International Journal of Biomedical and Health Sciences
Vol. 6, No. 4 December 31, 2010
Printed in Nigeria

0794-4748/2010 $12.00 + 0.00
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http://www.asopah.org

IJBHS 2010110/6405

Histological and biochemical effects of monosodium glutamate on the frontal lobe of adult Wistar rats

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(Received July 8, 2010; Accepted August 24, 2010)

ABSTRACT: Monosodium glutamate (MSG) is commonly consumed as a flavour enhancer or food additive and both animal model experiment and human clinical reports has established harmful effects. Group A_1 and B_1 rats was administered with 2mls and 1ml of 0.5g/ml MSG for 14 and 28 days respectively while Group A_2 and B_2 were respective withdrawal groups for A_1 and B_1 sacrificed 14 days post-administration. The control group (C_o) was administered with 1ml of distilled water for the period of the experiment.

Histological finding on the frontal lobe showed neurodegenerative changes in all the treated groups as compared with the control group. A correlating increased alkaline phosphatise activity indicating brain lesions was also observed in the treated groups. Withdrawal groups showed more histologically observed degenerative changes compared with the immediately sacrificed groups. Increased weight of the treated groups after sacrifice also signified probable indication for obesity.

Therefore, the non reversibility of the neurodegenerative changes caused by MSG is established in this study and a lighter dose seems to produce lesser degenerative changes.

Key words : Monosodium glutamate, neurodegeneration, brain lesions.

Introduction

Monosodium glutamate (MSG) is the sodium salt of the non-essential amino acid-glutamic acid, one of the most abundant amino acids found in nature (Francais Canada, 2008). Glutamate is thus found in a wide variety of foods, especially high protein foods such as dairy products, meat and fish and in many vegetables. Foods often used for their flavouring properties, such as mushrooms and tomatoes, have high levels of naturally occurring glutamate (Giacometti, 1979).

The human body also produces glutamate and it plays an essential role in normal body functioning[3]. Because of its flavour enhancing properties, glutamate is often deliberately added to foods – either as the purified monosodium salt (MSG) or as hydrolysed protein. Although once associated with foods in Chinese restaurants, MSG is now used by most fast food chains and in many foodstuffs, particularly processed foods (Moskin, 2008). In past times, monosodium glutamate was extracted from natural protein-rich foods such as seaweed. Today, this time-consuming practice is no longer used and monosodium glutamate is made from an industrial fermentation process (IFIC, 1997).

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González-Burgos and collaborators (2003) reported a dual effect of neonatal exposure to glutamate: an excitotoxic effect leading to cell death, and; a secondary neuroprotective effect, arising from the proliferation of glia cells and their subsequent uptake of glutamate, that favours the survival of the remaining neurons, and leads to a further hypotrophic effect on their dendritic processes. Eweka (2007) reported the distortion of the cyto-architecture of the renal cortical structures and cellular necrosis associated with the kidney**.** MSG consumption may have some deleterious effects on the cerebellum of adult wistar rats at higher doses and by extension may affect the functions of the cerebellum and may lead to tremor, unstable and uncoordinated movement, and ataxia (Eweka and Om'Iniabohs, *2*007).

