

## Effect of monosodium glutamate on the psychoneuroendocrine-immune system in Balb / c mice and their offspring

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### ABSTRACT

**Introduction:** Monosodium Glutamate (MSG) is used as a flavor enhancer, but its actions in health are a debated issue. Its effects on the Psychoneuroendocrine-immune system are not known.

**Objectives:** To determine the effect of monosodium glutamate on body mass, reproduction and lactation in Balb / c mice and their offspring.

**Materials and methods:** 20 mice in the neonatal period are administered subcutaneous GMS 4mg / kg diluted in 10 microliters of distilled water and others with 0.9% NaCl. At 90 days the Lee Index is calculated to determine the body weight, then they are paired in 4 groups of 5 mice where males and females are interbreed with GMS and 0.9% NaCl. The weight of the offspring in these crosses is compared to indirectly assess lactation.

**Results:** 100% of mice treated with MSG are obese because they have a Lee Index higher than 0.300. The females with GMS give birth to less than 4 offspring while the females (NaCl) mate with males (GMS) have an average offspring of 4-5 offspring. The weight of the offspring born of parents treated with MSG is lower than those not treated.

**Conclusions:** MSG administered subcutaneously in murine neonates induces obesity. Reproduction and lactation are affected in those treated with MSG since the number of offspring and the body weight of their offspring is lower than that of the untreated.

**Keywords:** Monosodium glutamate / Psychoneuroendocrinoimmunology / Obesity / Reproduction / Lactation /

## **INTRODUCTION**

Glutamic acid is a non-essential amino acid synthesized in the body. Its monosodium salt or monosodium glutamate (MSG) is used as a flavor enhancer for foods in different cultures. Its daily consumption added to food is estimated between 0.6-1.0 g in the United States; and 3.0 g in Asia. In Europe, 30 mg / kg / day of weight is established as an adequate level of consumption. (one)

The administration of MSG to rodents during the first 15 days of birth when the blood-brain barrier (BBB) is permeable, produces hypothalamic lesions. These mice develop disorders of metabolism and reproduction, hyperinsulinemia and obesity. In the Department of Biochemistry of the Institute of Basic and Preclinical Sciences "Victoria de Girón" the effect of MSG on obesity in rats has been evaluated. (two)

The objective of the present review is to describe the effects of monosodium glutamate on the neuroendocrinoimmune suprasystem in mice.

## **METHODS**

Twenty mice were selected in the neonatal period and administered subcutaneously to GMS 4 mg / kg of weight diluted in 10 microliters of distilled water, and a control group with NaCl. At 90 days the Lee Index was calculated to determine the body mass index, then they were separated into 4 groups each with 5 mice and crossed between parents with MSG and treated with 0.9% NaCl. The weight of the offspring was compared at those crosses to indirectly measure breastfeeding.

### **Ethical considerations**

The project was approved by the Center's Scientific Council and Ethics Committee, and is part of a branch project of the Ministry of Public Health, approved by the Ministry of Science, Technology and Environment. The animals were obtained from the National

Laboratory Animal Production Center of Cuba and treated in accordance with the regulations established for the care and use of them.

## **DISCUSSIONS**

The concentrations of GMS are very variable in the different compartments of the organisms. In the CNS, concentrations are higher within cells than in extracellular relationship, which allows neuronal and glial function. There are glutamate receptors in many organs such as: brain, spinal cord, nerves, heart, lungs, liver, testicles and spleen where it intervenes in cell signaling. (3)

In acute ischemic and hemorrhagic pathological conditions, trauma or in chronic neurodegenerative brain diseases, blood glutamate and intracerebral levels increase. Its plasma determination serves as a predictor of complications and unfavorable neurological conditions secondary to these pathologies. (one)

In the CNS the most important excitatory neurotransmitter is glutamate. It is synthesized and stored in glutaminergic neurons and is released to different stimuli. This is vital to regulate emotions, learning, memory, development and neuronal plasticity. (4)

Glutamate in the CNS is locally produced; because in physiological conditions it can not cross the BBB. Therefore, there are several sources to obtain it as the conversion of glutamine in astrocytes, metabolic sources of amino acid transamination and synthesis from alpha-ketoglutarate. (5)

The BHE restricts the entry of glutamate to the subluminal membrane by the action of high affinity transport proteins dependent on the Na + ion. The circumventricular organs are not protected by the BBB and are sensitive to plasma levels of glutamate. (6)

In animal models of neurotoxicity at key sites, MSG affects the coordinated action of the HHA-immune axis. T and B lymphocytes have receptors for glutamate which modulate their functions. In antigenic processing and presentation dendritic cells release glutamate that binds to the mGlu1R receptor on the T lymphocyte inducing its proliferation and the secretion of Th1 cytokines. Therefore, high levels of serum glutamate could induce abnormalities in the cellular and humoral immune response by promoting the secretion of proinflammatory cytokines. Perhaps this is one of the causes of the immune response damaging tissues of the body as it happens in rheumatological diseases.

The harmful effects related to the administration of GMS in murines are shown in Table 1.

System	
Nervous (Central and Periferic)	Seizures, slowing learning, hyperactivity, aggression, decreased motor activity and muscle strength, ataxic manifestations, increased neurotoxicity.
Endocrine	Alters the glucidic and lipid profiles, glucose intolerance, dysfunction of the pancreatic islets, obesity.
Reproductive	Morphological abnormalities of the spermatozoa, decreased spermatogenesis, testicular hemorrhage, destruction of the architecture of the seminiferous tubules. Significant reductions in the absolute and relative weights of the testicles, epididymis, prostate and seminal vesicle. It decreases the height of the seminiferous epithelium and the tubular diameter. In females it causes a decrease in oocytes, a sixfold increase in follicular ovarian cysts, a greater number of primary and total atretic follicles.
Immune	Involution of the thymic tissue. Increases the production of proinflammatory cytokines. Alters antigenic processing and presentation. It affects the integrity of the lymphoid tissue associated with the gastrointestinal mucosa (GALT). It decreases the production of secretory IgA in the lamina propria. (1.10)

So far in our research 100% of the animals treated with MSG developed obesity estimating the Lee Index which was greater than 0.300. The females that were administered GMS were the most affected in the reproduction because they had an average of 5 offspring, in addition these offspring had lower body weights in the first 21 days of life in relation to those not treated

## CONCLUSIONS

In murines, the administration of MSG by different routes in the first 15 days of birth when the blood-brain barrier is still permeable may affect the axes of the neuroendocrine-immune suprasystem, causing obesity and reproductive disorders.

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