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Effect of Treatment With Msg on Growth, Satiety and Epididymal Adiposity in Neonatal Rats

Leandro Coelho Lemos[1]; José Augusto Pochapski[1]; Allan Raczenski[1]; Luiz Augusto da Silva[2]; Thiago Emannuel Medeiros[3]; Palloma Almeida Soares Hocayen[4]; Janaina Ângela Turmina[2], Carlos Ricardo Maneck Malfatti[5*]

[1]Department of Physical Education, State University of Center-West, Irati, PR, Brazil.
[2]Pharmaceutical Science Postgraduate Program, State University of Center-West, Guarapuava, PR, Brazil.
[3]Physical Education Science Master Degree Program, State University of Santa Catarina, Florianópolis, SC, Brazil.
[4]Evolutive Biology Science Master Degree Program, State University of Ponta-Grossa (UEPG), Ponta Grossa, PR, Brazil.
[5]Department of Physiotherapy, State University of Center-West, Guarapuava, PR, Brazil.

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ABSTRACT

This study aims to evaluate the relationship between morphological and metabolic parameters in obese rats induced by MSG, using exercise to determine the glycemic response between animals. Were constituted by 10 adult female *Wistar* rats, 4-month-old boy with obesity induced by MSG. They measured levels of intake of food and water for a week, and after, there was a swimming test lasting 60 minutes. The results are expressed as mean and standard deviation. It was used the Student t-test for independent samples, a significant difference when considering $p<0.05$. Occur significant difference between the length of the small intestine, where the obese group has the gut lower 14% (13 cm) compared to the normal group ($p<0.05$). Regarding the body weight, the average weight of the MSG group was significantly lower (82%; 37g, $p<0.05$) compared to the Control group. The opposite occurred with visceral adiposity, performing significantly higher in MSG group (54%; 8g, $p<0.05$) from the average of the Control group. We conclude that the consumption of MSG may lead to obesity by increasing body fat and visceral also morphological differences in the size of the gut and body weight.

INTRODUCTION

Obesity is a major risk factor for metabolic syndrome. This syndrome involves a group of pathologies including insulin resistance, type 2 diabetes *mellitus* (T2DM) and hypertension (Coll *et al.,* 2009; Vergara-Rodriguez *et al.,* 2009)**.** Insulin resistance is not present in all the obese as well as non-obese and non-diabetic patients may develop it (Cahova *et al.,* 2007), however its relationship with obesity exists due to activation of the visceral fat is greater than subcutaneous fat. These results in major production of free fatty acids and high rates of this are associated with insulin resistance (Sinaiko, 2007). Obese individuals may develop insulin resistance in parallel with obesity, while it glucose tolerance remains normal, the pancreatic β cells to increase insulin production and secretion as a compensatory mechanism. With time, there is reduced insulin secretion and subsequent reduction glucose tolerance, which could cause the development of T2DM (Cahova *et al.,* 2007; Weyer *et al.,* 1999). In animal studies, obesity and insulin resistance induced by monosodium glutamate (MSG) has been described in literature (Hata *et al.,* 2012; Nawa *et al.,* 2011; Andreazzi *et al.,* 2011). The model has characteristic neurotoxic MSG, even with the blood-brain barrier not formed, when administered in the neonatal period in rats, causes damage to the arcuate nucleus of the hypothalamus, reaching to the circumventricular organs. The animals MSG are normofagics, hypercorticosteronemics, hyperleptinemics, have insulin resistance, have reduced production of grown hormone (GH), decreased activity of the protein of transporter glucose (GLUT4), are hyperinsulinemics, lower activity of brown adipose tissue and greater deposition of visceral fat (HIRATA, 1997).

It is known that the intestine is size 3-8 meters of length, and Hounnou et al. (2002), concluded that this size is correlated with weight and not the height of the individual.

** Corresponding Author*
Carlos Ricardo Maneck Malfatti, PhD
Department of Physiotherapy, Rua Simeão Camargo Varela de Sá, 03, 84015-430; Guarapuava– PR, Brazil.
Phone: +55 42 3621 1000; FAX: +55 42 3621-1090

The reduction of the intestine is a surgical technique used for both the treatment of obesity and for the T2DM. Different techniques applied that can reduce up to 65% of the length of the intestine, but there is likely to occur clinically significant complications such as malnutrition, difficult to control and deficiencies of some vitamins (Mun *et al.,* 2001).