According to Samuels (1999), the evidence of toxicity is overwhelming. Exposed laboratory animals suffer brain lesions and neuroendocrine disorders. Scientists studying retinal degeneration in mice treated with free glutamic acid have noted that these mice also became grotesquely obese following administration of free glutamic acid. The vulnerable hypothalamus in the brain regulates weight control, as well as other endocrine functions. When the brain is deluged with more free glutamic acid than it can handle, it is known that problems and diseases can develop as a diverse number of disease conditions such as ALS (amyotrophic lateral sclerosis- a progressive degeneration of neurons and motor cells of the brain), Alzheimer's disease, seizures, and stroke are associated with the glutamate cascade (Samuel, 1999). MSG is a member of the group of chemicals known as "excitotoxins that are known to interfere with brain chemistry and have been implicated in many neurological diseases, such as brain cancers, multiple sclerosis (MS), fibromyalgia, depression and hyperactivity (ADHD) (www.ezHealthyDiet.com, 2010). In fact, they overexcite brain cells to the point of cell damage and even cell death (NHIC, 2008). As a common ingredient in oriental cuisine, it has been associated with the Chinese Restaurant Syndrome (CRS). This comprises a number of symptoms that may arise from the consumption of MSG. They include headache, nausea, sweating, paresthesias, heart palpitations, chest pains and tremors (Resources for Life, 2009). Despite these, MSG has been declared safe for consumption by several international organisations and government institutions (Okwuraiwe, 2002). Therefore, this experiment aims to determine the effects of MSG consumption on the frontal lobe of adult wistar rats using histological and biochemical parameters.

Materials and Methods

Twenty five (25) adult Wistar rats of both sexes with average weight of 182g were randomly assigned into five groups A_1, A_2, B_1, B_2 and C_0 of five animals each. Groups A_1 and B_1 served as treatment groups that were immediately sacrificed after cessation of administration; Groups A_2 and B_2 served as respective withdrawal groups for A_1 and B_1 while Group C_0 was the control. The rats were obtained and maintained in the Animal Holdings of the Department of Anatomy, Faculty of Basic Medical Sciences, University of Ilorin, Ilorin, Nigeria.

The rats gained maximum acclimatization before actual commencement of the experiment. The rats in the treatment groups (A_1, A_2) and (B_1, B_2) were given 2mls and 1ml of 0.5g/ml MSG solution per day for 14 and 28 days respectively. The control group received 1ml of distilled water for the duration of the experiment. The rats in Group A_1 were sacrificed on the fifteenth day of the experiment; those in Groups A_2, B_1 and C_0 were sacrificed on the twenty-ninth day and rats in Group B_2 were sacrificed on the forty-third day of the experiment. The frontal lobe was quickly dissected out and fixed in10% formal saline for routine histological techniques. The tissues were dehydrated in an ascending grade of alcohol, cleared in xylene and embedded in paraffin wax. Serial sections of 7 microns thickness were obtained using a rotary microtome. The deparaffinized sections were stained routinely with haematoxylin and eosin. Photomicrographs of the desired sections were obtained for further observations.

Results

Biochemical Analysis

The concentration of acid phosphatase per litre of plasma in the experimental and control animals is as follows :

Table 1 – Concentration of acid phosphatase (in U/L)

Group	Mean	SEM
A_1	19.70	9.91
A_2	10.19	1.62
B_1	9.60	2.28
B_2	3.43	1.56
C_0	5.08	5.03

Histological Results

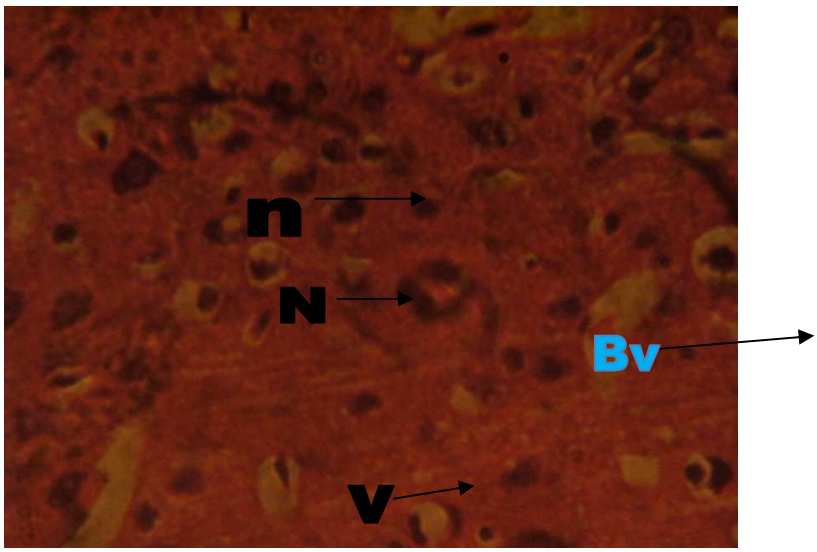

Figure 1: Photomicrograph of a transverse section through the frontal lobe of the control rat using H & E method at x400.

