc test.

Table 1. *Biochemical analysis of serum levels of glucose, tryglicerides, total cholesterol, HDL, LDL, VLDL in male offspring (postnatal day 60) from blood collected*

	60 days	
Substrates	C ($n = 10$)	W ($n = 10$)
Glucose (mg/dl)	123 ± 2	155 ± 2*
Tryglicerides (mg/dl)	49 ± 1	85 ± 2*
Total cholesterol (mg/dl)	75 ± 2	86 ± 2*
HDL (mg/dl)	50 ± 4	38 ± 3*
LDL (mg/dl)	15 ± 1	31 ± 2*
VLDL (mg/dl)	10 ± 0.1	17 ± 1*

HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low density lipoprotein.
Results are presented as the mean ± the standard error of the mean (S.E.M.).
*Differences were considered statistically significant if $P < 0.05$.

Furthermore, WD has more total fat, mainly saturated, sodium chloride and low dietetic fibers, which is characteristic of the WD. This kind of diet is widely consumed around the world and reproduces as far as possible human diet consumed in industrialized and urbanized countries, which has brought nutritional and epidemiological effects.[1,2,4]

Prenatal and early-life nutrition and stress are examples of adverse conditions that predispose offspring to metabolic and cardiovascular diseases in later life.[9,34] Reports performed in sheep and rat models of overnutrition found that *in utero* environment can substantially modify fetal genome expression, thereby exerting stimulatory or inhibitory effects on fetal growth and adiposity.[35–40]

In the present study maternal consumption of a WD at the beginning of gestation and through lactation, without pregravid obesity, produced offspring with high body weight, probably because of increased adiposity, as described.[41–43] Cross-fostering between dietary treatments has established that, in rodents, maternal consumption of a WD during the suckling period is critical and can cause obesity and is associated with metabolic consequences in offspring.[29,44] Furthermore, it is postulated that high lipid content diets may increase daily milk volume and lipid concentration, affecting milk fatty acid composition by increase in long-chain fatty acids to the detriment of medium-chain fatty acids.[45,46]

Offspring of rat dams fed a high-fat diet during the perinatal period also display a long-term upregulation in the expression of orexigenic peptides including galanin, enkephalin, and dynorphin in the paraventricular nucleus of the hypothalamus (PVN), and orexin and melanin-concentrating hormone in the perifornical lateral hypothalamus. Exposure to high-fat diet during gestation stimulates the proliferation of neuronal and neuroepithelial cells of the embryonic third ventricle of the hypothalamus and increases their migration to hypothalamic regions resulting in an increase in the proportion of neurons expressing orexigenic peptides.[47–50] Thus, in rodents we postulated that perinatal exposure maternal WD consumption results in disruption of the homeostatic feedback regulation

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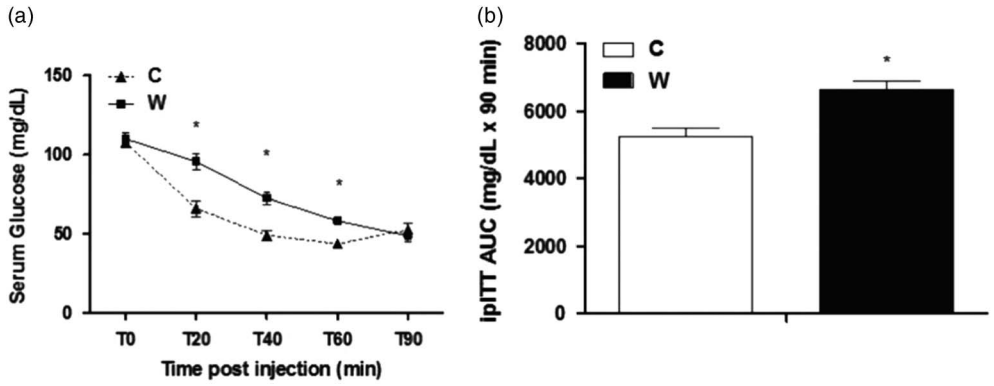

Fig. 3. Insulin tolerance test (*a*) and area under the curve for glucose (*b*) for the male pups from dams fed on either a control (C, $n = 6$, one pup from each of six litters per group) or westernized diet (W, $n = 6$, one pup from each of six litters per group) during pregnancy and lactation were calculated by using the trapezoidal rule. The values are presented as means ± S.E.M. $^*P = 0.05$ using two-way ANOVA, followed by Bonferroni's post-hoc test (A) or Student's *t*-test (B).

