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Original Research Article

Evaluating melatonin's neuroprotective effect on the cerebellar cortex of adult male albino rats following monosodium glutamate exposure: a comprehensive biochemical, histopathological and immunohistochemical study

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Abstract

Purpose: *To investigate neurotoxic effects of monosodium glutamate (MSG) on rat cerebellar cortices and evaluate potential neuroprotective action of melatonin.*
Methods: *Adult male albino rats (40) were randomly categorized into four groups of ten rats each comprising Group I (control), Group II (melatonin-treated, 6 mg/kg/day via intraperitoneal injection), Group III (MSG-treated, 4 mg/kg/day IP) and Group IV (co-treated with MSG and melatonin). After 14 days of injections, rats were sacrificed and blood samples were collected to determine serum glucose, total cholesterol (TC) and triglyceride (TG) levels. Cerebellar tissues were processed for histological examination, and homogenized specimens were used to estimate malondialdehyde (MDA), glutathione (GSH), tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) levels.*
Results: *Administration of MSG significantly ($p < 0.05$) increased serum glucose, TC, TG, MDA, TNF-α and IL-1β levels while significantly decreasing GSH level ($p < 0.05$). Histological analysis revealed that MSG exerted degenerative effects, including the presence of pyknotic Purkinje cells, with strong positive reactions for caspase-3 and glial fibrillary acidic protein as well as weak reactions for β-cell lymphoma-2 and synaptophysin. However, melatonin administration improved these parameters.*
Conclusion: *Monosodium glutamate induces neuronal injury in rat cerebellar cortex, but melatonin demonstrates a protective effect against these degenerative changes. There is a need for additional studies to understand the mechanisms of MSG and melatonin effects.*

Keywords: *Monosodium glutamate, Melatonin, Cerebellum, GFAP, Neuroprotective*

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INTRODUCTION

Monosodium glutamate (MSG), also known as China salt, is a crystalline compound made up of glutamic acid (78 %) and sodium (22 %). It is extensively used in canned soups, meats and vegetables to enhance taste, but its safe daily intake level remains undefined [1]. Consumption of MSG has been linked to various pathological conditions, including neurotoxicity, hepatotoxicity, reproductive and endocrine dysfunction and metabolic disorders. When dissolved in water, MSG is converted to glutamate, a neurotransmitter that enhances brain activity [2]. Glutamate interacts with N-methyl-D-aspartate (NMDA) receptors and affects brain functions such as memory, cognition and learning. However, excessive dietary glutamate levels may damage brain cells [3]. Moreover, extended exposure to elevated glutamate levels results in oxidative stress and subsequent damage to brain cells. Several neurodegenerative disorders, including Alzheimer's, Parkinson's and multiple sclerosis, are correlated with pathological increases in brain glutamate levels [3].

Cerebellum plays a crucial role in coordinating sensory inputs and motor responses for skeletal muscle control. Structurally, cerebellum includes deep nuclei and cortex and is made up of three layers, namely, the superficial molecular layer, middle Purkinje cells and deep granular layers housing various neurons and fibers. Glutamate is the primary excitatory neurotransmitter in the cerebellum and is released by parallel fibers in the cerebellar cortex to facilitate the transmission of nerve signals within its circuit. Melatonin, predominantly secreted by pineal gland and produced by sources such as blood lymphocytes, gastrointestinal tract and retina, modulates circadian rhythms and aging processes and influences endocrine and immune functions [4]. Melatonin is known for its anti-aging, anti-oxidant, anti-inflammatory and anti-apoptotic properties and offers protection against damage from free radicals [5]. Moreover, melatonin penetrates the blood–brain barrier, which highlights its therapeutic potential in the neurological field [6].

This study aimed to assess the biochemical, histopathological and immunohistochemical effects of intraperitoneal (IP) injection of MSG on rat cerebellar cortices. It further aims to examine the potential neuroprotective effects of concurrent melatonin administration. The findings are expected to enhance understanding of the pathogenesis of neurodegenerative conditions and offer potential therapeutic strategies.

EXPERIMENTAL

Animals

This study employed 40 adult male Albino rats weighing 200 – 230 g, sourced from the Animal House of the Laboratory Animal Centre in Cairo, Egypt. These rats were housed in sanitized plastic cages within a well-ventilated room, with free access to standard laboratory water and food *ad libitum*.

Environmental conditions were strictly controlled, room temperature was regulated in the range of 24 – 30 ºC and a strict 12-hour light-dark cycle was maintained. Before commencing the procedure, rats were acclimatized for two weeks.

Ethical approval

The study was authorized by the Institutional Animal Care and Use Committee at Assiut University, Cairo, Egypt (reference no. 0222961) and was conducted by following the guidelines in the care and use of laboratory animals [7]. The study implemented measures to minimize animal utilization and discomfort. Procedures were executed expediently and with precision to mitigate stress-induced alterations.

Tested compounds

Monosodium glutamate, with a purity level of up to 99 %, was procured from DØBELLA Food and Beverage in Egypt in a crystalline form. For administration, it was dissolved in distilled water, with one gram of MSG per milliliter of distilled water [8]. Melatonin (5 mg), purchased from Puritan's Pride in the European Union, was administered in pill form.

Design

Rats were categorized randomly into four groups (10 rats in each group) as follows: Group I served as control and was injected with distilled water (0.1 mL) via the IP route for 14 days [9]. Rats in Group II (Melatonin-treated) were injected IP with melatonin dissolved in 2.5 % ethanol at 6 mg/kg/day for 14 days.

Also, rats in Group III (MSG-treated) were injected IP with MSG after being dissolved in distilled water at a dose of 4 mg/kg/day for 14 days [9]. Lastly, rats in Group IV (MSG + Melatonin-treated) were injected IP with a combination of MSG (4 mg/kg/day) and melatonin (6 mg/kg/day) for 14 days.

Blood sampling

Blood samples were collected and sera were obtained and stored for biochemical analyses of serum glucose, total cholesterol (TC) and triglyceride (TG) using standard kits (Biodiagnostic, Giza, Egypt) according to the manufacturer's instructions.

