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Original Article

Histological Effects of Monosodium Glutamate on Brain of Infant Albino Swiss Mice *Mus Musculus*

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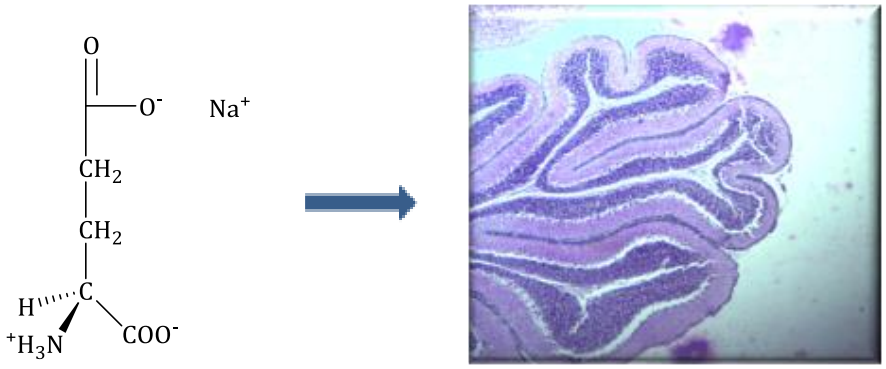
ABSTRACT

Monosodium glutamate (MSG) is one of additive compounds that can easily cross the placenta and affect brain development. The current study aims to investigate the detrimental effects of monosodium glutamate (MSG) on Albino Swiss Mice Mus musculus fetal brain during pregnancy and after delivery. Forty-eight pregnant mice were divided into two groups: control group(24) received only distilled water while the second group (treated group 24 mice) received 0.2ml/daily of MSG solution from the 17th days of pregnancy until the 21st days after birth (lactation period). Infant mice were randomly selected from each group and sacrificed in 15th, 21st, 30th and 60th days after birth. Histopathological examination of brain showed significant differences between treated and control groups. Histological lesions including: megakaryocyte, necrosis, blood capillary stenosis, fraction of nerve fiber and blood capillary collapsing, eosinophil cell, medullary necrosis and necrosis, eosinophilic nerve fiber, horseshoe shape nucleus, rosette shape pattern, acidophilic cytoplasm, swelling cell, gliosis, coalesces and occluded blood vessel. In conclusion, monosodium glutamate has clear histological effects on the brain of infant mice.

GRAPHICAL ABSTRACT



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Introduction

Monosodium Glutamate (MSG) is widely utilized as food-additives in most of commercial foods. The consumption of Monosodium Glutamate has elevated over time and this material is found in various ingredients and commercial foods that are sold in every market or food store. The MSG material gives a special flavor to the foods that is called umami in Japanese [1-2]. MSG is defined as sodium salt of glutamic acid. This salt is amino acid which is a major constituent of different proteins and various peptides, and is present in the most of body tissues [3]. Commercially, glutamic acid is made by molasses fermentation, and it is present in different products that are made by fermented proteins, like soy and hydrolyzed protein of vegetable. Glutamic acid is also synthesized and produced in tissues and has an important role in the metabolism process [3-4]. The MSG has been reported to be toxic substance for humans and experimental animals [5]. The adverse effects proved by different studies and researches including metabolic/digestive anomalies, respiratory disorders, circulatory diseases and nervous system problems. Glutamate is the primary excitatory amino acid neurotransmitter in the brain [6-7]. Previous studies reported that the administrated MSG at neonatal age can lead to severely injure their hypothalamic nuclei region (arcuate nucleus and ventromedial nucleus) thus causing increase in the body weight of rats, fat accumulation and deposition, reduce motor activity and growth hormone secretion in rats [8-10]. The present study aimed to demonstrate the histological effects of oral administration of 8g/kg/body weight doses of monosodium glutamate (MSG) on the brain of infant Albino Swiss Mice Mus musculus at different periods.

Material and methods

Animal model

Forty-eight adult female mice, (wt: 25±2 g with age: 10-14 Week) ordered from the Institute of Genetic Engineering and Biotechnology at the University of Baghdad/Baghdad/Iraq, and the animals were acclimatized for about a week to the laboratory environment before the initiation of the experiment, and fed on a standard diet (contain proteins, carbohydrates and lipids) and water ad libitum. The mice were housed in plastic cages in a temperature of (23±2 °C) and 12 hours light/dark.