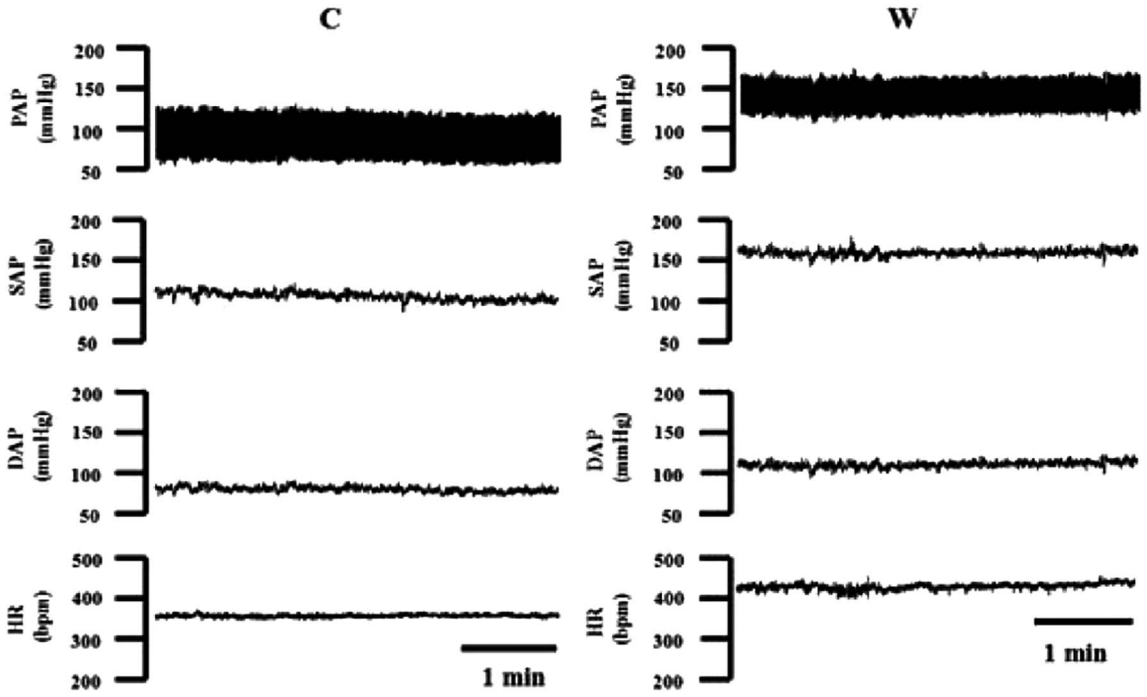

Fig. 4. Representative tracings of baseline arterial pressure of male pups at 60 days of age. Representative tracing of baseline pulsatile arterial pressure (PAP), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate (HR) in 60-day-old rats from dams submitted to a control diet (C, $n = 6$, one pup from each of six litters per group) or a westernized diet (W, $n = 6$, one pup from each of six litters per group) during pregnancy and lactation. All pups were fed on a standard chow diet at weaning.

and nutrient sensing capabilities of the hypothalamic feeding circuits leading to hyperphagia.

In addition, it is also well documented that, regardless of energy consumption, nutrient quality of diet is relevant as well. The increase in body weight was not only dependent of food energy intake, but also of a high-fat diet.[51] During perinatal life, a higher fat content in the maternal diet may have contributed to an increase in body weight of pups.

The W group presented hyperglycemia and decreased insulin sensitivity. A recent study using the same diet and protocol observed high levels of glycemia, fasting insulin, glucose intolerance, and increased visceral fat in pups born from mothers that were fed a WD.[52] Furthermore, an increase in visceral fat may lead to inflammatory conditions[53] which can decrease insulin sensitivity, suggesting insulin signaling, carbohydrate and lipid metabolism impairment in these animals.

High body weight and visceral fat[52] observed in the W group may also be associated with the high amount of simple sugars in WD which may promote increased insulin release. Hyperinsulinemia stimulates enzymes involved in lipogenesis and

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Table 2. *Mean arterial pressure (MAP); heart rate (HR); systolic arterial pressure (SAP); diastolic arterial pressure (DAP) at baseline level in male offspring (postnatal day 60)*

	Groups	
Parameters	C ($n = 6$)	W ($n = 6$)
MAP (mmHg)	117 ± 1	130 ± 3*
HR (bpm)	357 ± 10	428 ± 14*
SAP (mmHg)	130 ± 4	157 ± 2*
DAP (mmHg)	98 ± 2	111 ± 1*

Results are presented as the mean ± the standard error of the mean (S.E.M.).