Cerebellar collection

The body weights of rats were recorded at the commencement and conclusion of the experiment. After 14 days of IP administration, all animals were euthanized with a high dose of sodium thiopental (120 mg/kg, IP) to facilitate subsequent histological and biochemical analyses. Cerebella were perfused with 100 mL of heparinized saline via a cardiac catheter and subsequently excised and bisected. One-half was fixed in a 10 % formalin solution and processed into paraffin sections for histopathological and immunohistochemical studies. The other half was homogenized in a 20 % w/v cold potassium phosphate buffer (0.01 M, pH 7.4) and centrifuged at 5,000 rpm for 10 min at 4 °C. The resultant supernatant was used for the comprehensive assessment of malondialdehyde (MDA), glutathione (GSH), tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) levels.

Histological studies

Cerebella were dissected and fixed in 10 % formalin and then dehydrated in a graded alcohol series and cleaned with xylene. The tissues were embedded in paraffin and 4 µm-thick sections were made. After deparaffinization, sections were mounted on glass slides and stained with hematoxylin and eosin (H & E) according to the manufacturer's guidelines [10]. Stained sections from various groups were examined using an Olympus CX41 light microscope (Tokyo, Japan) to determine the mean thickness of granular cell layer, mean number of Purkinje cells and mean thickness of the molecular cell layer in 10 non-overlapping fields at ×400 magnification.

Immunohistochemical studies

Cerebellar cortex sections (4 µm thickness) were mounted on positively charged glass slides and subjected to deparaffinization, rehydration and incubation with trypsin, followed by washing with phosphate-buffered saline. Non-specific binding of endogenous peroxidase was inhibited using a 0.1 % hydrogen peroxide solution and Ultra V Block. The sections were then incubated overnight in a humid chamber with antibodies against glial fibrillary acidic protein (GFAP; Catalogue no. FNab03426, Wuhan Fine Biotech, Co., China, dilution 1:200), caspase-3 (Catalogue no. A11953, Abclonal Technology, dilution 1:200), B-cell lymphoma 2 (Bcl-2; Catalogue no. A16776, Abclonal Technology, dilution 1:200) and synaptophysin (Catalogue no. A6344, Abclonal Technology, dilution 1:100). Mean area fractions (%) of GFAP, caspase-3, Bcl-2 and synaptophysin-positive cells were quantified in different groups using ImageJ 22 software across ten non-overlapping fields at ×400 magnification with an Olympus CX41 light microscope (Tokyo, Japan).

Statistical analysis

All analyses were performed using the GraphPad Prism software (version 9). Mean and standard error of the mean were calculated for each group. A one-way analysis of variance (ANOVA) was used to determine significant differences among groups, which was followed by Tukey–Kramer post-hoc testing. The results were deemed statistically significant when *p*-values were < 0.05.

RESULTS

Rat body and brain weights

At the beginning of the experiment, no significant differences in rat body weights were observed among groups. However, at the end of the study, MSG-treated group exhibited a significant ($p < 0.05$) increase in body weight compared with control and melatonin groups. Moreover, no significant ($p > 0.05$) differences in brain weights were noted among groups (Figure 1).

Biochemical analysis

Evaluation of lipid profile and serum glucose levels

Rats exposed to MSG exhibited significantly ($p < 0.05$) higher TC and glucose levels than control, melatonin and MSG + melatonin groups. Moreover, MSG-exposed rats showed significantly ($p < 0.05$) increased TG levels compared with controls (Figure 2).

Evaluation of anti-oxidant and oxidative stress biomarkers

Rats exposed to MSG displayed significantly ($p < 0.05$) higher cerebellar tissue levels of MDA and a statistically significant ($p < 0.05$) reduction in GSH content in MSG group than in control,

melatonin and MSG + melatonin-treated groups (Figure 3).

Evaluation of proinflammatory cytokines

Rats exposed to MSG exhibited significantly higher cerebellar tissue levels of TNF-α and IL-1β than control, melatonin and MSG + melatonin groups (Figure 4).

Histological and histopathological results

Cerebellar sections from control and melatonin groups displayed folia comprising a white matter core and a mantle of cerebellar cortex, separated by deep fissures. The cerebellar cortex contains three distinct layers: the superficial molecular layer, the middle Purkinje layer and deep granular layer. Molecular layer exhibited tiny stellate and basket cells along with nerve fibers, while Purkinje layer had a single row of large pyriform cells with vesicular nuclei. On the contrary, the granular layer was characterized by clusters of small, darkly stained, spherical cell nuclei tightly packed together (Figure 5 and Figure 6).

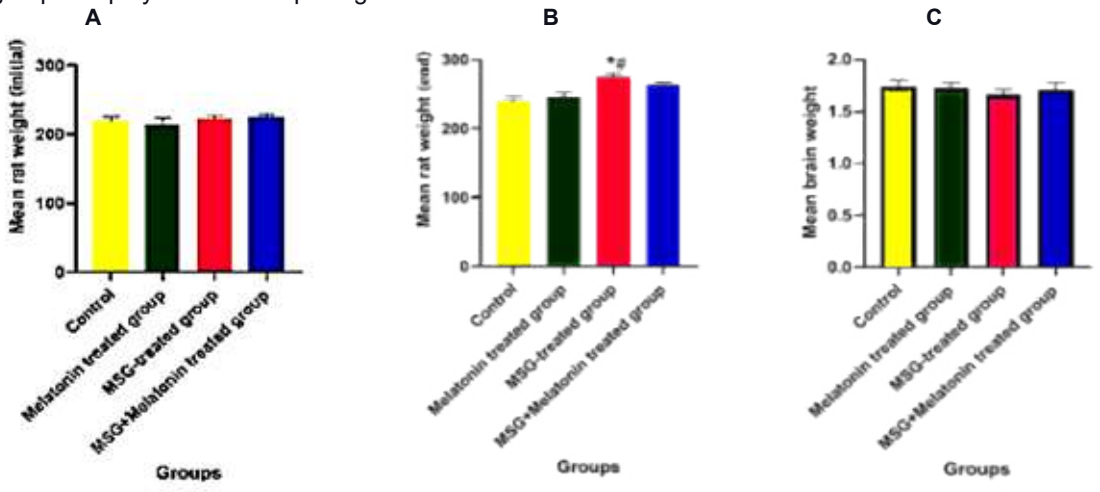

Figure 1: Comparison of mean rat weights at (A) start and (B) end of experiment, as well as (C) mean brain weights at end. **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, $p < 0.05$