Chemicals

Monosodium glutamate substance (formula: $C_5H_9NO_4Na$) with purity of 99% NT was used in the current study (8 mg/kg MSG) to detect if there were side effects.

Experiment design

Forty- eight experimental female mice divided into two groups (24 mice as control group and same number of mice for MSG administration). Each group was subdivided into 4 subgroups with six mice in each subgroup. MSG was orally administered to pregnant mothers from day 17th of pregnancy, and continued until day 21st after birth. Pups were dissected in four different periods after the birth (15th, 21st, 30th and 60th day). This procedure can be summarized as following point: Control groups: containing 6 pregnant mice for each group, which received (0.5 ml/day) distilled water until dissected .

- Control groups: twenty-four pregnant mice received orally (0.2 ml/day) of distilled water and pups dissected at day (15th, 21st, 30th and 60th) after the birth.
- Day 15th group: contain six pregnant mice received (0.2 ml/daily) MSG solution from 17th of pregnancy until 15th day after birth, and pups were dissected the same day MSG was stopped.
- Day 21st group: contain six pregnant mice received (0.2 ml/daily) MSG solution from day 17th of pregnancy until day 21st after birth, and pups were dissected the same day MSG was stopped.
- Day 30th group: contain 6 pregnant mice received (0.2 ml/daily) MSG solution from 17th of pregnancy until 21st day after birth, and pups were dissected on day 30th after birth.
- 60-day group: contain 6 pregnant mice received (0.2 ml/daily) MSG solution from 17th of pregnancy until 21st day after birth,

and pups were dissected the on day 60th after birth.

Histological examination

Brains were obtained from the infant mice killed by anesthetized in a laboratory glass desiccator using chloroform, and fixed overnight in 10% formalin. The fixed tissues were embedded in paraffin blocks using automated processing and embedding equipment. Tissue sections of 5 µm thick were cut and mounted onto glass slides, which were stained with hematoxylin and eosin [11-12].

Result and Dissection

Histological examination of control group section shows normal structures of Blood vesicles in cerebrum (Figure 1) and normal view for medulla, molecular layer, purkinji layer and granular layer (Figure 2). Different degree of histological changes was recorded in treated group according to the dissection periods.

In 15th day group, cerebellum show eosinophil cells and medullary necrosis (Figure 3) and in cerebrum show eosinophil cells, swelling of cells, Occluded blood vesicle and infraction (Figure 4). While, in cerebrum show giant cells and necrosis. Whilst, in the cerebrums of same treated group, megakaryocytes were seen, eosinophils infiltrations, morphological changes in cell size such as swelling, occluded blood vessel and necrosis as shown in figure 5 .

In comparison, the second group (day 21st group) the histological changes in the cerebellums were: the presence of eosinophilic nerve fibers, occluded blood vessels with evidence of edema, megakaryocytes also shown as well as necrosis (see Figure 7-9 subsequently).

Compared to previous groups, brain sections taken from mice of 30th day group show swelling of megakaryocytes, presence of apoptotic cells and tissue necrosis was seen (Figure 12 and 13).

Cerebellum sections showed megakaryocytes and nuclear morphology changes such as coalesces of granular nuclei, horseshoe shape nucleus, swelling cells and rosette shape pattern and necrosis as shown in Figure 14.

In 60th day group, cerebellum sections show gliosis, presence of microglia cells and eosinophilic cells with acidophilic cytoplasm, swelling of cells was seen in general (figure 15 and figure 18). While cerebrum sections of same treated group show dilation in blood vessels, swelling of cells, occluded blood vessels, and necrosis. (Figure 16 and 17).

Glutamate, the main component of MSG, is a neurotransmitter distributed ubiquitously in the mammalian brain tissue and it was linked to symptoms of neurological when taken in excess [13-14]. The results of current study show obvious changes in all treated groups as compared with the control mice. Mild changes recorded in the brain of group 15th day, which include eosinophil cells, medullary necrosis, swelling of cells, occluded blood vesicles and giant cells and megakaryocytes,. In 21st and 30th day groups, severe changes were reported, including; occluded blood vesicle with edema, giant cell and necrosis deeply eosinophilic nerve fiber, occluded vesicle , swelling of glial cell, megakaryocytes,, apoptosis, glial coalesces, coalesces of granular nuclei, horseshoe shape nucleus and rosette shape pattern. The results of this study agree with observations described by other studies [15-18]), they record necrosis in the hypothalamic (arcuate nucleus) neurons of neonatal mice given MSG systemically. Furthermore, other studies have shown that neonates treated with MSG caused neuronal cell death with decrease of photoreceptor and glial cells [19]. Several studies have also found neurodegenerative changes after MSG administration in various rodent species, usually when the compound was administered subcutaneously or by forced gavage [20]. Although MSG administration was stopped, but its affects were still present on the pups brain of 60th day and show many changes, like; gliosis, macrophage, eosinophilic cells, acidophilic cytoplasm, swelling of cell, coalesces , dilation in blood vessels, occluded blood vessels and necrosis.