The intestine has the capacity to modulate the secretion of insulin by pancreas by certain substances secreted (Ahren, 2003; Drucker, 2006; Deacon e Holst, 2002). The size of the intestine may influence the etiology of obesity and insulin resistance because a small intestine has a better absorption of nutrients and best metabolic process, due the amount of nuclear receptors that are responsible for regulating absorption (Wit *et al.*, 2008; Kondo *et al.,* 2006).

In the intestine, enterocytes are stimulated to improve secretion of signaling molecules, how the glucagon-like peptide 1 (GLP-1) and the glucose-dependent insulinotropic polypeptide (GIP), capable of increased production and secretion of insulin in a dependent on glucose (Holst, 2008; Ahren, 2003; Drucker, 2006; Deacon and Holst, 2002).

Thus, the size or weight of the intestine may or not enhance the secretion of insulin-dependent glucose and may increase satiety and gastric emptying. This study aims to evaluate the relationship between morphological and metabolic parameters in obese and nonobese rats, using the exercise to determine the blood glucose response between animals.

METODOLOGY

Animals

It was used ten females rats *Wistar*, maintained in the Laboratory of Biochemistry of Exercise (LABE/I), of State University of Center-West. After weaning, were distributed in collective cages under controlled conditions of temperature (25°C) and inverted light/ dark cycle (12h/12h) with water and food *ad libitum*.

This study was approved by committee of ethics in animal use of State University of Center-West (P.026/2012).

Obesity Induced

Half of the newborn animals (n=5), approximately 6 g of body weight, received monosodium glutamate (MSG) via subcutaneous (4.0 mg/g of body weight) for 5 consecutive days to induce obesity. The other half (n=5) was trated with salina (0,9% NaCl).

Measurement of Water and Food Intake

After four months of induction of obesity, the animals had their blood glucose monitored and spent seven days in metabolic cage to measure urine and fecal volume. For samples of blood glucose was collected blood from the distal end of the tail of each rat, using a glucosimeter Accu-Chek Advantage II.

Experimental Protocol

From six days, the animals performed 20 min of swimming/day at 6% of the weight of body for adaptation to exercise protocol. After fasting for eight hours and measurement of blood glucose, the animals performed a swimming test in a pool with depth of approximately 50 cm, filled with heated water kept at around 30°C to 32°C. The test lasted 60 minutes. At the end of the exercise the animals were sacrificed with a guillotine following the guidelines of the ethics committee for animals for analysis of biochemical parameters and internal structures. The animals were weighed on digital scales, and then positioned on the operating table in supine position. After trichotomy of anterior abdominal wall with laparotomy the intestine was removed, together with visceral adipose tissue. The length of the intestine was measured with scale in a vertical position. Finally, both the intestine and visceral fat have been weighed in a high precision balance.

Statistical Analysis

Data are expressed as means ± SEM. Statistical significance was determined using an unpaired Student's t-test. The correlation coefficient was determined by linear regression. Differences were regarded as statistically significant when the $p<0.05$.

RESULTS

There is significant difference between the length of the intestine, where the obese intestine is 14% (13 cm) smaller compared to normal group (Table 1). There was no significant difference between the levels of intake, both feed and water intake between the groups. There was no significant difference between urine and fecal volume.

In relation to the body weight, the average weight of group obese was less (16%; 37g) but not significant difference. The same occurred with visceral adiposity, which was higher in the obese group (42%; 8g) but not being significant.

Table. 1: Morphological and physiological characteristics between groups.

Characteristics	Obese	Normal	p
Blood Glucose (mg/dL)	91.2 ± 11.49	93.2 ± 15.3	0.81
Intestine Weight (g)	4.04 ± 0.48	5.65 ± 0.22	0.90
Visceral adiposity (g)	20.5 ± 1.33	12.19 ± 2.09	0.32
Body Weight (g)	220.4 ± 7.43	257.6 ± 8.32	0.86
Water Ingestion (ml)	24.06 ± 5.51	29.15 ± 8.14	0.75
Food Ingestion (g)	11.31 ± 1.9	11.37 ± 4.6	0.63
Fecal Volume (g)	3.82 ± 1.01	4.01 ± 1.4	0,88
Urine Volume (ml)	9.87 ± 2.93	7.57 ± 2.96	0,65

Values expressed as mean ± SEM. *Statistically significant (p<0,05).