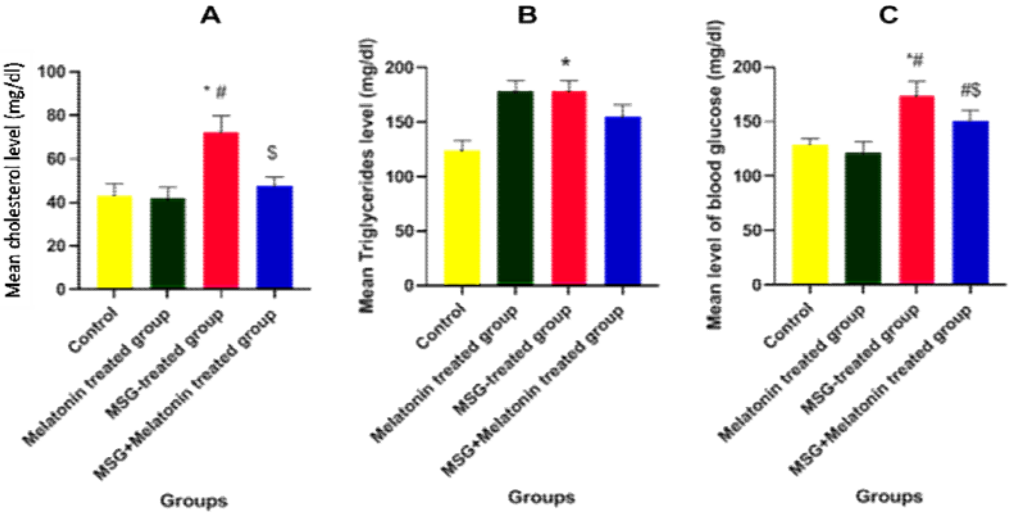

Figure 2: Evaluation of (A) mean cholesterol, (B) triglyceride and (C) blood glucose levels. **Key:** *, # and $ indicate significant differences from the control, melatonin, and MSG groups, respectively, at $p < 0.05$

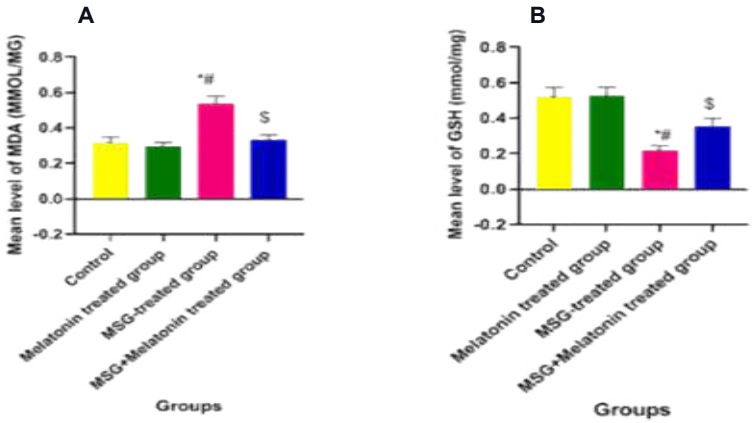

Figure 3: Evaluation of (A) mean malondialdehyde (MDA) and (B) glutathione (GSH) levels. **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

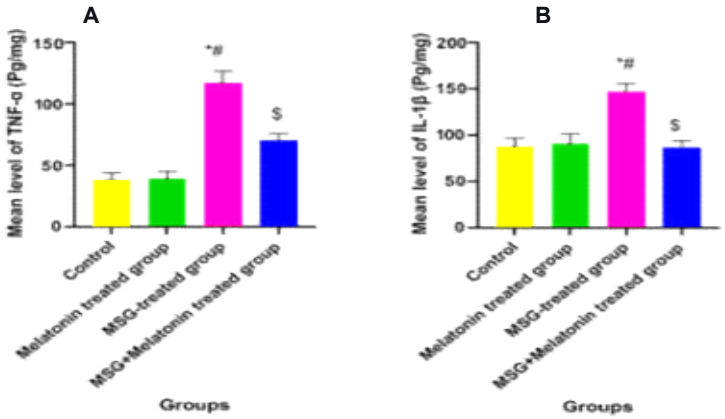

Figure 4: Determination of (A) TNF-α and (B) IL-1β mean. *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

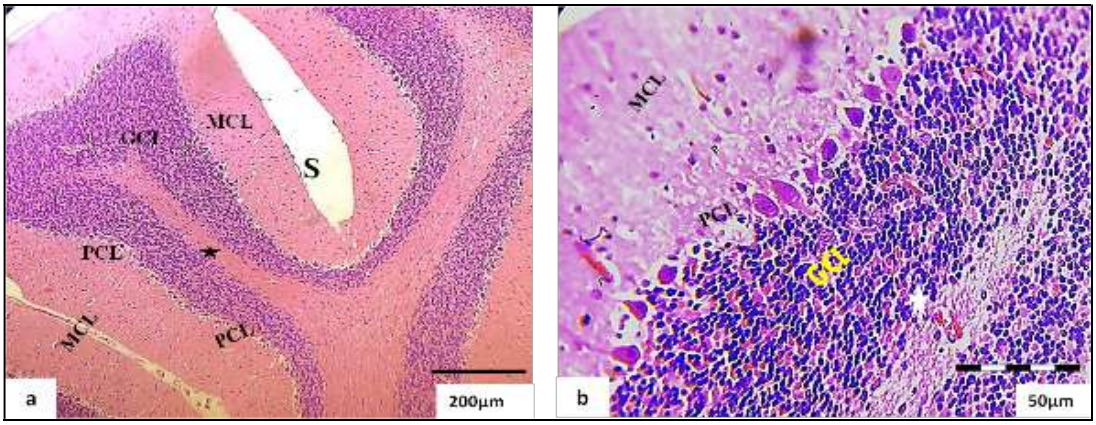

Figure 5: Photomicrographs of cerebellar cortex from control group: a) The molecular cell layer (MCL) and Purkinje cell layer (PCL) are arranged in a single row, with a densely packed granular cell layer (GCL) and a well-defined core of white matter (asterisk). Cerebellar folia are separated by deep, long fissures (S). b) MCL and PCL feature large flask-shaped cells arranged in a single row, while GCL comprises small spherical granular cells. (H&E ×100, scale bar = 200 µm; ×400, scale bar = 50 µm)