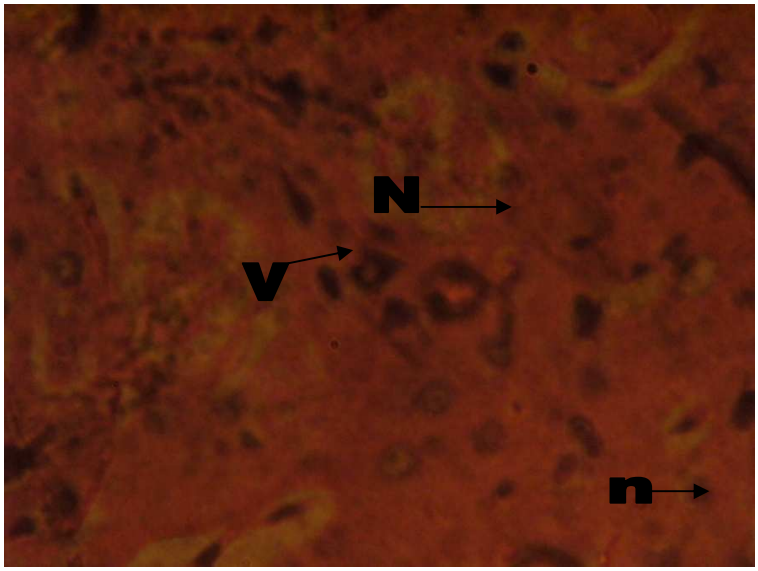

Figure 2: Photomicrograph of a transverse section through the frontal lobe of the experimental rat administered 2mls of 0.5g/ml MSG per day and sacrificed after 14 days of administration using H & E method at x400.

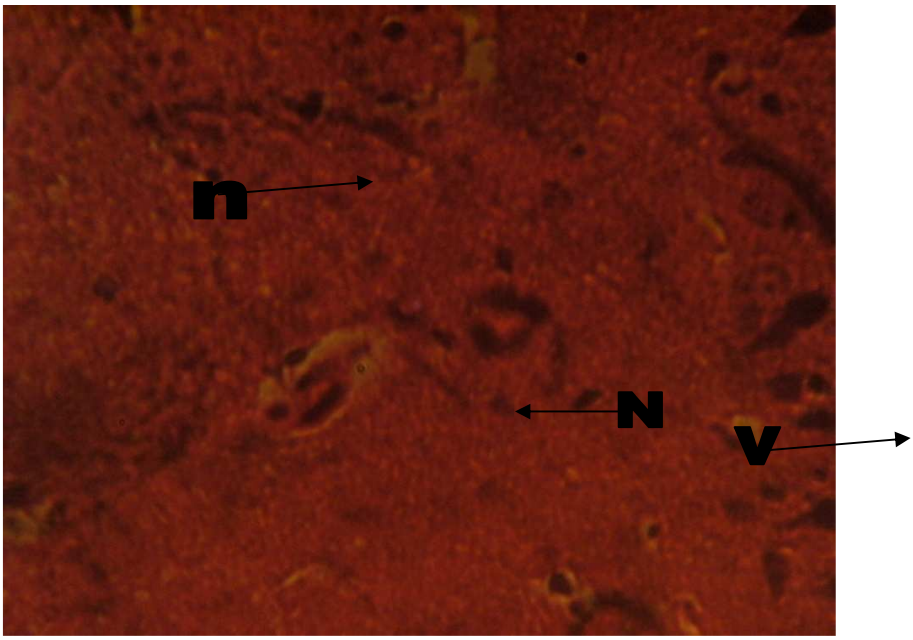

Figure 3: Photomicrograph of a transverse section through the frontal lobe of the experimental rat administered 2mls of 0.5g/ml MSG per day for 14 days and then withdrawn for 14 days using H&E method at x400.