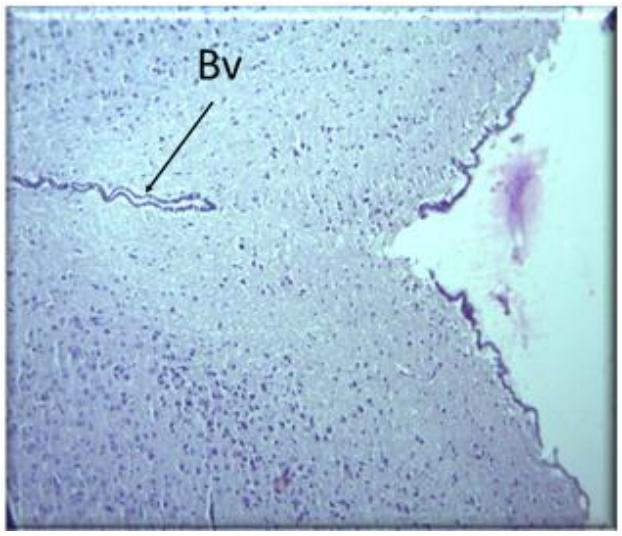

Figure 1: Transvers section of 15-day mice control cerebrum, showing blood vesicles (Bv). (H&E, 100 x)

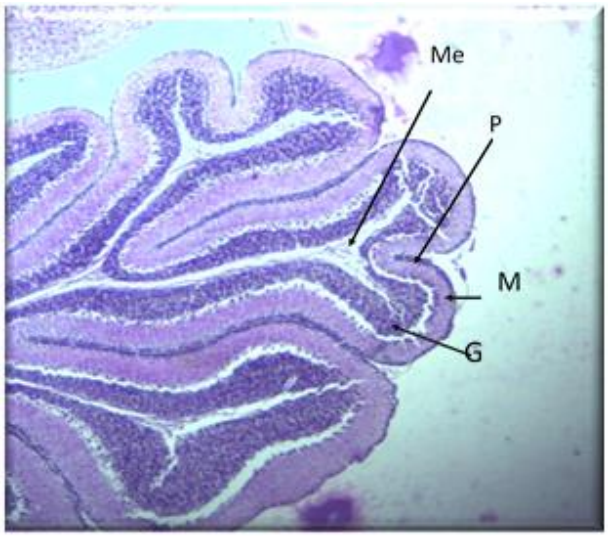

Figure2: Transvers section of 15-day mice control cerebellum, showing medulla (Me), molecular layer (M), purkinji layer (P) granular layer (G).). (H&E, 40 x)

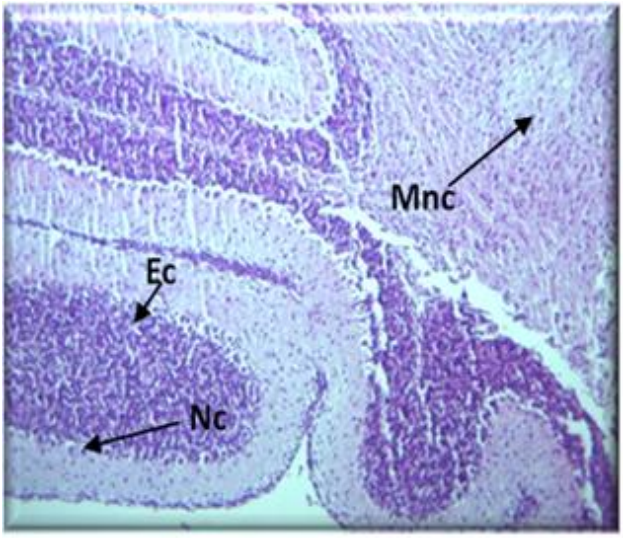

Figure 3: 15day, shows eosinophil cell (Ec), medulla necrosis (Mnc) and necrosis (Nc).(H&E, 100 x)