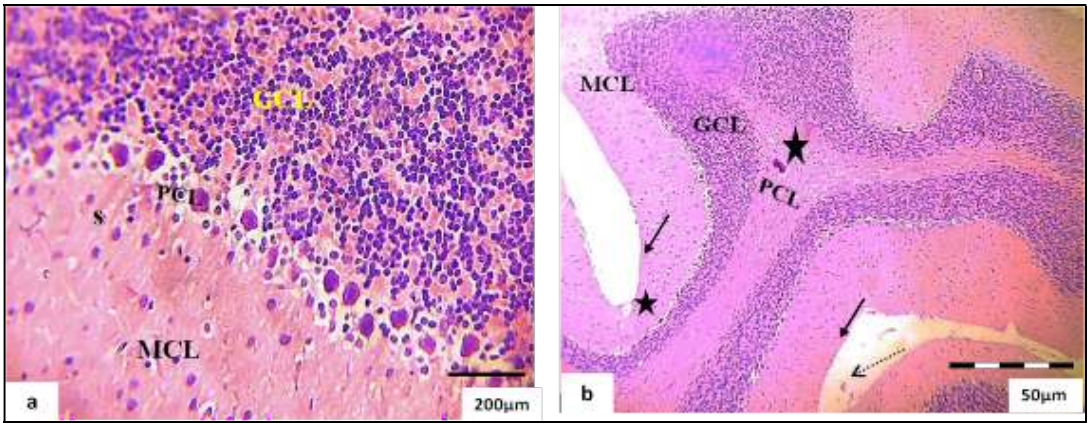

Figure 6: Photomicrographs of cerebellar cortices from melatonin group: a) Molecular cell layer (MCL) and Purkinje cell layer (PCL) are arranged in a single row, with a densely packed granular cell layer (GCL) and a distinct core of white matter (asterisk). Cerebellar folia are separated by deep, long sulci (S). b) MCL consists primarily of nerve fibers (asterisks), with a few basket cells and stellate cells (black arrows) and blood capillaries (dotted arrows). PCL features large flask-shaped cells with vesicular nuclei arranged in a single row, while GCL contains small, rounded, granular cells. (H&E ×100, scale bar = 200 µm; ×400, scale bar = 50 µm)

The MSG-exposed group showed a considerable decrease in thickness of all cerebellar cortical layers (Figure 7 a) and prominent histological changes, especially in Purkinje cell layer, marked by the loss of some Purkinje cells, which resulted in empty spaces. Certain Purkinje cells appeared pyknotic, while others lost their characteristic pyriform shape (Figure 7 b). However, melatonin administration improved cerebellar cortical layers, which regained a nearly normal appearance. Nonetheless, some Purkinje cells remained degenerated and pyknotic (Figures 8 a and b). Quantitative analysis of mean thickness of molecular and granular cell layers and number of Purkinje cells revealed that MSG-exposed rats had significantly reduced values than control and melatonin groups (all $p < 0.0001$). In MSG + melatonin group, co-administration of melatonin led to a significant increase in these parameters compared with MSG alone group ($p < 0.0001$; Figure 9).

Immunohistochemical results

Immunohistochemical analysis of control and melatonin groups using anti-GFAP antibodies indicated the presence of thin, regular glial fibers and a small number of GFAP-positive, star-shaped astrocytes (Figures 10 a and b). In contrast, MSG group displayed increased cytoplasmic GFAP expression in large astrocytes, with several thick and elongated processes (Figure 10 c). Conversely, MSG + melatonin group possessed thinner glial processes, with a considerable reduction in quantity and intensity of GFAP-positive astrocytes (Figure 10 d). Quantitative analysis of mean area fraction of GFAP immunoreactivity revealed a significant increase in MSG group compared with control and melatonin groups ($p < 0.001$). Although the MSG + melatonin group also showed elevated GFAP expression compared with control and melatonin groups, it exhibited a significant decrease relative to MSG group (all $p < 0.001$; Figure 10 e).

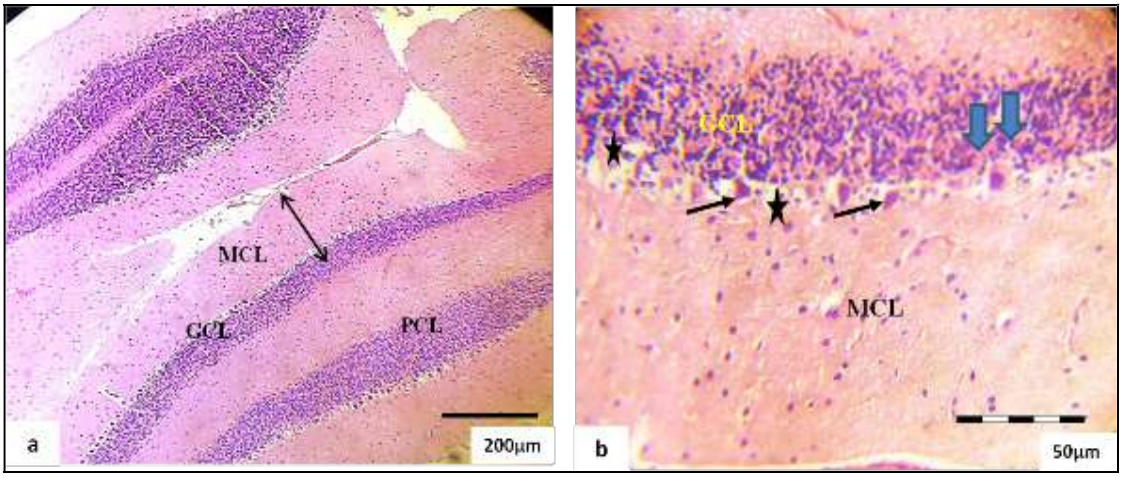

Figure 7: Photomicrographs of cerebellar cortex from the MSG-exposed group: a) Double-headed arrow indicates a noticeable decrease in thickness of cortical layers. b) Molecular cell layer (MCL) shows a reduced number of Purkinje cells, which appear pyknotic and are arranged in a single row (arrows), with areas of Purkinje cell loss (thick arrows) and vacuolation around Purkinje cells (asterisk). Granular cell layer (GCL) is densely packed with small, rounded granular cells. (H & E ×100, scale bar = 200 µm; ×400, scale bar = 50 µm)

