EFFECT OF MONOSODIUM GLUTAMATE ORALLY ADMINISTERED TO MALE WISTER RATS ON THE BRAIN LIPID

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Abstract

Monosodium glutamate (MSG) of brand name "Ajinomoto" was administered to forty wistar rats, randomly divided into four groups and housed in different cages. The rats were administered with varying doses (500, 1000 and 1500 mg/kg body weights) of MSG for 28 days. Standard operational procedures (SOPs) were used to investigate its effects on the brain lipids of the test animals. The result showed significant, dose–related difference ($P < 0.05$) in the level of the brain lipids (cholesterol, triacylglycerol, and Total lipids) assayed in test groups compared with control group. The significant reduction in the brain lipid levels of the test groups compared to the control may cause depression state of the brain, suggesting that MSG is toxic to the brain.

Keywords*: Monosodium glutamate, "Ajinomoto", total lipid, cholesterol, triacylglycerol,*

INTRODUCTION

Monosodium glutamate (MSG) is the sodium salt of the amino acid, glutamic acid. It is sold as a fine white crystalline substance, similar in appearance to table salt (NaCl) and sugar. It does not have a distinct taste and how it adds flavour to other foods is not fully understood (FASEB & FDA, 1995). Asians originally used a seaweed broth to obtain the flavour enhancing effect of MSG, but today MSG is made by a fermentation process using starch, sugar, beets, sugar cane or molasses (George, 2004). It is used as a flavour enhancer in a variety of foods prepared at homes, in restaurants and by food processors (FASEB & FDA, 2005). Monosodium glutamate is widely used as a food additive and flavour enhancer in a variety of foods prepared at homes, in restaurants and by food processors in today's world (FASEB, 1996; FDA, 1996), although its effect on the body chemistry remains controversial (George, 2004). This compound is suspected to interfere with the brain chemistry and has been implicated in many neurological diseases (Blaylock, 1997). It has been shown experimentally that prolonged high levels of glutamate in the blood causes glutamate to seep through the blood brain barrier (BBB) and this results in acute neuronal necrosis (Allent *et al.*, 1987).

In the brain, glutamate serves as a neurotransmitter (Fernstrom, 1994). It also plays a general role in protein and energy metabolism, (Fernstrom, 1994). The body uses glutamate as a neurotransmitter in the brain and there are glutamate responsive tissues in other parts of the body as well (Choi, 1988). Neurotransmitters are stored in nerve endings and are used by nerve cells to inhibit or excite target cells, such as muscle or endocrine cells, (Tarasoff & Tara, 1993). Indeed, since the 1980s, processed free glutamic acid has been used as an ablative tool to selectively kill brain cells in a bid to facilitate the study of, and develop drugs for endocrine dysfunction, neurodegenerative diseases and other disorders involving the brain (Ishikawa *et al.*, 1997). Injections of glutamate into laboratory animals have resulted in damage to the nerve cells in the brain (Kubo *et al.*, 2004). Glutamate has a trophic function in the developing central nervous system (CNS); it regulates proliferation, migration and survival of neuronal progenitors. A number of diseases, seizures and stroke are associated with the glutamate cascade (Blaylock, 1997). The ever–expanding use of MSG by the food industry raises a great concern because MSG over stimulates brain cell activity. It is neither a necessary additive, nor a harmless flavour enhancer like common table salt. MSG actually tricks the brain into thinking that the food tastes good.

This study is aimed at evaluating the possible effect of MSG on the brain by assaying the cholesterol, triacylglycerols and total lipid levels after its administration to wistar rats for a period of 28 days. The results can then be extrapolated to what is expected to happen to human on consumption of the flavour enhancer.