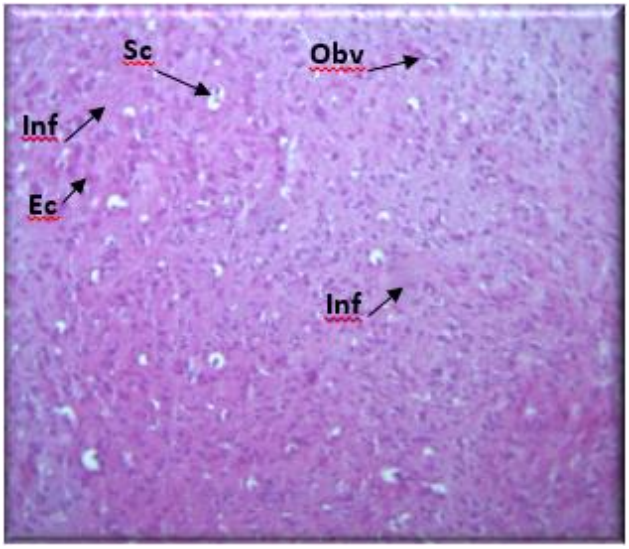

Figure 4: 15day mice cerebrum, shows eosinophil cell (Ec), swelling cells (Sc), Occluded blood vesicle (Obv) and infraction (Inf). (H&E, 100 x)

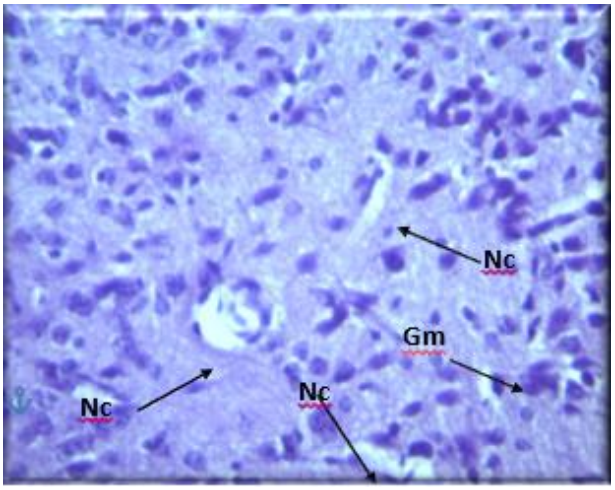

Figure 5: 15-day, cerebrum, showing giant cell (Gc) and necrosis (Nc). (H&E, 400 x)

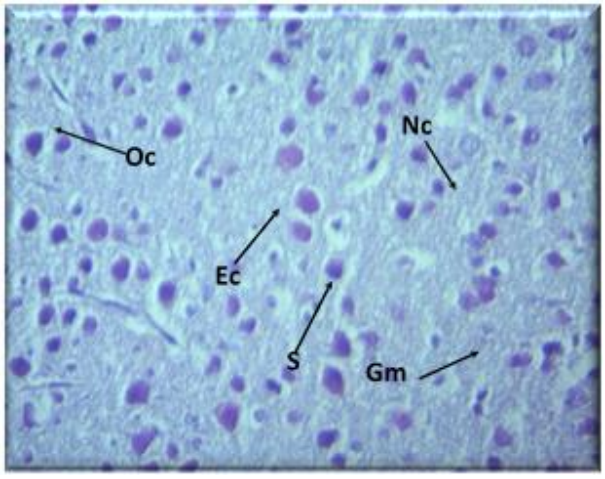

Figure 6: 15-day, cerebrum, showing giant macrophage (Gm), eosinophilic cell (Ec), swelling cell(S), occluded blood vesicle (Oc) and necrosis (Nc). (H&E, 400 x)

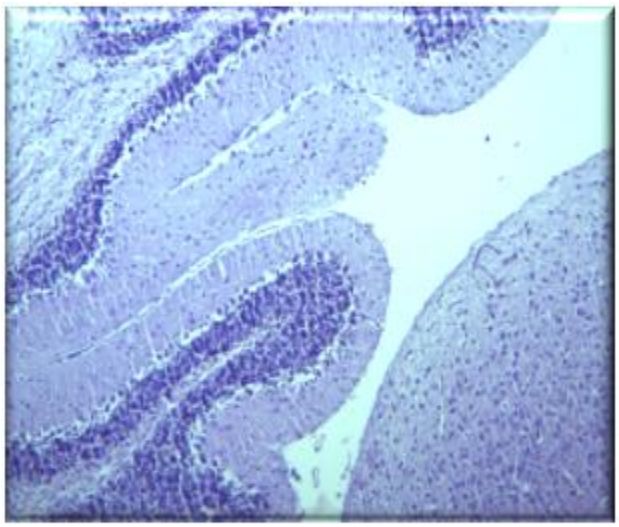

Figure 7: 21-day control mice, (H&E, 100 x)