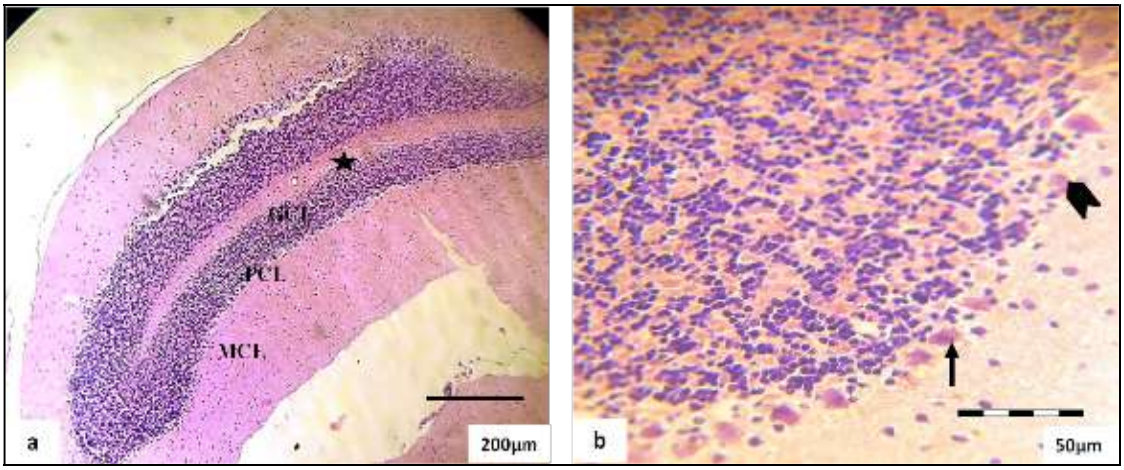

Figure 8: Photomicrographs of cerebellar cortices from MSG + melatonin treated group, displaying nearly typical histological architecture: a) Molecular cell layer (MCL), Purkinje cell layer (PCL) arranged in a single row and a densely packed granular cell layer (GCL) with a distinct core of white matter (asterisk). b) MCL shows a Purkinje cell layer containing some degenerated and pyknotic cells (arrowhead) alongside normal cells (arrow). The GCL is densely packed with small, rounded granular cells. (H&E ×100, scale bar = 200 µm; ×400, scale bar = 50 µm)

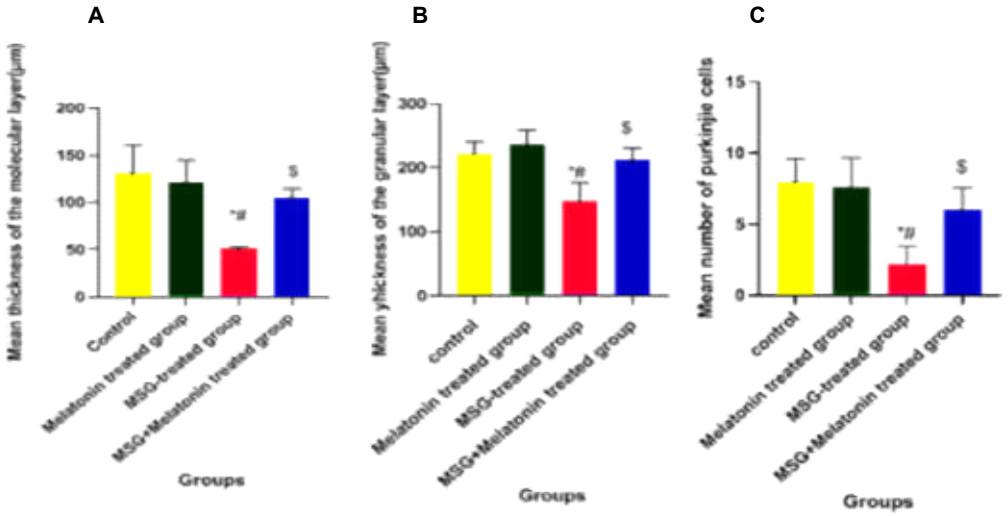

Figure 9: Chart showing (A) mean thickness of molecular layer, (B) mean thickness of granular cell layer, and (C) mean number of Purkinje cells in rat cerebellar cortex at ×400 magnification. **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