MATERIALS AND METHODS

Procurement and Management of Animals

The animals used for the study were 8 weeks old adult male Wistar rats weighing between 110 g and 230 g, obtained from the animal houses of the Faculty of Veterinary Medicine and Faculty of Pharmaceutical Sciences, University of Nigeria Nsukka (UNN). The feeds used for the study were normal rat diet chow bought from King size feed and mill flour limited, Nsukka

Experimental Design/Treatment of Animals

Forty rats were acclimatized to the laboratory environment for seven days and then assigned to four groups of ten rats each. Administration of MSG was by oral intubation. The rats were maintained on normal rat chow bought from King–size and flour mill Ltd, Nsukka, Enugu State.

The animals were fed *ad libitum* on the chow and water throughout the duration of the experiment. The groups were as follows:

- Group I was the control group and was administered distilled water only (2 ml/kg).
- Group II was administered with 0.5 g/kg body weight of monosodium glutamate dissolved in distilled water (250 mg/ml).
- Group III was administered with 1.0 g/kg body weight of monosodium glutamate dissolved in distilled water (250 mg/ml).
- Group IV was administered with 1.5 g/kg body weight of monosodium dissolved in distilled water (250 mg/ml).

The rats in groups II, III and IV were given MSG 3 times a day, 7 days a week for 4 weeks.

Animal Sacrifice and Sample Collection

All rats were sacrificed on day 28. The skull was opened and the brain excised and washed in phosphate buffered saline (PBS). A portion of the brain from rats in each group were taken and blotted with filter paper, homogenized and used for the assay. The extraction of brain lipids was according to the method described by Schweisguth *et al.* (1989). Assay of brain cholesterol was by the method described by Richmond (1973), total lipids by the process of South (2002) and triacylglycerol assay was by the method described by Andrikopoulos (2002).

RESULTS AND DISCUSSION

As shown in Table 1, there was a decrease in the brain cholesterol levels of the test groups administered 500 mg/kg, 1000 mg/kg and 1500 mg/kg body weight of MSG compared to the control group. The decreases which appeared to be dose dependent were statistically significant ($P < 0.05$) only in the group administered 1000 mg/kg and 1500 mg/kg body weight of MSG. Table 2 shows that there was an increase in brain triacylgylcerol levels of the groups administered 500 mg/kg, 1000 mg/kg, and 1500 mg/kg body weight of MSG compared to the control group. The increases in brain triacylglycerol levels of the various treatment groups compared to control group were statistically significant ($P < 0.05$).

Table 1: In vivo effect of varied concentration of MSG on brain cholesterol of Wistar Rats

Group	Dose (g/kg b.w)	Cholesterol (mg/100 ml)	% change of cholesterol
1	0.00	184.47± 2.65	0.00
2	0.50	178.06 ± 2.43	– 3.3
3	1.00	125.92 ± 2.02	– 32.1
4	1.50	113.29 ± 2.92	– 38.6

n = 10, Results are means ± S.D.

Table 2: In vivo effect of varied concentration of MSG on brain Triacylglcerol of Wistar Rats

Group	Dose (g/kg b.w)	Triacylglcerol (Mmol/L)	% change of Triacylglcerol
1	0.00	0.11± 0.02	0.00
2	0.50	0.33 ± 0.03	200
3	1.00	0.33 ± 0.07	200
4	1.50	0.46 ± 0.03	318.2

n = 10, Results are means ± S.D.

Table 3: In vivo effect of varied concentration of MSG on brain total lipids of Wistar Rats

Group	Dose (g/kg b.w)	Total Lipids (Mg/100 ml)	% change of Triacylglcerol
1	0.00	0.48± 0.02	0.00
2	0.50	0.18 ± 0.01	– 62.5
3	1.00	0.23 ± 0.01	– 52.1
4	1.50	0.25 ± 0.01	– 47.9

The result in Table 3 shows that there were decreases in the level of the total lipids in the brain of all the test groups. The reduction in brain total lipid level of the test groups were statistically significant ($P < 0.05$) compared to the control group and was highest in the group given 500 mg/kg body weight of MSG.

