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3 authors, including:

Mohamed Abdelhamid
National Research Center, Egypt

Samah Khalil
Benha University

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THE DELETERIOUS EFFECTS OF MOBILE PHONE RADIATION (900 MHZ) ON BEHAVIOR PROFILE OF MICE: THE EFFECT OF ALTERNATIVE THERAPY IN NEUROPROTECTION

Mohamed F. Abdelhameed [1], Nabil Ashry Ibrahim Elnahas[2] and Samah Ahmed Mohammed Khalil[2*.]
[1] Department of Pharmacology, Medical Division, National Research Centre, Dokki, 12622, Giza, Egypt
[2] Department of Architecture, Shoubra Faculty of Engineering, Benah University
Corresponding author: Samah Ahmed Mohammed Khalil
E-Mail: samah.khalil@live.com, samah.khalil@feng.bu.edu.eg

ABSTRACT

The cognition is a very critical process even for animals, enables them to recognize each other, their owner, feeding space requirement and help them in the vital behaviors as mate choice, foraging, on the other hand, the surrounded mobile phone radiation (MPR)and its increased application even for animal farms management and feeding can radiate inside the farms leading to the threaten animals' health especially vital organs so this will reflect negatively on the farm income. Our study aimed to evaluate the effect of some famous historical architectural shapes on cognitive state and spatial memory impairment induced by effects of the mobile phone radiation, (900 MHz) for 8 weeks and possibility to create healthy and high efficient architectural farm designs. Thirty-two (32) Swiss Albino male mice were randomly divided into 8 groups (n = 8), they housed in 4 cages with various shapes. Group I & II housed in a traditional cage, Group I served as a control which did not subject to a mobile phone but groups (II-IV) are exposed to mobile phone radiations. Our result revealed that these changes in architectural shapes as housing in pyramid shape can induce positive effects on cognitive state and spatial memory impairment induced by MPR, it also retains the antioxidant capacity total antioxidant (TAC), malondialdehyde (MDA) and nitric oxide (NO), reduced glutathione (GSH), catalase (CAT) plus it alleviate the neurodegenerative effect of MPR on hippocampus and cortex in histopathology, it concluded that housing under pyramidal architectural shape may have a positive effect on cognition and spatial memory impairment induced by the hazard of electromagnetic waves and this study can be useful for architects and advised to be used in the creation of healthy architecture buildings for either human or animal farms.
Keywords: Architectural shapes, spatial memory, cognitive booster, Mice, Mobile phone radiation.

Introduction

The recent decades changed the peoples' concepts about veterinary services Therefore, it became the responsibility of the veterinary service providers to take care not only of animal disease, but also animal welfare (Pirrone *et al*., 2019). Animal welfare is a "multidimensional state, comprising good health, comfort, expression of behavior, and so on" (Botreau *et al*., 2007). The expression of animal behavior is closely related to its cognitive state where it plays an important role in mate choice, foraging, and many other behaviors(Shettleworth, 2010)**.** Cognition is a mental action or process that enables both animals or humans to react with others and translate thought, experience, and the senses to acquiring knowledge and understanding(Shettleworth, 2001). The cognitive process is highly affected by stressors (Sandi, 2004) that may cause cognitive impairment which in turn negatively affects animal productivity(Curtis and Stricklin, 1991).

Many studies reported that mobile phone radiation (MPR) is a highly biological stressor that negatively affect all livestock's health by an oxidative stress (Nazıroğlu *et al*., 2013), these surrounding electromagnetic radiation (EMR) that compulsorily produced from using of technologies in all fields especially its application and networking even in farm management, subjecting our environment to huge source of EMR which in turn affect human health(Adebayo *et al*., 2014), domestic animals (Ebrahimi *et al*., 2018; Everaert and Bauwens, 2007; Hässig *et al*., 2014), (Wenzel *et al*., 2002) noted the abnormal behavior in cattle such as lying, pasture and ruminating behaviors as daily behavior profile, also there are the other notable effects recorded in poultry as embryo mortality especially between 9th and 12thdays of incubation (Batellier *et al*., 2008), chicks myocardium pathological changes, DNA damage and increased mortality(Ye *et al*., 2016), these impacted effect also included the wild livestock in form of animal populations decline and deterioration (Balmori, 2009). The biological analyses to these effects explained various effects include anxiety-like behaviors and oxidative stress(Shehu *et al*., 2016) so a number of studies have concerned to EMR hazards, reported that EMR affects mainly the brain causing neural damage (Hussein *et al*., 2016), disturbed permeability of blood-brain barrier BBB (Sirav and Seyhan, 2016; Sırav and Seyhan, 2016), affected memory performance (Brzozek *et al*., 2018), Increasing incidence of the carcinogenic potentiality especially the heart and brain tumors (Falcioni *et al*., 2018), disturbed urogenital function (Türedi *et al*., 2017), decreasing the reproductive capacity of both males (Gautam *et al*., 2019) and females (Shahin *et al*., 2017), induced hormonal disturbance(Asl *et* *al*., 2019; Stephen *et al*., 2019) and liver damage (Moradpour *et al*., 2020).

All these radiation-related potential symptoms and other insults including decreased body weight (Qi *et al*., 2015), as well as male and female re-productivity plus fetal health(Fragopoulou *et al*., 2010; Kesari and Behari, 2012; La Vignera *et al*., 2012; Nazıroğlu *et al*., 2013)which in turn affect farm income and productivity so that the search in prevention and protection against this problem become a national goal, to have led veterinarians to cooperate with architects presenting a novel solution to reduce these negative effects, recently use the term of "alternative therapy" for reliable solve uncontrolled problems by replacing the undesirable effects of chemical drugs in form of "shape power" or architectural spaces geometry(Rao, 1997; Shemesh *et al*., 2017).

The thinking in the use of the most permanent factor (architectural space) where all livestock spends most of all times within architectural interior spaces, surrounded by radiation sources, this idea also derived from what called Sick Building Syndrome (Redlich *et al*., 1997), the architect in turn, concerned in any change possibility of the shape, proportions, or angles of the space to create a safe and healthy space and study its effective role in the solve of some problems(Elbaiuomy *et al*., 2019).