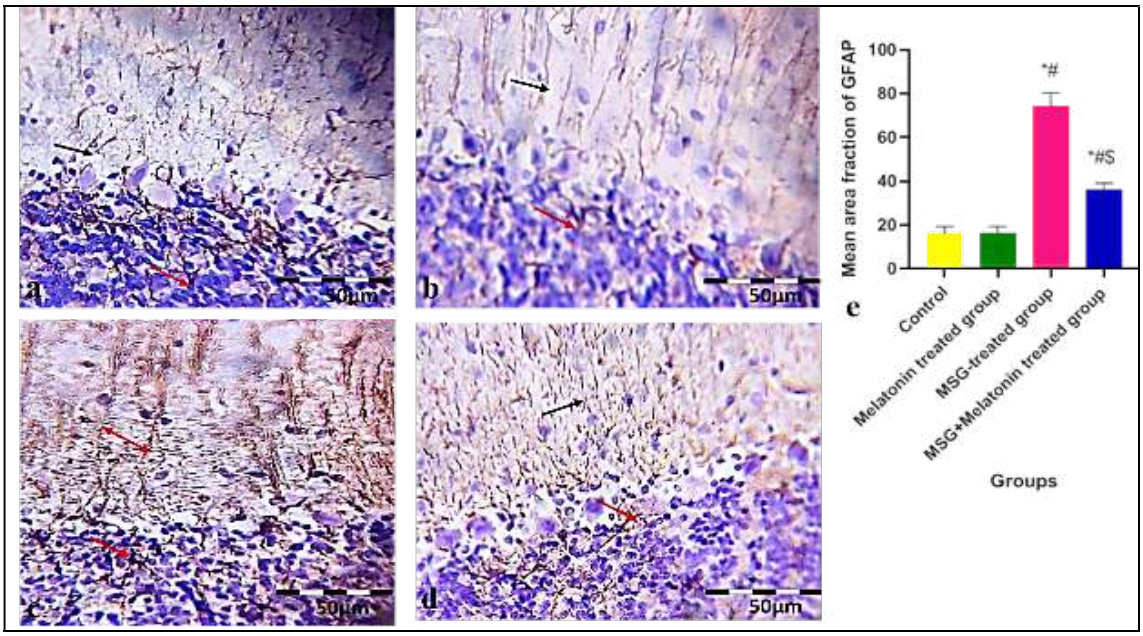

Figure 10: Representative photomicrographs of GFAP immunostained sections of rat cerebellar cortex. Control (a) and melatonin (b) groups show positive immunoreactivity in small-sized astrocytes (red arrows) and their thin processes (black arrows). The MSG group (c) exhibits intense GFAP cytoplasmic immunoreactivity in large astrocytes (red arrow), along with an increase in the number and thickness of their processes (double-headed arrow). The MSG + melatonin group (d) shows positive GFAP immunoreactivity in small astrocytes (red arrow) with a decrease in the thickness of their processes (black arrow). **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

Immunohistochemical results for cleaved caspase-3

Immunohistochemical analysis using anti-cleaved caspase-3 antibodies revealed negative-to-weak caspase-3 immunoreactivity in cerebellar cortex layers (molecular, Purkinje and granular) in control and melatonin groups (Figure 11 a and b). The MSG group demonstrated significantly increased positive cytoplasmic immunoreactivity in granular and Purkinje cell layers (Figure 11 c). Conversely, in MSG + melatonin group, moderate positive cytoplasmic immunoreactivity was observed in certain granular and Purkinje cells (Figure 11 d). Quantitative analysis of mean area fraction of

anti-cleaved caspase-3 immunoexpression showed a significant increase in MSG group compared with control and melatonin groups ($p < 0.001$). Also, MSG + melatonin group exhibited a significant increase compared with control and melatonin groups. Nevertheless, expression was significantly lower compared with MSG group (all $p < 0.001$; Figure 11 e).

Immunohistochemical results for Bcl-2 and synaptophysin

Immunohistochemical analysis using Bcl-2 antibodies revealed enhanced cytoplasmic staining in control and melatonin groups across all cerebellar cortex layers (Figures 12 a and b). While MSG group displayed a considerable reduction in Bcl-2 staining (Figure 12 c), MSG + melatonin group showed moderate positive immunoreactivity in certain granular, Purkinje and molecular cells (Figure 12 d). For synaptophysin, control and melatonin groups exhibited improved staining in all layers (Figures 13 a and b), whereas MSG group had significantly reduced levels (Figure 13 c). The MSG + melatonin group showed moderate positivity in some cells (Figure 13 d). Quantitative analysis indicated a significant decrease in Bcl-2 and synaptophysin expression in MSG group compared with controls ($p < 0.001$), with MSG + melatonin group showing significant increases over MSG group ($p < 0.001$; Figure 12 e and Figure 13 e).

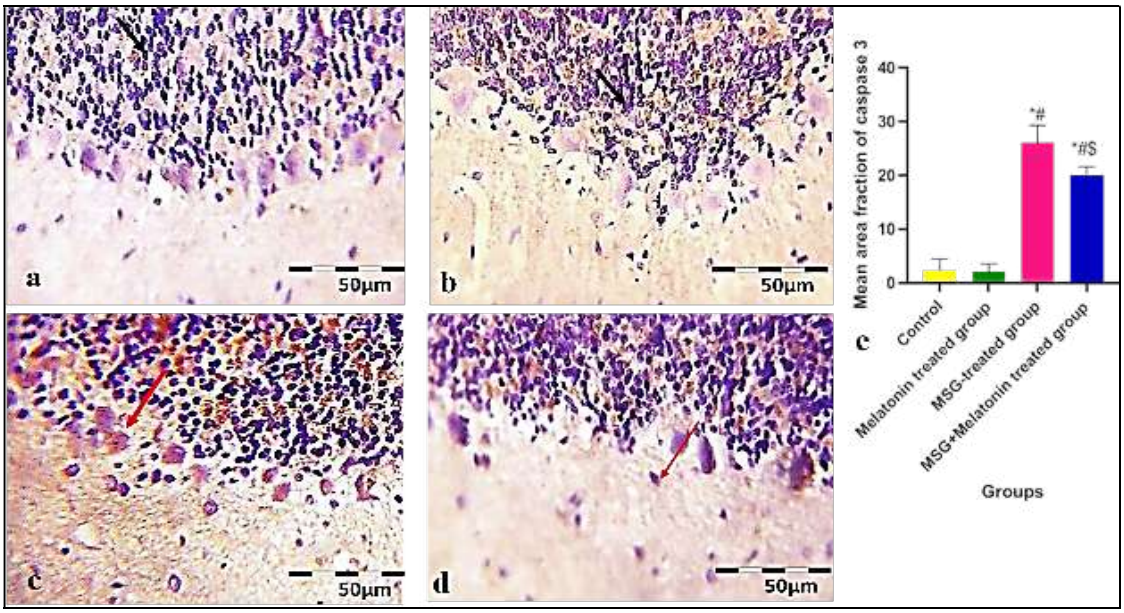

Figure 11: Photomicrographs of caspase-3 immunostained sections of rat cerebellar cortex: The control (a) and melatonin (b) groups show negative to weak caspase immunoreactivity. The MSG group (c) exhibits positive cytoplasmic immunoreactivity in cells of granular layer (black arrow) and some Purkinje cells (red arrow). The MSG + melatonin group (d) demonstrates moderate positive cytoplasmic immunoreactivity in some Purkinje cells (H&E ×400). (e) Quantitative analysis of mean area fraction (%) of caspase-3 positive cells at ×400). **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