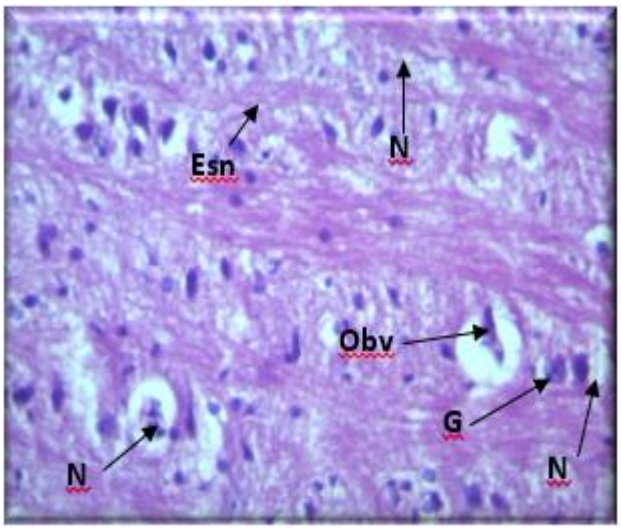

Figure 8: 21-day, shows eosinophilic nerve fiber (Esnf), occluded blood vesicle with edema (Obve), giant cell (Gc), and necrosis (Nc). (H&E, 400 x)

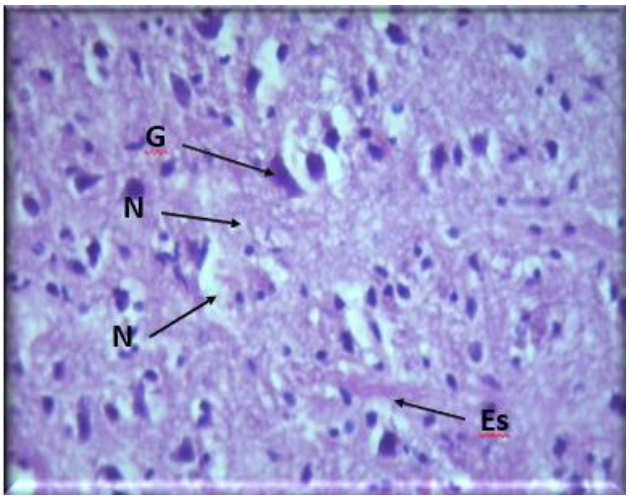

Figure 9: 21day, shows eosinophilic fiber (Esf), giant cell (G) and necrosis (N). (H&E, 400 x)

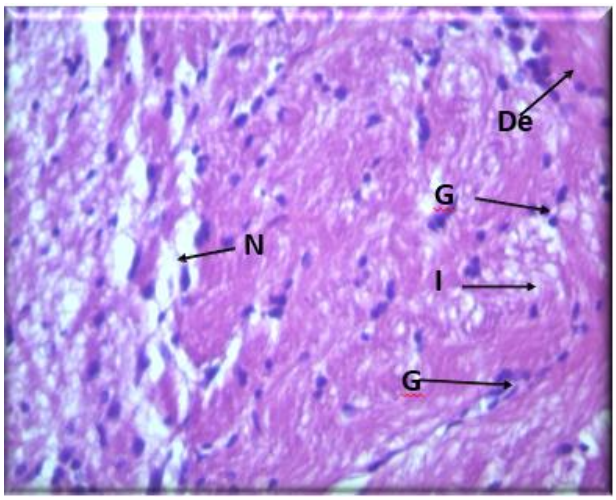

Figure 10: 21day, shows deeply eosinophilic nerve fiber (De), giant cell (G) and necrosis (N).(H&E, 400 x)