The architectural space benefits were reported in some previous studies including its healthy role in healing potentiality of incisional wounds within a wooden pyramid cages (Rao, 1997) improvement of conscious level (Elbaiuomy *et al*., 2019), also housing of animals in pyramid counteracts neuroendocrine and oxidative stress(Bhat *et al*., 2007).The energy of pyramidal shapes might improve some biological parameters reflecting in tumor growth retardation (Nahed *et al*., 2010), improvement of activity and better relaxation (MI *et al*., 2013), reduced also prenatal stress (Murthy *et al*., 2013) not healthy role only but also another agriculture role as long time food and milk preservation(Abdelsamie *et al*., 2014; Gopinath *et al*., 2008). The slight modification of architectural space as bio-geometrical spaces induce improvement of the immunity status of animals and the support of self-healing (health improvement) by protective energy balance. (Sharaf *et al*., 2014)

Therefore, the present study concerned to investigate this novel trends to assess the ability of the number of famous historical architectural Pyramidal shape cage and gold ratio rectangle base forms to improve memory and cognition function and protect against deleterious effects produced by mobile phone (900 MHz) using biochemical parameters, oxidative parameters, histopathological and object recognition test and y-maze in adult male mice.

Material and Methods

Animals

Healthy adult male Swiss Albino mice weighing 24 ± 2 g, were purchased from the Animal Breeding House of the National Research Centre (NRC), Dokki, Giza, Egypt. Animals were housed in clean acrylic cages in the laboratory animal room (23 ± 2 °C), on standard pellet diet and tap water *ad-libitum*, a minimum relative humidity of 40 %, and a 12 h dark/light cycle. Mice were allowed to acclimate to laboratory conditions for one week.

Ethics statement

The experimental work on mice was performed with the approval of the Animal Care & Experimental Committee, National Research Centre, Giza, Egypt, and the international guidelines for the care and use of laboratory animals of the National Institutes of Health (NIH No. 85:23 revised 1985).

The cage design

All the cages used in our study had nearly the same volume and were made from acrylic material. The color of the acrylic material was white to neutralize or to avoid the influence of the colors in our paradigm. Two of the shapes (G I & II) were identical and looked like the traditional laboratory cages with a volume of 22040 cm³ (40cm*29cm*19cm). While the other two architectural forms selected were known to contain special capabilities across different ages, civilizations, and cultures for health. The names and shapes of cages were depicted in Fig. 1.

Animal grouping and experimental protocol

The experimental study aimed to assess the effect of the exposure to MPR on the oxidative stress parameters and behavioral observations of male mice, and to evaluate the effect of the geometric shapes of architectural voids in terms of shape, angle, and proportions on cognitive state and spatial memory. Thirty-two (32) adult male mice were randomly divided into 4 groups (8 mice/cage). The groups were housed in cages with various architectural shapes as follows (Fig. 1):

- G I: served as a negative control, mice housed in a traditional cage at a separate room with the same conditions, but without MPR (ordinary shape cage - MPR).

  However, the mice in the experimental groups (G II- G IV) were exposed to a mobile phone as a source of Radiofrequency Electromagnetic Radiation (900 MHz) from an active GSM (Global system for mobile communications)for 24 hours per day for eight weeks with a daily 50 missed calls. The missed call duration equaled 45 seconds while the intervals between the two successive missed calls equaled 15 seconds. Besides, the missed calls were set on a silent non-vibrating mode to avoid disturbance or stress.

- G II: positive control, mice housed in a traditional cage but exposed to MPR (ordinary shape cage + MPR).
- G III: mice housed in Pyramidal shape cage (with the same proportions of the great pyramids) (Pyramidal shape cage + MPR).
- G IV: mice housed in a cage with a gold ratio rectangle base (gold ratio rectangle base + MPR).

  The cages were placed at axes corresponding to the four coordinate directions, with an average distance of at least one and a half meters from each other as shown in Fig. 2. Besides, the two phones were placed in the middle of the shapes at equal distances (1.38 m) from all shapes as represented in Fig. 2.

The radiation source

The radiation source used in our study came from two commercial identical mobile phones (ALCATEL 1066G, GSM 900 MHz). Thus, instead of using models of digital mobile phone signals with constant parameters (frequency, power), we used real GSM signals (Vodafone, Egypt) which are never constant since there are continuous changes in their intensity.

Electromagnetic field (EMF) measurements- dosimetry

The electrical field produced by the mobile phone was monitored by the Smart Field meter, EMC Test Design RPF-04, LLC test lab, National Physical Laboratory, UK, having a band of 900 MHz and the reading was 29-32 V/m within the various cages, depending on the sound level or distance variation. The shape places were changed periodically every three days to ensure equal exposure to radiation. The specific absorption rate (SAR) for the whole body of the exposed mice can be approximately calculated according to the equation:

$$\mathbf{SAR} = \sigma E^2 / \rho$$

Where E is the root mean square value of the electrical field measured within the cages, σ is the mean electrical conductivity of the tissues, and ρ is the mass density [21, 22]. The SAR is a parameter widely used by most authors to compare the absorbed energy in different biological tissues. The SAR values ranging from 0.65 to 0.84 W/kg were calculated using the above equation by applying the measured electrical field density 29–33 V/m, σ = 0.8 S/m and mass density ρ = 1040 kg/m3.

Behavioral study

Object recognition test

The test apparatus was designed as described by (Ennaceur and Delacour, 1988) Three days before testing, each rat was allowed to explore the apparatus for 2 min, while on the testing day, a session of two trials, 2-min each was allowed. In experiment 1 (EX-1), two identical objects were placed in two opposite corners of the apparatus. A rat was placed in the apparatus and was left to explore these two identical objects. After EX-1, the rat was placed back in its home cage and an inter-trial interval of 1 h was given. Subsequently, experiment 2 (EX-2) was performed. In EX-2, a novel object (N) replaced one of the objects that were presented in EX-1, then rats were exposed again to two different objects: the familiar (F) and the novel one (N). Exploration was defined as follows: directing the nose toward the object at a distance of no more than 2 cm and/or touching the object with the nose. From this measure, a series of variables were then calculated: the total time spent in exploring the two identical objects in T1, and that spent in exploring the two different objects, F and N in T2. The discrimination between F and N in T2 was measured by comparing the time spent in exploring the F with that spent in exploring the N is the discrimination index (DI) and represents the difference in exploration time expressed as a proportion of the total time spent exploring the two objects in T2. DI was then calculated; DI = (N - F)/N + F.

Y-maze spatial working memory assessment

Although it is basic in its design is assessed according to the protocol of (Kraeuter *et al*., 2019), the Y-maze can be used to assess short-term memory in mice. For example, spontaneous alternation, which measures spatial working memory, this requires interaction across several different regions of the brain, such as the hippocampus and prefrontal cortex (Sarnyai *et al*., 2000; Swonger and Rech, 1972). Testing is carried out using a Y-shaped maze with three light-colored, opaque arms orientated at 120° angles from each other. The mouse is introduced at a particular position on the maze and allowed to explore the arms freely over a short time period. An entry occurs when all four limbs of the mouse are within an arm.

An alternation is defined as consecutive entries into all three arms. Then, the number of arm entries and alternations are recorded to calculate the percentage of alternation behavior.