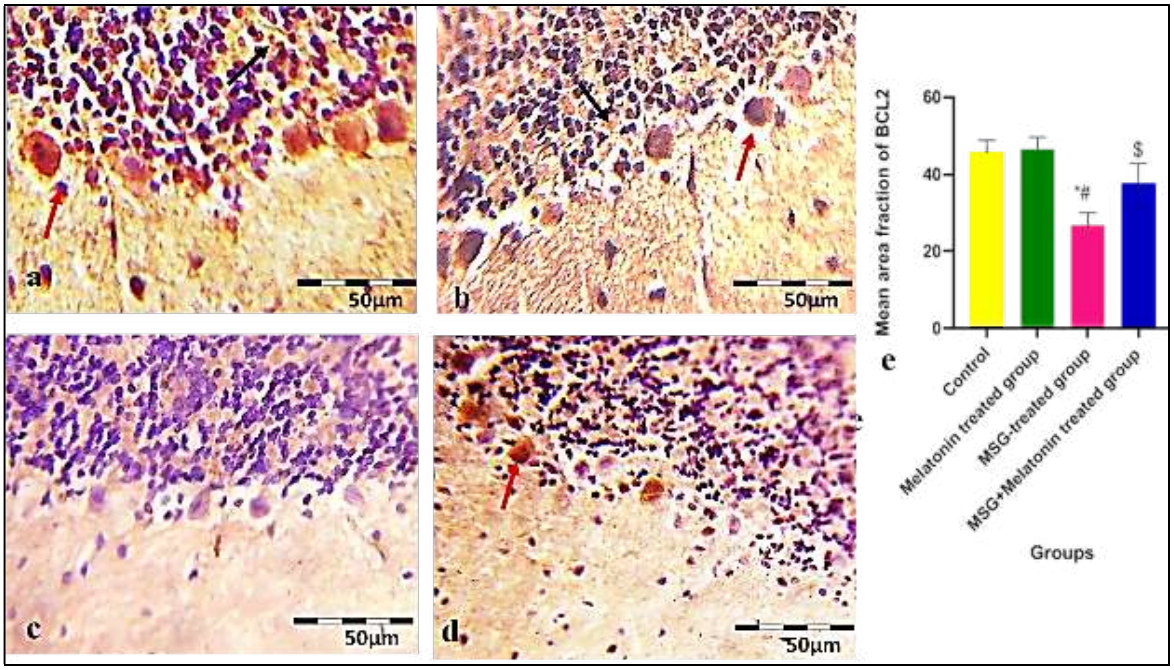

Figure 12: Representative photomicrographs of Bcl-2 immunostained sections of rat cerebellar cortex. Control (a) and melatonin (b) groups show positive immunoreaction for Bcl-2 in granular layer cells (black arrow) and some Purkinje cells (red arrow). MSG group (c) exhibits negative to weak positive cytoplasmic immunoreactivity for Bcl-2 (arrows). MSG + melatonin group (d) shows increased Bcl-2 cytoplasmic immunoreactivity (H&E ×400). (e) Quantitative analysis of mean area fraction (%) of Bcl-2 positive cells at ×400. **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

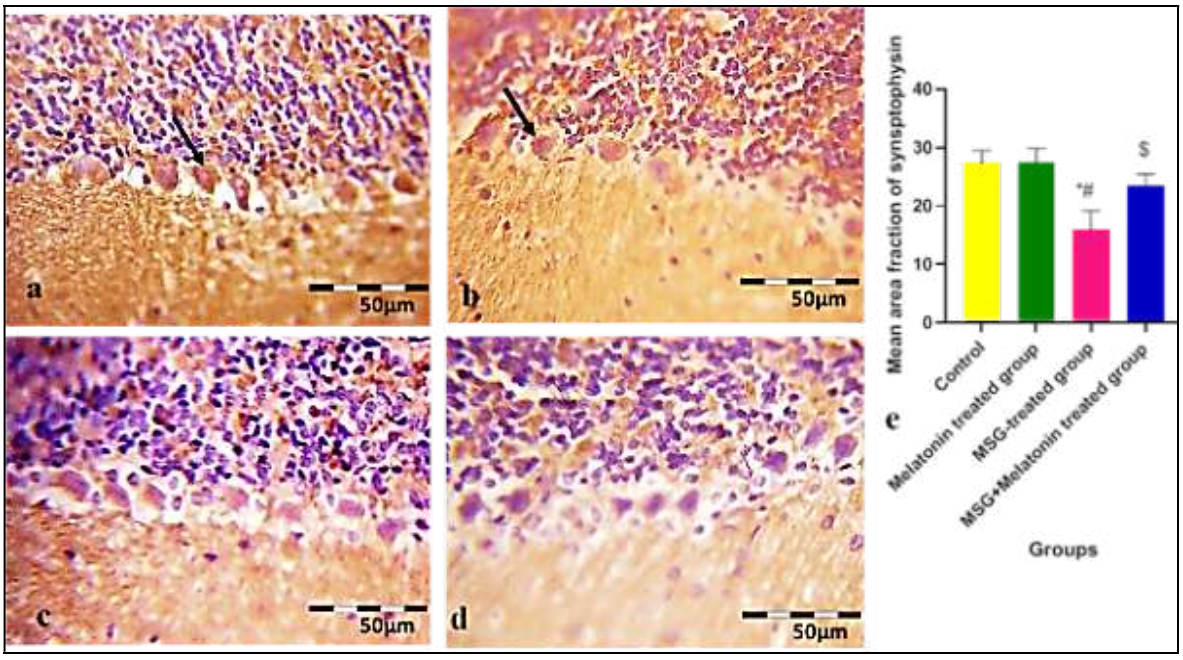

Figure 13: Representative photomicrographs of synaptophysin immunostained sections of rat cerebellar cortex. Control (a) and melatonin (b) groups show positive immunoreaction for synaptophysin in Purkinje cells (red arrow). MSG group (c) exhibits negative to weak positive cytoplasmic immunoreactivity for synaptophysin (arrows). MSG + melatonin group (d) shows increased synaptophysin cytoplasmic immunoreactivity (H&E ×400). (e) Quantitative analysis of mean area fraction (%) of synaptophysin positive cells at ×400. **Key:** *, # and $ indicate significant differences from control, melatonin, and MSG groups, respectively, at $p < 0.05$

DISCUSSION

Monosodium glutamate, a white crystalline powder and sodium salt of amino acid L-glutamic acid is commonly added to both processed and unprocessed foods. However, this addition raises concerns regarding elevated glutamate levels from MSG consumption [11]. The compound is converted to sodium and L-glutamate, an excitatory neurotransmitter that induces N-methyl-D-aspartate (NMDA) receptors. Excessive glutamate synthesis results in excitotoxicity, a key factor in neurodegenerative diseases such as Alzheimer's disease and multiple sclerosis [12].