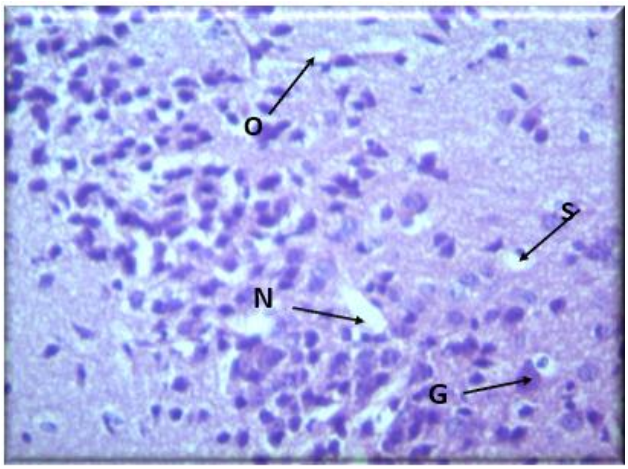

Figure 11: 21-day, showing occluded vesicle (O), swelling cell (Sc), giant cell (G) and necrosis (N). (H&E, 400 x)

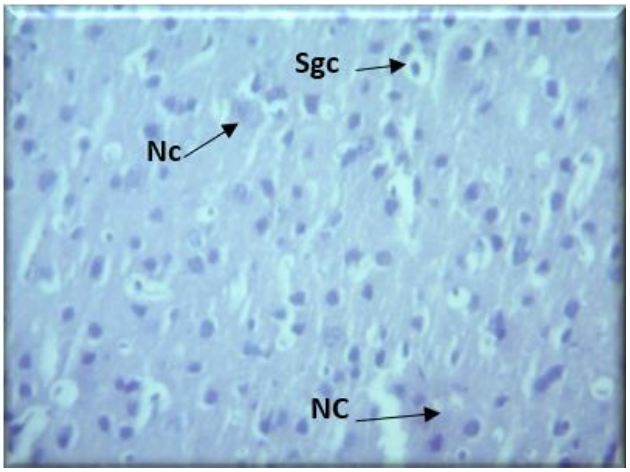

Figure 12: 30-day, showing swelling glial cell (Sgc), and necrosis (Nc). (H&E, 400 x)

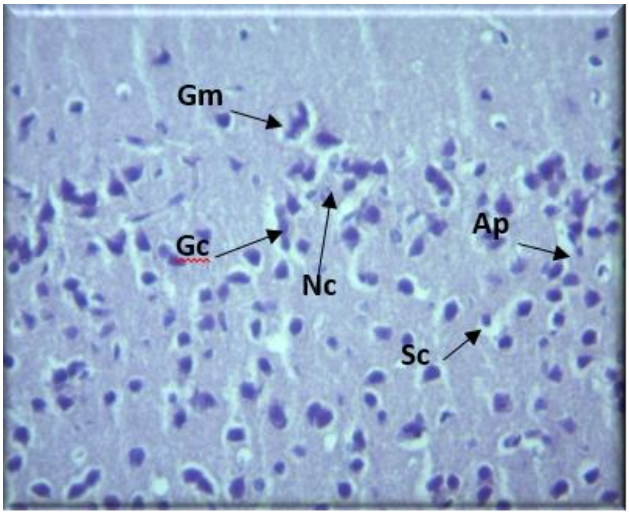

Figure 13: 30-day, cerebrum, showing giant macrophage (Gm), apoptosis (Ap), swelling cell (Sc), glial coalesces (Gc) and necrosis (Nc). (H&E, 400 x)

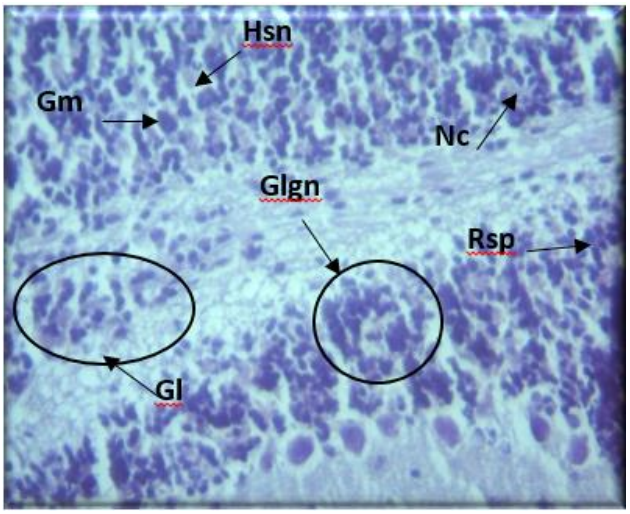

Figure 14: 30-day, cerebellum, showing giant macrophage (Gm), coalesces of granular nuclei (Glgn) horseshoe shape nucleus (Hsn), swelling cell (Sc), rosette shape pattern (Rsp) and necrosis (Nc). (H&E, 400 x)