It can be assessed by allowing mice to explore all three arms of the maze freely A mouse with a good working memory will remember the arms of the maze that it has already visited and will show a tendency to enter a less recently visited arm, A high percentage is taken as good working memory as this indicates that the mouse has recalled which arms it has already visited. The percent (%) alternation was calculated using the following formula:

%Alternation=(Number of Alternations/[Total number of arm entries−2])×100

Y-maze spatial reference memory assessment

It can be tested by placing the test mouse into the Y-maze with one arm of the maze closed off during training (Training session). This arm is designated as the novel arm. After a certain time interval (Inter-trial interval, ITI), during which the mouse is removed from the maze, the mouse is placed back into the maze with the blockage removed (Testing session). The length of the ITI will strongly influence the performance of the animal in this task, as longer ITIs require higher memory load. Commonly used mouse strains usually perform well in this task with ITI up to 4 h. Some investigators use 24 h ITI to tap into long-term spatial memory. The mouse should remember based on distal spatial cues and their relation to its present location in the Y-maze which arm it has not explored previously and should visit this novel arm more frequently than the other arms.

It can be assessed by counting the number of entries into the novel arm then compared to the entries into the other arms to assess the degree of spatial memory. A mouse that shows no preference for any of the arms during the Testing session is an indication of an impaired spatial memory, which may indicate impaired functioning of the hippocampus.

Blood collection and tissue preparation

Blood samples were collected from the retro-orbital venous plexus of mice under light ether anesthesia and collected in clean test tubes, allowed to clot, then centrifuged for 10 minutes at 3000 r.p.m. Serum samples were separated and stored into Eppendorf tubes at - 20 °C to be used for biochemical analysis. After collection of blood samples, mice were sacrificed by cervical dislocation and their whole brains were immediately removed. Brains of mice were kept at (-80 °C) for the determination of its MDA, GSH, NO, and CAT content.

Antioxidant parameters of brain tissue homogenate.

GSH was estimated in brain tissue homogenate tissue according to the method described by (Beutler, 1963). CAT activity was evaluated according to the methods of (Aebi, 1984). MDA was estimated as a marker for lipid peroxidation according to the method suggested by (Ohkawa *et al*., 1979). NO was evaluated by the method described by (Montgomery and Dymock, 1961). All the above biochemical parameters were assayed by using local commercial kits purchased from Biodiagnostic, local distributor, Giza, Egypt.

For the histopathological study, small pieces of brains were excised, fixed in 10% neutral buffered formalin solution, prepared in paraffin blocks, cut into sections of 5-6 µm in thickness, and stained with haematoxylin-eosin(Shapiro *et al*., 1983).

Statistical analysis

In the present study, all results were expressed as mean ± standard error of the mean. Data analysis was achieved by a one-way analysis of variance (ANOVA) followed by Tukey comparison test using software program graph pad prism 7. Difference was set at P<0.005.

Result

Exposure of male mice to GSM-900-MHz mobile phones radio-frequency electromagnetic radiation resulted in several biological effects. Except for anxiety, there were no obvious signs of toxicity observed in experimental animals.

Effect of architectural space on MPR-affected memory using the object recognition test

Within EX-1 and EX-2, no differences in total exploration time were seen among the different groups. In contrast with the particular exploratory activity exhibited in EX-1, a decrease of it in EX-2 was observed in all rats except those housed in ordinary cages and subjected to MPR that represent as GII (Fig. 3.a). Positive group mice explored the novel and familiar objects almost similarly. Exploration time in EX-2 showed that mice housed in a pyramid cage (GIII) were the best group explored the new object significantly more than the familiar one as shown in Fig. 3.b. The mice housed in pyramid cage (GIV) exhibited some improvement in exploration time in EX-2 where they explored also the new object significantly more than the familiar one as shown in (Fig. 3.c). That reflected to DI that demonstrated a failure of those housed in an ordinary cage and subjected to MPR (GII) to discriminate between a familiar and a novel object in the second part of the test session, while all other rats significantly discriminated the novel object better than the familiar one (Fig. 3.c).

Line crossing that explained in (fig. 3.d). Showed that rat housed in ordinary cages and subjected to MPR (GII) significantly increased line crossing as a result of hesitation with increased motor activity, however, those housed in pyramidal shape cages did less line crossing as mice not subjected to MPR did.

Y-Maze for of Spatial Working and Reference Memory in Mice assessment

a- Spontaneous alternation

Within Experiment number-1 (spontaneous alternation) (Fig. 4. A,B,C) Which measures spatial working memory, there are no significant differences in the percentage of the alternation behavior were seen among the different groups.

Spatial reference memory

Within Experiment number-2 (Spatial reference memory) (Fig. 4.D), mice housed in ordinary cages or gold ratio rectangle base cage and subjected to MPR (GII) have a poor spatial memory in comparison to the negative control group (GI) that revealed by a significant decrease in discrimination between novel and other arms.

While mice housed in pyramidal cages(GIII) have a good spatial memoryin comparison to the positive control group (GII) where mice could significantly differentiate between arms achieved the maximum entries in the novel one.

Oxidant and antioxidant capacity

Measurement of lipid peroxidation

Mice exposure to mobile phone radiation in G II group resulted in a significant increase (p <0.001) lipid peroxide (Fig. 3C) as evidenced by the increase in MDA levels in brain tissue compared to G I. However, housing mice in pyramidal shape cage significantly mitigated these changes (Table 1).

Antioxidant capacity (GSH, NO, and catalase)

Determination of reduced glutathione

GSH works in reduced form as one of the most important antioxidant in the body,compared to the control group, a significant decrease (P<0.001) was found in the GSH content (Fig. 3B), in brain tissue of mice housed in an ordinary cage and subjected to mobile radiation G II (Fig. 3A). Whereas, the use of cages of pyramidal architectural shapes improved the declined levels in the brain tissue of exposed mice (Table 1).

Determination of enzyme activities (CAT)

Catalase aimed to antioxidant state in the tested tissue, there is a significant decrease (P<0.001) was found in enzyme activities (CAT) in (GII) mice in comparison to the control group (GI). Whereas, the housing in pyramidal architectural shapes (GIII) improved the lowered CAT enzymatic activities in the brain tissue of exposed mice (Table 1).

Determination of nitric oxide assay (NO)

Our result revealed a significant decrease (P<0.001) in brain tissue homogenate (NO) of (GII) mice compared to the control group (GI). These assay explained improved the lowered NO in the brain tissue of those housed in pyramidal architectural shapes (GIII)(Table 1).

Histopathological examination

The histopathological finding explained the effect of mobile phone radiation (900 MHz) on mice hippocampal and cortical brain regions. (Fig. 5, 6, 7)

Discussion

The main purpose of our study was to investigate the ability of the housing in several famous historical architectural shapes (pyramidalshape group and gold ratio rectangle base.) to boost cognition state and enhance spatial memory impairment induced by exposure effects of RFR produced by mobile phone radiation (900 MHz) on mice brain.