*Differences were considered statistically significant if $P < 0.05$.

increases its expression.[54,55] Furthermore, alterations in insulin signaling promote changes in enzymes that regulate lipid metabolism, leading to increased levels of VLDL-c due to increased synthesis and lower breakdown of TAG by liver, decreased content and increased catabolism of HDL-c due to a higher concentration of TAG and high amount of LDL-c.[56]

Fatty acids polyunsaturated precursors are essential for cellular structures especially to the central nervous system during pregnancy and lactation.[57] Furthermore, heart is the first functional organ, and this fact is important to promote growth and offspring development.[58] Furthermore, the introduction a 60% fat diet to mices on the perinatal period promotes alterations expression pattern of several genes involved in the energy metabolism regulation, circadian clock, and inflammation in offspring heart and liver.[59] However, essential nutrients deficiency and saturated fat excess during critical periods of developmental may predispose the offspring to cardiovascular disease in adulthood.

The present study also observed the effects of a WD on cardiovascular parameters. The WD in the perinatal period induced tachycardia and hypertension with increased cardiac and vascular sympathetic modulation in the juvenile offspring. The consumption of fructose increases levels of adenosine-5′-triphosphate (ATP) in rostral ventrolateral medulla (RVLM) promoted an increase in activity of the sympathetic premotor neurons are highly sensitive to ATP, when the ATP synthase was blocked decreased in central sympathetic outflow and hypertension.[60] This data suggests that manipulation dietetic during perinatal period caused an intrauterine programming increasing the activity sympathetic in the offspring through consumption fructose.

The W group presented decreased insulin sensitivity, hyperinsulinemia[52] and glucose intolerance.[52] Also we observed reduction of BRS coupled with autonomic misbalance and hypertension. It has been demonstrated that hyperglycemia stimulates PVN and increases sympathetic activity through activation of corticotropin-releasing factor receptors in the RVLM. Furthermore, high glucose level increases c-Fos expression in tyrosine hydroxylase neurons within RVLM and promotes catecholamines synthesis.[61]

Insulin receptors are highly expressed in the PVN and arcuate nucleus (ArcN).[62–64] PVN and ArcN project to cardiovascular control regions within the brainstem, such as the RVLM promoting sympathoexcitatory effects.[65,66] In addition, glucose has been shown to exert effects on neurons in the nucleus of the solitary tract, the main brain stem site that receive baroreceptor and visceral afferents.[67–71]

Glucose injection into the hypothalamus, an important brain site for metabolic homeostasis and autonomic regulation, has been shown to decrease the firing rate of the superior vagus nerve and presumably impact baroreflex control of the heart.[72] Taken together, these findings suggest that hyperglycemia promotes autonomic misbalance by stimulation of sympathetic and reduction in parasympathetic control of the heart leading to a decrease in cardiac BRS.

Furthermore, It's been documented that diabetes mellitus promotes endothelial dysfunction. In this setting, hyperglycemia increases reactive oxygen species generation through activating protein kinase C-mediated NAD(P)H oxidases[73] and peroxynitrite-mediated oxide nitric synthase endothelial uncoupling,[74] which also leads to reduced NO bioavailability. In addition, hyperglycemia increases endothelial apoptosis[75] and release vasoconstrictors such as prostanoids and endothelin-1 through protein kinase C-mediated pathway in response to hyperinsulinemia and hyperglycemia appears to precede changes in vascular complication or NO production.[76,77] In the current study, we suggest that high levels of glucose promote alterations in endothelium function, contributing as one of the pathophysiological mechanisms associated with hypertension in W group.

The mechanisms to explain how maternal obesity and nutrients excess in the uterus increase the risk of future metabolic disease are poorly understood. Probably the quality and quantity of fetal nutrient supply in combination with genetic and epigenetic mechanisms are involved. *In utero* environment can substantially modify fetal genome expression, thereby exerting stimulatory or inhibitory effects on fetal growth and adiposity.[78] Many phenotypic changes observed in offspring exposed to a high-fat diet in rodent models may thus be linked to alterations in the epigenome.[79,80]

Histone modifications in the adiponectin and leptin genes have been examined in offspring exposed to a maternal high-fat diet.[81] Furthermore, previous studies have demonstrated alterations in the gene expression and methylation of the hypothalamic areas that are associated with energy balance and motivated feeding behavior of offspring of dams exposed to a maternal high-fat diet.[82] This suggests that genes related to metabolism homeostasis may also be important keys to understand mechanisms underlying the development of hypertension and biochemical alterations, however further studies are necessary to clarify an influence of nutritional programing on epigenetic states.