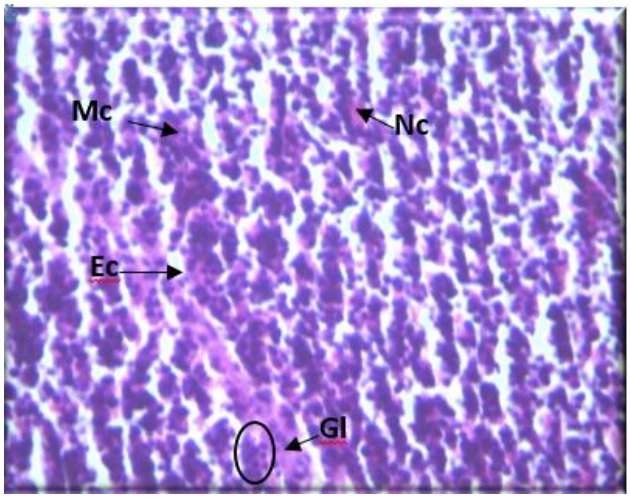

Figure 15: 60day, shows gliosis (Gl), macrophage (Mc), eosinophilic cell (Ec) and necrosis (Nc). (H&E, 400 x)

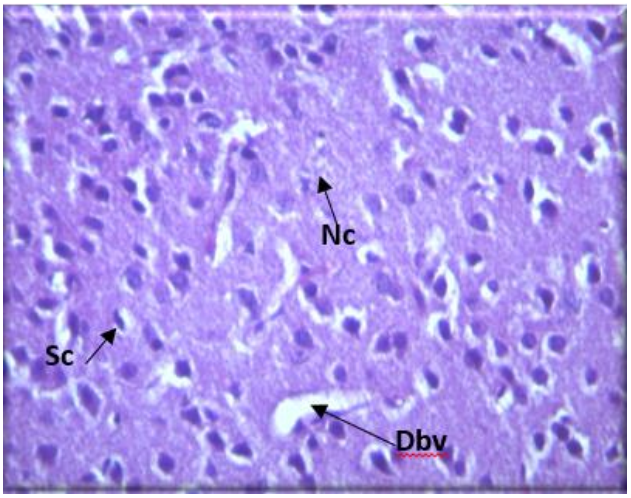

Figure 16: 60day, cerebrum, shows dialation in blood vessel (Dbv), swelling cell (Sc) and necrosis (Nc). (H&E, 400 x)

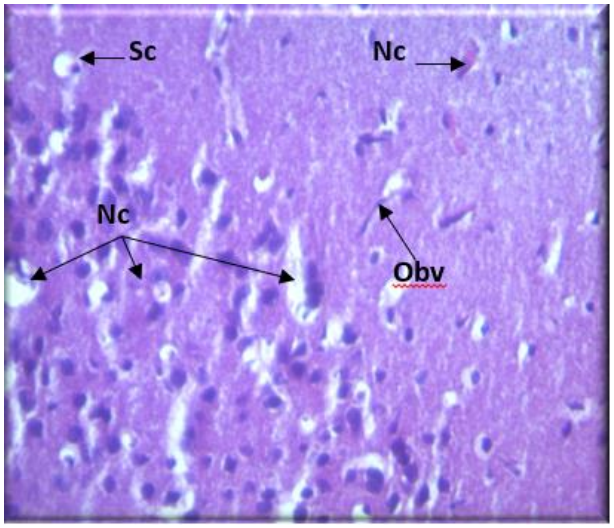

Figure 17: 60-day, showing occluded blood vessel (Obv), swelling cell (Sc) and necrosis (Nc). (H&E, 400 x)

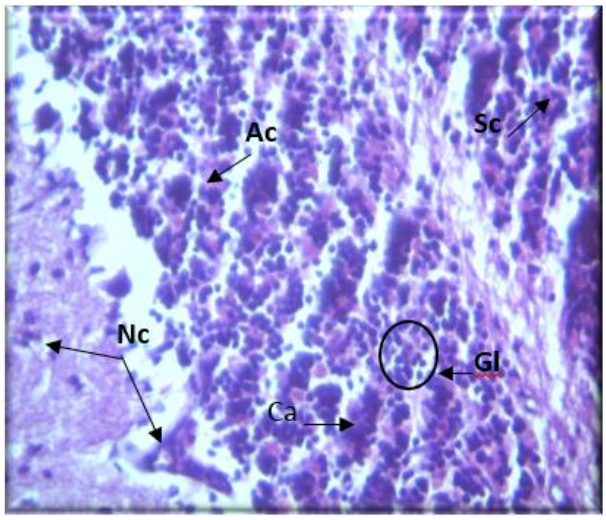

Figure 18: 60-day, showing acidophilic cytoplasm (Ac), swelling cell (Sc), gliosis (Gl) coalesces (Ca) and necrosis (Nc). (H&E, 400 x)