Same as the weight difference between the groups are not significant when correlated with the length of the intestine, it is possible to note a tendency for higher weight related to the size of higher intestine (figure 1). The blood glucose at rest and during exercise was not significantly different between the normal group and obese group **Figure 2.**

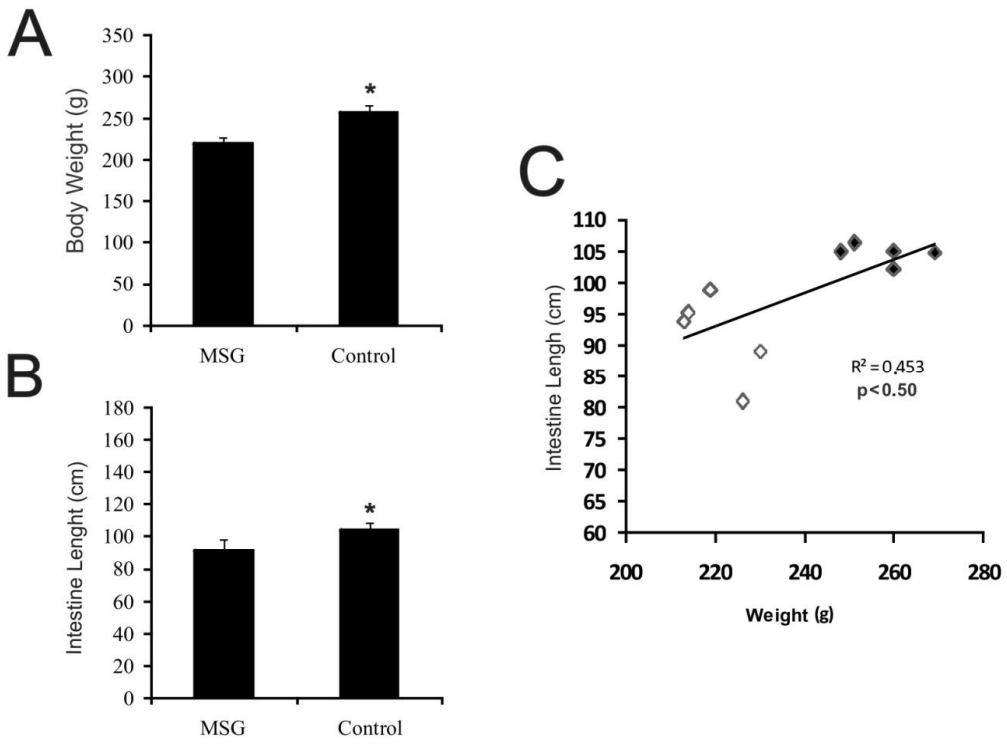

Fig. 1: A: Values of body weight between groups expressed as mean ± SEM; B: Values of the length of the intestine between groups expressed as mean ± SEM; C: Correlation between body weight and length of the intestine (r = 0.453, p<0.67), ◇ obese group; ◆ normal group.

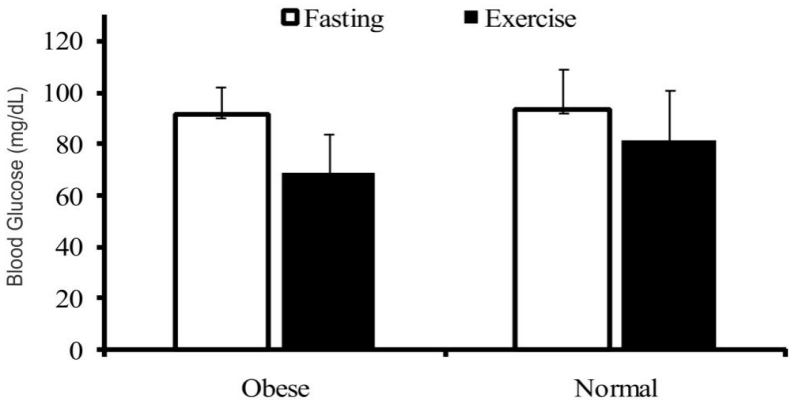

Fig. 2: Values of blood glucose before and after exercise. Values expressed as mean ± SEM.