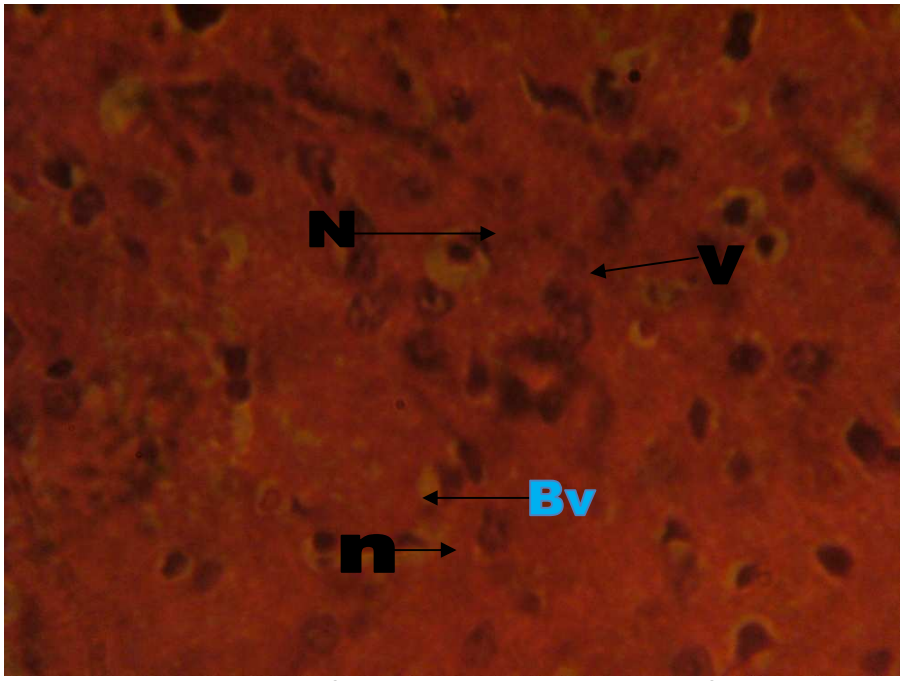

Figure 4: Photomicrograph of a transverse section through the frontal lobe of the experimental rat administered 1ml of 0.5g/ml MSG per day for 28days using H&E method at x400.