Pre-clinical study of mouse models has been beneficial in the examination of the underlying pathophysiology of dementia and cognitive impairment, as well as in the inspection of novel trends as apart of cognition impairment solutions (Webster *et al*., 2014).

The choice of ORT and Y-maze in assessment of mice cognitive state and spatial memory returned to that exploring activity of novel objects is an important behavior of mice to react with the surrounding environment (Leger *et al.*, 2013). This behavior is related to the innate curiosity of rodents to reconnoiter previously unvisited areas (Lalonde, 2002) also previous literature choose Y-maze as a behavioral test to assessment equine prospective memory (Murphy, 2009) also this apparatus used to determine feeding space requirements of the dairy cow (Rioja-Lang *et al.*, 2012).

There is a tight link between neural degeneration of some brain region and behavioral impairment (Greene-Schloesser *et al.*, 2013) and its expression and assessment must be in a controlled environment (Krakauer *et al.*, 2017). This relation is more prominent especially between the memory of both humans/rodents and their hippocampus which responsible for memory formation (Eichenbaum *et al.*, 1992). So any hippocampal damage affects negatively not only memory but also may include very critical disorders starting with prolonged stress (Garrido, 2011).These critical actions may be induced by the actions of oxidative stress and depletion of GSH that resulted in inflammation and end with hippocampal apoptosis and neuronal damage (Méndez-Armenta *et al.*, 2014) which is highly related to heavy o_2 consumption of neurons (Friedman, 2011). For hippocampal importance, the scientist interested with hippocampal function improvement factors especially physical ones (Chieffi *et al.*, 2017; Garthe *et al.*, 2016).

Our results presented in this study provide a poor cognitive state and spatial memory impairment of mice that housed in ordinary cages and exposed to mobile phone radiation (900 MHz) that is previously discussed by(Narayanan *et al.*, 2015)who suggested that mobile phone altered spatial cognition. These results are also supported by the potentiality of mobile phone radiation (900 MHz) to induce oxidative damage ROS in mice brain of G II. This oxidative damage was cleared by increased lipid peroxidation, attrition of enzymatic antioxidant (CAT) and non-enzymatic antioxidant (GSH) levels, and lowering nitric oxide content that in turn extensively degenerate neuronal structure in selective areas of hippocampus (CA1, CA3) and the cerebral cortex (Saikhedkar *et al.*, 2014).

The present observations are indicative of oxidative stress parameters which are in line with many previous studies that implies a correlation between exposure to EMR and formation of reactive oxygen species either in rabbit (Irmak *et al.*, 2002), rat (Dasdag *et al.*, 2009; Hussein *et al.*, 2016) and this oxidative stress is highly reflected to behavioral deficits (Narayanan *et al.*, 2014).

However, the housing of mice in the selected cage with different geometrical shapes attenuated such perturbations supposing the effect of angles distribution that may disturb or disperse the radiated waves by the effect of pyramidal power “as a supernatural source of power” as suggested with a pyramidal shape, it supposed that this pyramidal power made its action by the emission of waves that have specific wavelength and frequency which mitigate the hazard effect of MPR(Nagy, 2007; Nahed *et al.*, 2010). Where those mice seemed good cognitive state and spatial memory by testing with ORT or Y-maze and matching also with mitigating of oxidative stress of MPR supported by retaining of antioxidant capacity for mice housed especially in cages designed as pyramidal shape (GIII), showed decreased MDA, improving of enzymatic antioxidant (CAT) and non-enzymatic antioxidant (GSH) levels and increasing nitric oxide content what is the same line with(Bhat *et al.*, 2003) who reported that pyramidal environment alleviates oxidative stress and improved antioxidant defense in rat, that in turn reflected to alternated areas of apparent intactpyramidal neuronal structure in selective areas of hippocampus (CA1, CA3) and showed moderate protective records with alternated areas of apparent intact neurons the cerebral cortex that previously reported by (Murthy *et al.*, 2013) who also explained the hippocampal improvement for mice that subjected to prenatal stress but housed under the pyramidal shape.

The change in the shape is meaning the change in both power or energy emitted from this surrounding shapes and angles distribution that may disperse the electromagnetic radiation (Karim, 2007) where above mentioned improvement not reported with mice housed in gold ratio rectangle base cages (GIV) that has nearly similar angular construction and angles distribution as ordinary cages so it explicates its failure to retain enzymatic antioxidant and non-enzymatic antioxidant capacity that reflected to some neurodegeneration of hippocampal regions and also explained the cognitive and spatial memory impairment.

However, housing the animals in cages of historical architectural shapes was capable of nearly induce significant alterations in the pyramidal shapes. The above results suggested that electromagnetic radiation from mobile phones caused increases in the levels of oxidative stress in the brain tissue of mice. However, the possible mechanism behind these alterations is still unclear and our study may be the pioneer in discussing these points but it suggests further study on another stressful model to prove pyramidal shape capability in mitigating ROS production and biological function improvement.

Conclusion

Our data suggested that electromagnetic radiation from mobile phones induced perturbations in hippocampal function especially cognitive state and spatial memory by induction of oxidative stress in the brain tissues of mice. The idea of the construction of farms as well as buildings near the radiofrequency station in form of pyramidal architecture may be represented as a solution to alleviate MPR cognitive impairment and may improve the spatial memory of animals. However, the precise mechanism underlying these effects is still unclear. Eventually, this study may advice to scientists to cooperate to find a possible and applicable control to uncontrolled surrounding hazards.

Table (1): Effects of architecture shapes on brain oxidant/antioxidant capacity (MDA, GSH, CAT, and NO) of mice exposed to mobile phone radiation (900 MHz).

	GI	The exposure groups		
		GII	GIII	GIV
MDA	54.7±1.9	95.9±1.41[a]	62.4±4.25[b]	76.8±2.88[ab]
GSH	89.6±2.26	52±5.5[a]	84.3±2.66[b]	62.7±4.24[a]
NO	267±18.4	153±4.37[a]	257±11.8[b]	183±15.4[a]
CAT	0.93±0.01	0.37±0.11[a]	0.85±0.01[b]	0.47±0.02[ab]

Data were expressed as mean ± SE (n=8). Statistical analysis was carried out by one-way ANOVA followed by Tukey's multiple comparisons test. a = significantly different from negative control (GI) at P<0.001 & b = significantly different from positive control (G II) at P<0.001 ab = significantly different from negative control (GI) at P<0.001 and also significantly different from positive control (G II) at P<0.001. G I: negative control ((ordinary shape cage - MPR)); G II: positive control (ordinary shape cage + MPR); GIII: Pyramidal shape cage + MPR; GIV: Gold ratio rectangle cage+ MPR.