In this study, MSG was administered IP because oral glutamate administration is associated with considerable metabolic issues in the bloodstream [13]. Rats exposed to MSG demonstrated a statistically significant increase in mean body weight after 2 weeks compared with control group receiving distilled water. This finding aligns with a previous study that observed increased body weight in rats after MSG administration [14]. Moreover, MSG intake has been associated with obesity in both animal models and humans, which could be ascribed to its stimulatory effect on appetite centers and disrupting the hypothalamic signaling axis of leptin action [15].

The group treated with MSG exhibited a significant metabolic increase in serum glucose, TG and TC levels compared with controls. These findings agree with a study that reported elevated TC levels in MSG-exposed rats. These changes were attributed to the mobilization of free fatty acids from the adipose tissue [16].

Monosodium glutamate adversely affects hepatic lipoprotein metabolism by activating coenzyme A reductase, a key enzyme in cholesterol synthesis, increasing TG and TC levels in serum. Increased serum glucose levels could result from enhanced hepatic gluconeogenesis and decreased tissue sensitivity to insulin [17]. Conversely, co-administration of melatonin with MSG significantly reduced TC and glucose levels in serum. High TC levels in serum have been linked to increased production of reactive oxygen species, contributing to neurodegenerative disorders. In this study, MSG administration for two weeks considerably increased MDA levels and reduced GSH in rat cerebellar tissues, which suggests that MSG induces oxidative stress, resulting in lipid peroxidation and diminished anti-oxidant defense. A decrease in GSH levels could be attributed to its role in neutralizing excess free radicals and hydrogen peroxide. Neuroglial cells use a cystine/glutamate antiporter, and hence, elevated extracellular glutamate limits cystine availability for GSH synthesis.

After 14 days of MSG exposure, levels of TNF-α and IL-1β were significantly increased but were restored after melatonin administration. Excessive glutamate exposure has been shown to increase levels of pro-inflammatory cytokines, such as TNF-α, at the transcriptional level in the brain and intestines [18]. Monosodium glutamate has been reported to stimulate oxidative stress and inflammatory responses, leading to brain dysfunction. An animal study established a correlation between MSG intake and cognitive impairment, as the brain is particularly vulnerable to oxidative damage owing to its high metabolic activity and unique lipid composition [18].

This study observed that IP administration of MSG for two weeks caused neurodegenerative changes in cerebellar cortex. Light microscopic examination indicated spacing, shrinkage and cellular loss in Purkinje cell layer, along with a statistically significant reduction in number of Purkinje cells compared with controls, which agrees with previous reports [19]. Structural alterations noted in cerebellar cortex of MSG-treated rats could be ascribed to glutamate accumulation, which over-activates glutamate receptors and results in excessive intracellular calcium levels and subsequent neuronal damage. In addition, MSG adversely affects neuronal membranes, which results in sustained depolarization.

Chronic MSG administration has been shown to disrupt cortical cytoarchitecture, which suggests a potential neurotoxic effect [20]. In contrast, MSG + melatonin group exhibited significant improvements across all layers of cerebellar cortex, especially in Purkinje cell layer. Cells maintained a more normal appearance, with fewer necrotic features and an increased cell count compared with MSG group. This study observed strong GFAP expression in cerebellar cortices of MSG-treated rats, signifying astrocyte activation and reactive gliosis, which are characteristic of neurodegeneration. An increase in number and size of astrocytes was observed in MSG group, which agrees with a previous study [19].

Conversely, co-administration of melatonin reduced number and size of astrocytes, which implies that melatonin mitigates astrogliosis and down-regulates pro-inflammatory cytokine expression.

Rats exposed to MSG demonstrated significantly elevated caspase-3 activity, a crucial mediator of

apoptosis, which could be attributed to MSG-induced oxidative stress. Melatonin administration significantly reduced caspase-3 immunoreactivity, which emphasizes its neuroprotective properties. Bcl-2 expression was significantly decreased in MSG group but increased in MSG + melatonin group, which establishes the role of melatonin in preventing apoptosis.

Decreased synaptophysin expression in MSG-exposed group could have resulted from inhibited protein biosynthesis, while positive synaptophysin staining was observed in MSG + melatonin group. These findings imply that sustained high levels of glutamic acid led to neurotoxicity. However, melatonin may alleviate oxidative stress, as evidenced by reduced MDA levels and increased GSH levels in cerebellar tissue. Therefore, MSG content in food products should be carefully regulated.

Limitations of this study

Use of a singular dosage of monosodium glutamate (MSG; 4 mg/kg/day) and melatonin (6 mg/kg/day) restricted evaluation of dose-dependent impacts. Future studies should consider varying doses to offer a more thorough understanding. Moreover, histological evaluations on fixed tissue samples may not fully depict dynamic alterations associated with neurodegeneration or neuroprotection.

CONCLUSION

The findings from this study indicate that IP administration of MSG significantly alters body weight, lipid profile, MDA, GSH, TNF-α and IL-1β levels as well as histopathology and immunohistochemistry of cerebellar cortex, indicating oxidative damage. Conversely, melatonin suppresses body weight gain induced by MSG and offers protection against and restores MSG-induced cerebellar cortex injury by inhibiting oxidative damage. There is a need for additional studies to understand the mechanisms of MSG and melatonin effects.

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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