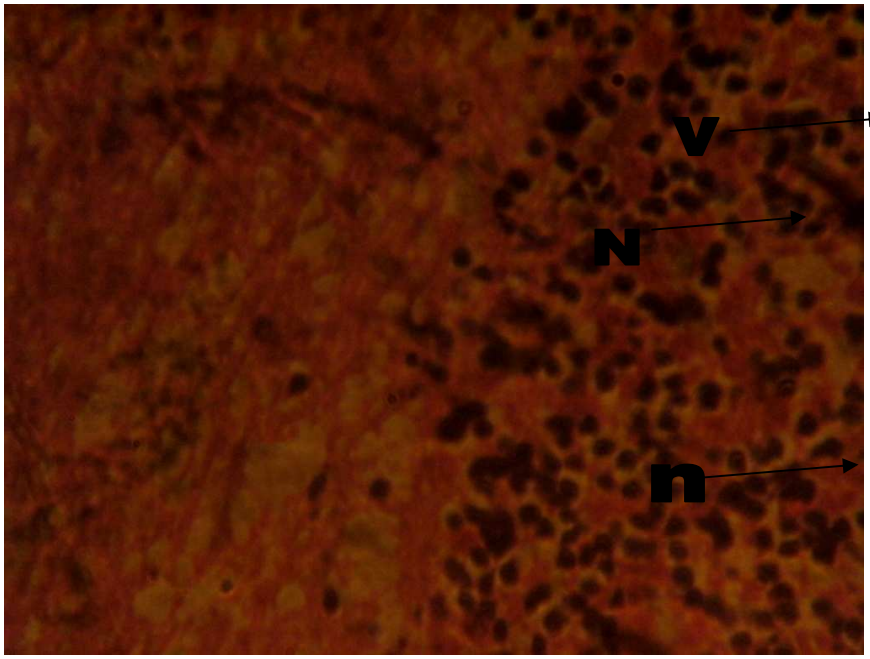

Figure 5: Photomicrograph of a transverse section through the frontal lobe of the experimental rat administered 1ml of 0.5g/ml MSG for 28 days and then withdrawn for 14 days using H&E method at x400.

LEGEND
N - Neuron
n - Neuropil
Bv – Blood vessel
V - Vacuole

Observations

It was observed from the biochemical analysis that the activity of acid phosphatase was higher in most of the treatment groups when compared with the control. This activity was seen to be lower in the withdrawn groups compared with the immediately sacrificed groups. It was also observed that the levels of acid phosphatase activity resulting from the administration of a heavier dose for a shorter duration are higher than those resulting from the administration of a lighter dose for a longer duration.

The control sections of the frontal lobe showed normal histological features with the normal neurons, neuropil and blood vessels visible.

The treatment sections of the frontal lobe showed some histological changes that were at variance with those obtained in the control. There were evident neurodegeneration, nerve sparsity and chromatolysis with greater severity in the withdrawal groups. This is the result of continued degeneration during the withdrawal interval and failure of regeneration to occur during this period. It was also observed that the severity of degeneration was greater with the administration of an heavier dose for a shorter duration compared with that obtained with a lighter dose for a longer duration.

Discussion

All the treated groups showed some degree of degenerative changes with the changes being more marked in Group A_1 than in B_1, more marked in Group A_1 compared to A_2, and more distinct in Group B_1 compared to B_2. It can be inferred from the damage of neurons observed being more severe in Group A_1 than in B_1 that the same total mass of MSG (14g) consumed over different time ranges and at different quantities per day has not produce the same effects. It is deduced that ingestion of a smaller dose for a longer time period may be safer than consuming a higher dose over a shorter time period. It is also seen from histological observation that the withdrawal groups show changes which did not heal or show signs of regeneration after withdrawal. This might mean that the retention of MSG in the blood was high enough to cause continued damage even after cessation of administration. Biochemical analysis showed an increase in the activity of acid phosphatase (ACP) in three of the treatment groups compared with the control group. The increased level of ACP is observed to reduce in the withdrawal groups when compared to the Groups A_1 and B_1. This might mean that the activity of the enzyme reduced and approached normal during the withdrawal period. It can be inferred from this increase that MSG consumption could result in brain lesions as ACP levels rise when brain lesions occur.

In this experiment, sudden withdrawal of the rats from MSG seems to have resulted in more degenerative changes. A gradual withdrawal might have produced a different result. The tremor, unstability and uncoordinated movement, and ataxia inference of Eweka and collaborators (2007) might be linked to the frontal lobe lesions effect reported in this work. Memory deficit, reasoning disorder , locomotion deficiency and impulse instability may also be associated with the frontal lobe lesions.

Conclusions and Recommendations

The side effects of its consumption on the frontal lobe have been shown from this study based on the biochemical and histological alterations observed. It has been shown that nerve cell degeneration and brain lesions result from MSG consumption. These changes might affect locomotion, reasoning, memory, language, and social and sexual behaviour. With these results, it is feasible that the functions of the frontal lobe as the organ for executive decision may be adversely affected.

It is recommended that further research be carried out investigating the effects of MSG on specific areas of the frontal lobe (for instance, Broca's speech area) and other parts of the brain. It is also recommended that the absorption, kinetics and mechanism of action of MSG in animals and humans be studied.

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