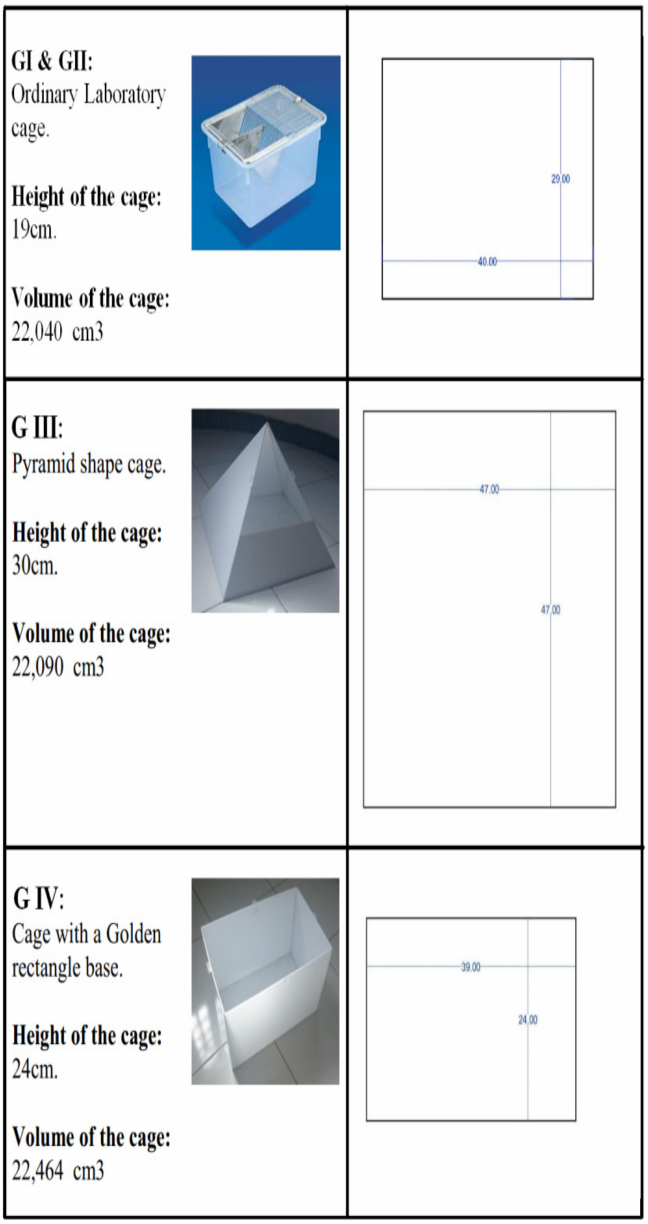


Fig. 1 : Architectural shapes of cages designed for mice exposed to a mobile phone radiation (900 MHz) protocol.

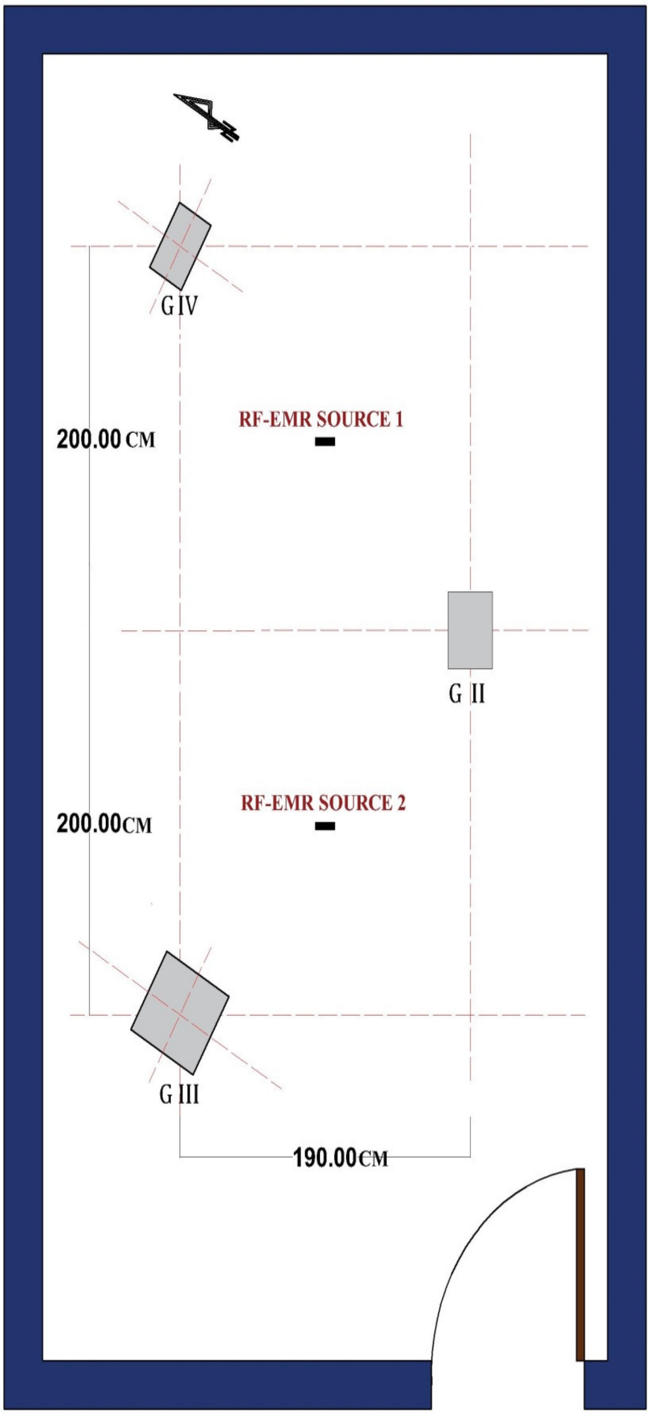
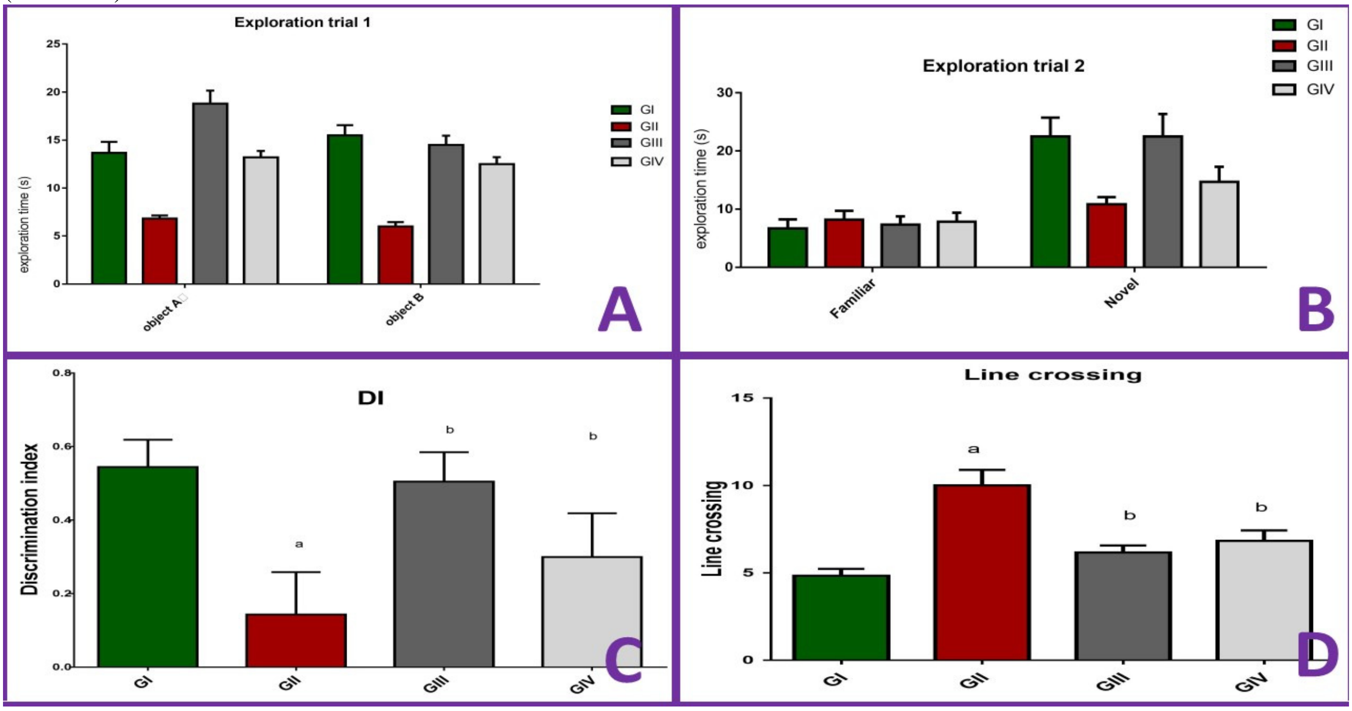