Glutamate, an excitatory amino acid and neurotransmitter is abundantly present in the brain of mammals as well as in dietary proteins (Babu *et al.*, 1994). This study examined the effect of MSG on brain lipids and selected biochemical parameters of adult albino rats. Monosodium glutamate was administered at varying doses (500, 1000 and 1500 mg/kg body weight) to the rats for 28 days. The brain lipids were evaluated. The administration of MSG to the rats at 1000 and 1500 mg/kg body weight significantly decreased ($P \leq 0.05$) the brain cholesterol level relative to the control. This is in agreement with the work of South (2002). This result is also consistent with the work of Blaylock (1997) which showed that high levels of glutamate in the brain causes Alzheimer's disease whose pathogenesis has been linked to the altered cholesterol homeostasis in the brain. The significant increase ($P < 0.05$) in the level of brain cholesterol of the control group compared with the groups administered 1000 and 1500 mg/kg body weight of MSG is consistent with the work of Dietschy & Turley (2004) and Guizzetti (2007) which showed that the brain contains a high level of cholesterol which is synthesized in situ, and that there is no evidence for the net transfer of sterols from the blood into the brain or spinal cord. Cholesterol is an essential component of cell membranes and plays an important role in signal transduction. Therefore MSG may be one of the causes of poisoning in the brain.

There was a significant increase ($P \leq 0.05$) in brain triacylglycerol levels of the test groups administered varying doses of MSG compared to the control group. This result is at variance with the findings of Bawari *et al.* (1995) which shows that MSG depletes brain triacylycerol levels. This discrepancy might be due to the age of the animals used for this study or the doses (500 mg/kg, 1000 mg/kg and 1500 mg/kg body weight) of MSG administered to the rats in this study while Bawari *et al*. (1995) used neonate rats and administered 4mg/g body weight of MSG. There was a significant depletion ($P < 0.05$) in brain total lipids levels of the test groups administered varying doses (500 mg/kg, 1000 mg/kg and 1500 mg/kg body weight) of MSG compared with the control group. This result is consistent with the work of Bawari *et al.* (1995) and Laura *et al.* (2004) which showed that MSG depletes brain total lipids thereby producing neuronal damage in circumventricular organs of the rat brain. It is also in agreement with the work of Babu *et al.* (1994) and Blaylock (1997) which equally showed that MSG alters brain total lipids level in adult rats.

Approximately, 25 % of the total amount of cholesterol present in humans is localized in the brain, most of it in the myelin. Almost all brain cholesterol is produced in situ there, with the blood brain barrier effectively protecting it from exchange with lipoprotein cholesterol in circulation (Bjorkhem *et al.*, 2003). Thus there is a highly efficient apolipoprotein dependent recycling of cholesterol in the brain (Bjorkhem *et al.*, 2003). In adults, the rate of synthesis exceeds the need for a new structural sterol, so that net movement of cholesterol out of the CNS must take place. Two pathways are used in this excretory process with formation of 24 – hydroxycholesterol (Dietschy & Turley, 2004). This reaction is catalyzed by a cytochrome P450 (CYP 461AI) cholesterol 24–hydroxylase (24–hydroxylase) which is selectively expressed in the brain. Cholesterol diffuses out of the cell across the blood brain barrier (BBB) and is cleared by the liver (Kotti *et al*, 2006). Recently it has been shown that this occur not only within the brain but also with other tissues and organs as well (liver and red blood cell) (Blaylock, 2007). This could cause some sorts of degenerative diseases such as coronary heart disease, artherosclerosis, arthritis as well as induce cancer formation (Blaylock, 2007).

CONCLUSIONS

The results shown in this work suggests that MSG may have been hazardous to the health of the test animals used in the work. The varying doses 500 mg/kg, 1000 mg/kg and 1500 mg/kg body weight of MSG significantly reduced the brain lipid levels of the test groups, hence might lead to depression state of the brain. These results support the initial findings that MSG is toxic to the brain. This toxic effect to the brain may be slow and cumulative.

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