Conclusion

This study provides evidence that oral consumption of MSG at acceptable daily doses may promote injuries in brain of infant mice. Severe damage occurred in the brain cell including; megakaryocyte, necrosis, blood capillary stenosis, fraction of nerve fiber and blood capillary collapsing, eosinophil cell, medullary necrosis and necrosis, eosinophilic nerve fiber, horseshoe shape nucleus, rosette shape pattern, acidophilic cytoplasm, swelling cell, gliosis, coalesces and occluded blood vessel.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

References

[1]. Xiong, J.S., Branigan, D. and Li, M., *Int. J. Clin. Exp. Med.,* 2009, **2**:329 [Google Scholar], [Publisher]

[2]. Niaz K., Elizabeta Z., Jonathan S., *EXCLI J.,* 2018, **17**:273 [Google Scholar], [Publisher]

[3]. Kurihara K., *Am. J. Clin. Nutri.,* 2009, **90**:719 [Crossref], [Google Scholar], [Publisher]

[4]. Bera T.K., Sanjit K.K., Prem K.Y., Prithwiraj M., Shankar Y., Bishal J., *World J. Pharm. Sci.,* 2017, **5**:139 [Google Scholar], [Publisher]

[5]. Tawfik M.S., Al-Badr N., *Food Nutr. Sci.,* 2012, **3**:651 [Crossref], [Google Scholar], [Publisher]

[6]. Geh R.S., Beiser A., Ren C., Patterson R., Grammar L.C., Ditto A.M., Harris K.E., *J. Nutr.,* 2001, **130**:1038 [Crossref], [Google Scholar], [Publisher]

[7]. Nicholas J., *J. Nutr. Health,* 2001, **58**:365 [Crossref], [Google Scholar], [Publisher]

[8]. Nakagawa T., Ukai K., Ohyama T., Gomita Y., Okamura H., *Exp. Anim*., 2000, **49**:239 [Crossref], [Google Scholar], [Publisher]

[9]. Pelaez B., *Arch Neurol.,* 2001 **14**:165 [Google Scholar], [Publisher]

[10].Rivera M.C., *J. Neurosci. Res.,* 2004, **76**:678 [Crossref], [Google Scholar], [Publisher]

[11]. Tala'a A.A., Hussin A.M., OJVR, 2019, **23**:414 [Google Scholar]

[12].Ibrahim M.N., Abdullah S.A.H., *Tikrit J. Pure Sci.,* 2017, **22**:49 [Google Scholar], [Publisher]

[13]. Ganesan K., Sukalingam K., Balamurali K., Radziah S., Alaudeen S., Ponnusamy K., Ariffin I.A., Gani S.B., *J. Pharm. Chem. Biol. Sci.*, 2013, **3**:1257 [PDF], [Google Scholar]

[14]. Hinoi E., Takeda T., Ueshima T., Tsuchihashi Y., Yoneda Y., *Eur. J. Biochem.,* 2004, **271**:1 [Crossref], [Google Scholar], [Publisher]

[15].Gill S.S., Mueller R.W., McGuire P.F., Refined O.M., *Toxicol. Pathol*., 2000, **28**:277 [Crossref], [Google Scholar], [Publisher]

[16]. Carlton S.M., *Curr. Opin. Pharmacol.,* 2001, **1**:52 [Crossref], [Google Scholar], [Publisher]

[17].Park J.H., Choi T.S., *Lab. Anim*., 2016, **50**:94 [Crossref], [Google Scholar], [Publisher]

[18]. Husarova V., Ostatnikova D., *JMED Res.,* 2013, 2013 [Crossref], [Google Scholar], [Publisher]

[19]. Stephen A.U., Ushie A.M., Wilson O.A., *Environ. Dis.,* 2021, **6**:17 [Crossref], [Google Scholar], [Publisher]

[20].El-Shobaki F.A., Mahmoud M., Attia A., Refaat O., El-Haggar E., *Der Pharma Chemica,* 2016, **8**:44 [PDF], [Google Scholar]

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