Fig. 2 : The top view of the exposure system setup was used in the study. Two mobile phones, as sources of Radiofrequency Electromagnetic Radiation (RF-EMR), were placed at the canter surrounded by the mice residing in the various cages. The mice were exposed to RF-EMR of 900 MHz frequency for 24 h/day for 8 weeks at SAR of 1.1 W/kg.

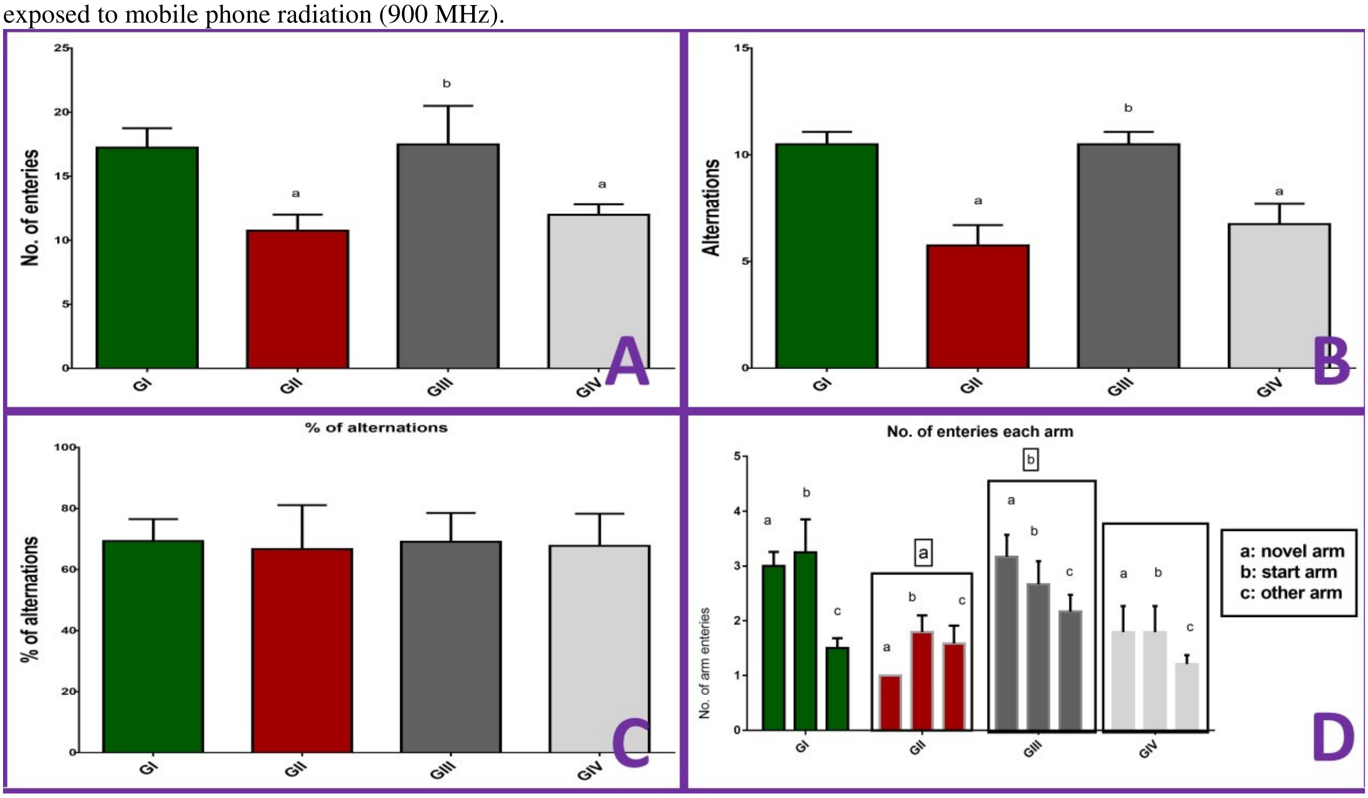
G I: negative control ((ordinary shape cage - MPR)); **G II**: positive control (ordinary shape cage + MPR); **GIII**: Pyramidal shape cage + MPR; **GIV**: Gold ratio rectangle cage+ MPR

Fig. 3 : Effects of architecture shapes on cognitive state expressed in ORT of male mice exposed to mobile phone radiation (900 MHz).