In summary the present data showed that quality of maternal diet during pregnancy and lactation are important for the

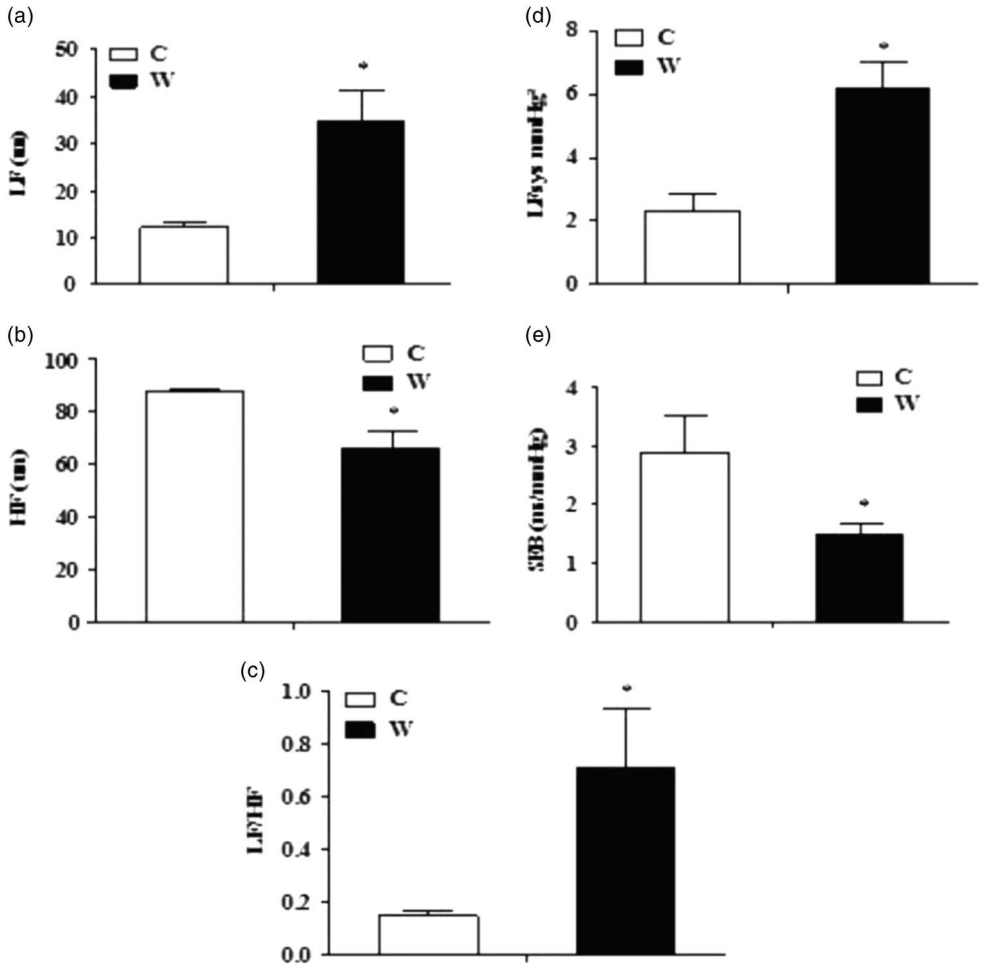

Fig. 5. Perinatal westernized diet increased power of PI spectra at low-frequency band (LF) (*a*), LF/HF ratio (*c*), power of SAP spectra at LF (*d*) and decreased high-frequency band (HF) (*b*) and baroreflex sensitivity (BRS) (*e*) in 60 days of westernized diet (W, $n = 6$, one pup from each of six litters per group) and (C, $n = 6$, one pup from each of six litters per group) from dams submitted to a control diet (18% of lipids) or a westernized diet (32% of lipids) during pregnancy and lactation. Male pups were fed on a standard chow diet at weaning. Values are means, with their standard errors represented by vertical bars. *Mean values were significantly different from those of the WD group in basal condition at 60 days ($P = 0.05$; unpaired Student's *t*-test).

physiological development of offspring. The consumption of WD in the perinatal period caused endocrine and autonomic nervous system alterations. These findings provide insights into the effects of maternal diet and suggest that a higher body weight, autonomic misbalance and insulin resistance are the possible risk factors for the development of arterial hypertension.

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Conflicts of Interest

None.

Ethical Standards

The study was approved by the Ethics Committee for Animal Research (CEPA) of the Federal University of Sergipe and followed the Guidelines of the National Council for the Control of Animal Research (CONCEA) and International Principles for Biomedical Research Involving Animals.

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