DISCUSSION

After the trial period, was observed that the model of obesity induced in rats, produced some morphological changes in animals. The framework consists of obesity on body weight gain, increased blood glucose levels (hyperglycemia) and increased intake of water and food (Zhao *et al.,* 2003; Jorgensen *et al.,* 2001). Results related to body weight, glycemia end, water and food intake were the same as those found in the literature for this model of obesity induction (Nawa *et al.,* 2011; Andreazzi *et al.,*2011; Kondoh and Torii, 2008; Iwase *et al.,* 2000). According Hermanussen and Tresguerres (2003), the influence of MSG on GH production results in reducing the size of the animal and its organs. Iwase et al. (2000) found in their study with induction of obesity by MSG, increase in visceral fat percentage and body weight reduction. In the study presented by Voltera et al. (2008), neonatal administration of MSG was able to produce visceral fat accumulation in mice, increasing from 32% compared to normal mice. The present study was difference of 54% (8g) in visceral adiposity to the MSG group compared to the control group. The administration of MSG in newborn rats causes a destruction of the arcuate nucleus and ventro-medial hypothalamus region of the bearing mice develop obesity due to lack of control between absorption and energy expenditure (Hermanussen *et al.,*

2006). In the study by Voltera et al. (2008), mean arterial pressure (mmHg) and heart rate (bpm) were significantly higher compared to control rats. The implications are the main cardiovascular risk attributed to metabolic syndrome (Jonsson *et al.,* 2002), by virtue of its relationship with other risk factors such as hypertension, insulin resistance and dyslipidemia (Carneiro *et al.*, 2003). Even if the cardiovascular variables have not been verificas by this research studies indicate that visceral fat is related to the development of cardiovascular diseases due to stimulation of the sympathetic nervous system through the insulin, leptin and hypothalamic neuropeptides, play a role which important in the regulation of appetite and metabolism in obese subjects (Mark *et al.,* 1999; Eikelis *et al.,* 2003). At the end of the trial period, the model of obesity by MSG promoted morphological changes in the small intestine and weight of the animals. The data collected indicated decreased of 14% (13 cm) in intestinal length, and for body weight difference was 82%; 37g among obese mice compared to normal mice. In the study by Smith et al. (2006), there was an increase in the percentage of visceral fat, along with the size and weight of the intestine in MSG model in male rats. Humans are poorly adapted to the abundance of readily absorbable nutrients, which are causing, among other evils, a lack of nutrients in the distal segments of the intestine, causing serious endocrine and metabolic. Due to modern hypercaloric diet, low in fiber, easily digested, the small intestine is inadequately long as the stomach, a stock chamber, inadequately broad. In parallel, our food instincts, developed in times of famine and scarcity, remain increased, while our everyday physical exertion is diminished (Santoro, 2003). Exercise, in turn, exerted no influence on blood glucose. It is well studied the influence of exercise on blood glucose levels, and this factor is very important to be controlled in obese people because it can evolve from a case of insulin resistance caused by weight gain (Yang e Smith, 2007; Grundy *et al.,* 2004) the framework of T2DM. One week aerobic exercise training may improve insulin sensitivity in individuals with T2DM (Winnick *et al.,* 2008). In skeletal muscle, aerobic exercise can increase the enzyme glycogen synthase activity and protein expression of GLUT4 without the insulin signaling (Christ-Roberts *et al.,* 2004).

CONCLUSION

Through the analysis performed in this study, it was concluded that the model of obesity by monosodium glutamate (MSG) interfered with the size of the animals, characteristic of the induction model of obesity and shown by several studies in the literature. There was no statistically significant difference was between intestine length and body weight between the control group and the group MSG. There was also a significant increase in visceral adiposity to the MSG group compared to the control group. We conclude that the consumption of MSG may lead to obesity by increasing body fat and visceral also morphological differences in the size of the gut and body weight, however, further studies are required to elucidate the subject.

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