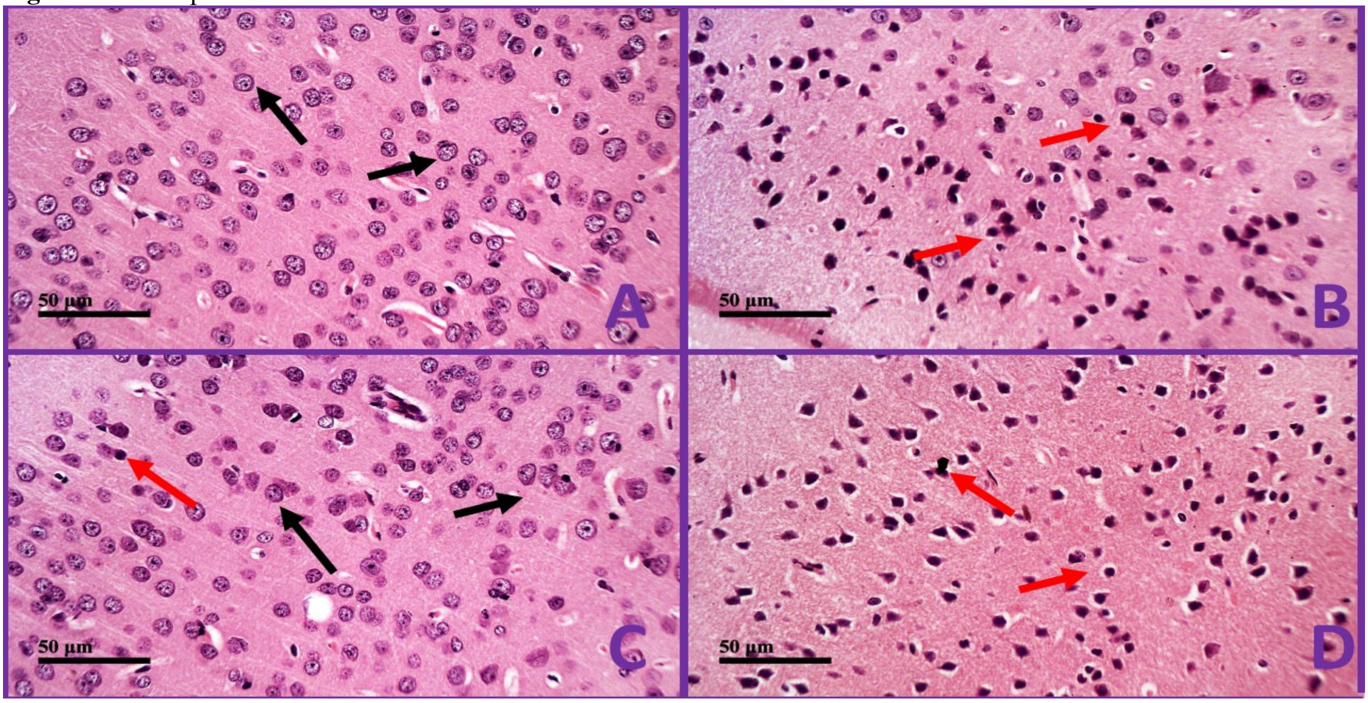
Data were expressed as mean ± SE (n=8). Statistical analysis was carried out by one-way ANOVA followed by Tukey's multiple comparisons test. a = significantly different from negative control (GI) at P<0.001 & b = significantly different from positive control (G II) at P<0.001 ab = significantly different from negative control (GI) at P<0.001 and also significantly different from positive control (G II) at P<0.001. **G I**: negative control ((ordinary shape cage - MPR)); **G II**: positive control (ordinary shape cage + MPR); **GIII**: Pyramidal shape cage + MPR; **GIV**: Gold ratio rectangle cage+ MPR.

Fig. 4 : Effects of architecture shapes on spatial working memory and reference memory expressed in y-maze of male mice exposed to mobile phone radiation (900 MHz).



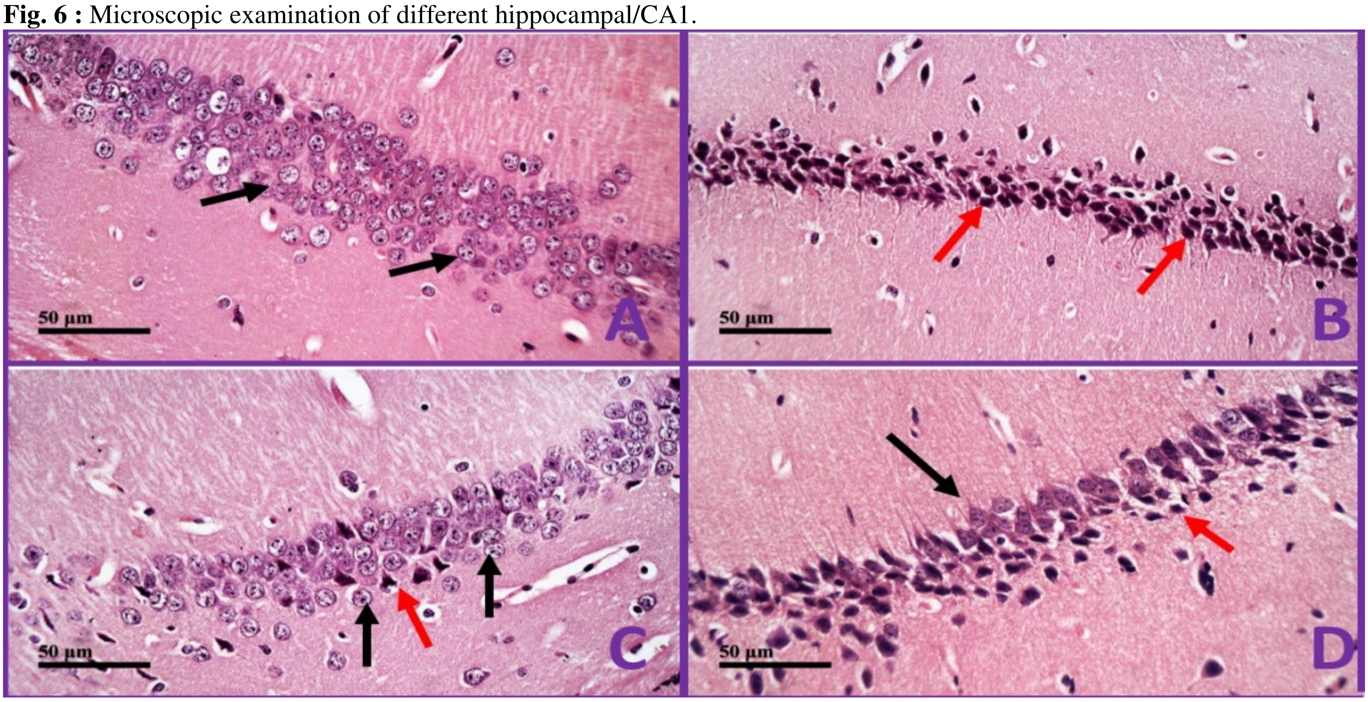
Data were expressed as mean ± SE (n=8). Statistical analysis was carried out by one-way ANOVA followed by Tukey's multiple comparisons test. a = significantly different from negative control (GI) at P<0.001 & b = significantly different from positive control (G II) at P<0.001. **G I**: negative control ((ordinary shape cage - MPR)); **G II**: positive control (ordinary shape cage + MPR); **GIII**: Pyramidal shape cage + MPR; **GIV**: Gold ratio rectangle cage+ MPR

Fig. 5 : Microscopic examination of different brain cortex.



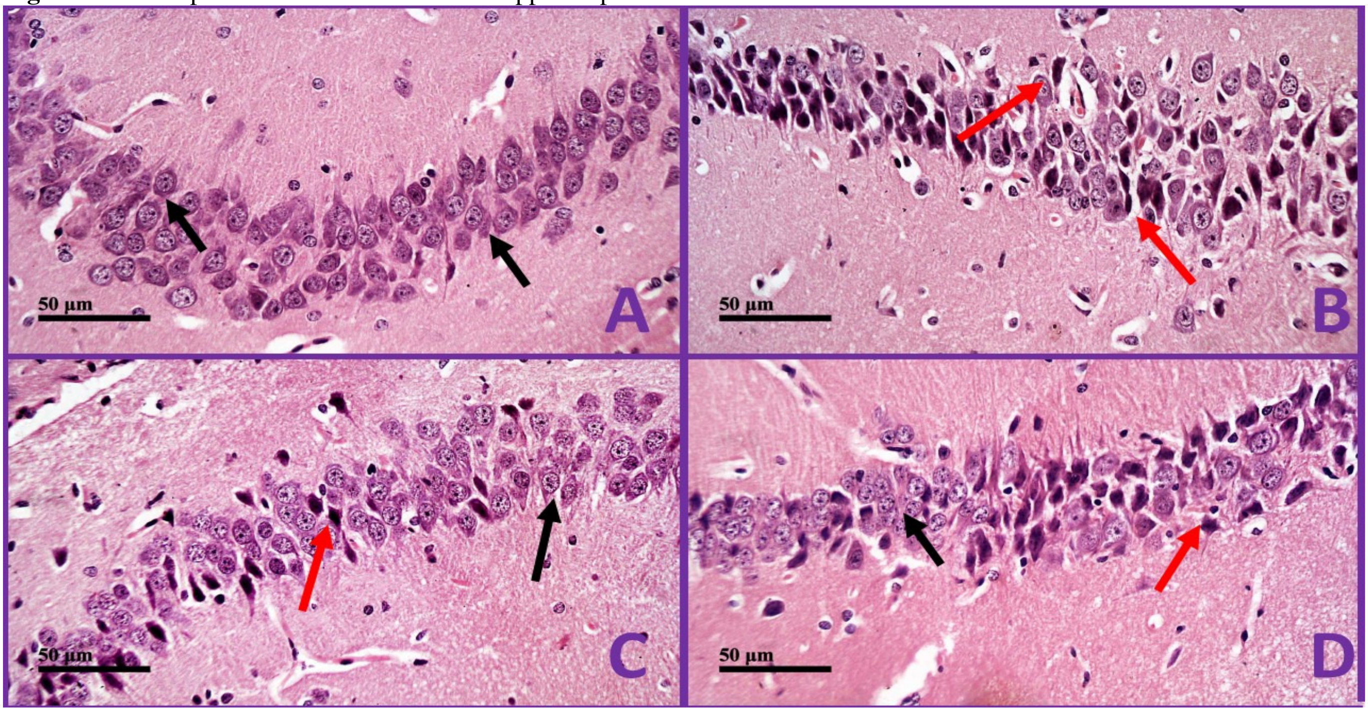
Microscopic examination revealed (**A)** normal organized morphological features of outer and deep cortical layers with many apparent intact neurons with intact cellular details (black arrow) and intercellular tissue, **(B)** showed marked diffuse degenerative changes of outer cortical neurons with many dark, shrunken and pyknotic and necrotic neurons (red arrow) accompanied with mild intercellular edema, (**C**) showed moderate protective records with alternated areas of apparent intact neurons (black arrow) or degenerated cells (red arrow) were observed with mild higher glial cells infiltrates (arrow head), **(D)** showed marked diffuse degenerative changes of outer cortical neurons with many dark, shrunken and pyknotic and necrotic neurons (red arrow) accompanied with mild intercellular edema, **A=G I**: negative control ((ordinary shape cage - MPR)); **B=G II**: positive control (ordinary shape cage + MPR); **C=GIII:**Pyramidal shape cage + MPR; **D=GIV**: Gold ratio rectangle cage+ MPR.

Fig. 6 : Microscopic examination of different hippocampal/CA1.



Microscopic examination revealed (**A**) demonstrated normal morphological features of hippocampal layers with apparent intact pyramidal neurons (arrow) with minimal degenerative changes records, **(B)** showed sever degenerative changes of most of pyramidal neurons with many shrunken and pyknotic neurons (red arrow) and mild intercellular edema., (**C**) showed few scattered records of neuronal degenerative changes (red arrow) records with many apparent intact neurons (black arrow) were observed., **(D)** showed alternated areas of apparent intact (black arrow) or damaged and degenerated pyramidal neurons (red arrow) with mild intercellular edema., **A=G I**: negative control ((ordinary shape cage - MPR)); **B=G II**: positive control (ordinary shape cage + MPR); **C=GIII:** Pyramidal shape cage + MPR; **D=GIV**: Gold ratio rectangle cage+ MPR.

Fig. 7 : Microscopic examination of different hippocampal/CA3.



Microscopic examination revealed (**A**) demonstrated normal morphological features of hippocampal layers with apparent intact pyramidal neurons (arrow) with minimal degenerative changes records., **(B)** showed alternated areas of apparent intact (black arrow) or damaged and degenerated pyramidal neurons (red arrow) with mild intercellular edema as well as glial cells infiltrates. (**C**) showed variable records between samples (Fig. 1 showed more apparent intact neuronal records, Fig. 2 showed many degenerated neurons with minimal intact neurons) **(D)** showed alternated areas of apparent intact (black arrow) or damaged and degenerated pyramidal neurons (red arrow) with mild intercellular edema as well as glial cells infiltrates., **A=G I**: negative control ((ordinary shape cage - MPR)); **B=G II**: positive control (ordinary shape cage + MPR); **C=GIII:** Pyramidal shape cage + MPR; **D=GIV**: Gold ratio rectangle cage+ MPR.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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Authors' Contribution

All authors contributed to the design and implementation of the work.

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