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Research Paper

Environmental Effect of High-voltage Towers on the Cerebellum and Cognitive Impairments in the Monkey

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ABSTRACT

Introduction: Today, high-voltage (HV) lines create a pernicious environment for humans living or working in the vicinity and even under these lines. The male rhesus monkey is used to investigate the effects of fields produced by HV towers. This study examines the function and level of impact in rhesus monkeys' brains from the cerebellum's cognitive, biological, and structural perspective.

Methods: Two monkeys have been used, one as a control and the second as a test. The monkey under test was subjected to a simulated HV electrical field of 3 kV/m, 4 hours a day, for 1 month. Behavioral tests were performed using a device designed and built for this purpose. Concentration analysis of adrenocorticotropic hormones (ACTH) and inspection of glucocorticoid receptor gene's (GR) expression were performed by the reverse transcription polymerase chain reaction method. Changes in cerebellar anatomy were examined with magnetic resonance imaging (MRI). All tests were performed before and after the study period and compared with the control monkey.

Results: Cognitive tests showed a significant reduction for the monkey exposed to the HV electrical field in the first week after imposition compared with the same time before. Also, the expression of the *GR* gene decreased, and the concentration of ACTH hormone in plasma increased. Surveying the level of cerebral MRI images did not show any difference, but hemorrhage was evident in a part of the cerebellum.

Conclusion: The tested monkey's cognitive, biological, and MRI results showed a decrease in visual learning and memory indices.

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Highlights

• Exposure to high-pressure electrical fields induces cognitive changes in the male rhesus monkeys, which is associated with an elevated susceptibility to neurological disorders.

• There is a significant reduction in the prefrontal cortex after exposure to high-pressure electrical fields.

• Neurological disorders are correlated with behavioral anomalies in male rhesus monkeys.

• Exposure to high-pressure electrical fields can provoke immune system dysfunctions, manifesting as weakness and fatigue.

Plain Language Summary

The ELF around high-voltage power towers has significant detrimental effects on the brain and cognitive functions of both animals and humans. The main purpose of this research was to investigate the biological and cognitive effects on the brain, behavior, and other directly related parameters in monkeys exposed to high-voltage fields created in the lab environment. The results of the study demonstrated significant changes in behavioral, cognitive, and biological aspects in monkeys exposed to these high-voltage fields. These findings indicate a potential risk for individuals as well as employees of occupations living or working near these high-voltage towers.

1. Introduction

Studies have shown that the frequency of electromagnetic waves that are propagating in high-voltage towers in residential areas can cause problems in blood and brain and even disability for residents living on the margins of the affecting magnetic fields (Aliyari et al., 2022; Aliyari et al., 2019b; Aliyari et al., 2019a; Crespi et al., 2016; Draper et al., 2005; Kazemi et al., 2018; Lowenthal et al., 2007).

The electromagnetic field (EMF) of high-voltage (HV) towers threatens the ecosystem as an environmental hazard and affects animals and cell division. They also cause biological effects, including changes in cell and tissue functions, human bone marrow function, and heart rate (Garip & Akan, 2010). The EMF activates the reactive oxygen species (ROS), which can produce peroxides and hydrogen oxides, causing toxicity inside the neuron cells. The impact of EMF on the production of free radicals by ROS in neurons causes toxicity within them and impairs the function and structure of the neurons. The results of these abnormal changes are neurological diseases and symptoms, including Huntington, Alzheimer, and depression (Goraca et al., 2010; Lohmann et al., 2003). Alzheimer disease is a severe defect in the function and structure of the hippocampal neurons, which is accelerated by the ROS (García et al., 2008). Another neurological disorder caused by HV tower fields is an increase in the prevalence of Alzheimer. This neurological disorder occurs in older people, which weakens concentration and impairs remembrance of memorabilia and memory. Research shows that workers who are more exposed to the EMF are more likely to afflict with this disease (García et al., 2008; Haddad et al., 2007; Sobel & Davanipour, 1996).

In addition, studies on experimental animals and domestic animals, as well as humans, have shown that wavelength, duration of exposure, and distance from EMF affect cell proliferation, interfere with DNA replication, cause various mutations, and increase the incidence of congenital defects and reproductive disorders (Aliyari et al., 2022; Hardell et al., 2008; Hardell & Sage, 2008; Kazemi et al.; Mihai et al., 2014). One study involved up to 30000 matched case-control pairs of children living in the United Kingdom. It was found that children living in homes as far as 600 m from HV power lines had an elevated risk of leukemia. An increased risk of 69% for leukemia was found for children living within 200 m of power lines, while an increased risk of 23% was found for children living within 200 to 600 m of the lines (Draper et al., 2005). The severity of this disorder was proportional to the duration of the proximity to the EMF and the wave type (Crespi et al., 2016; Lowenthal et al., 2007). According to the research, living near these lines doubles the risk of leukemia in children (Hardell et al., 2008a; Hardell et al., 2008b; Liburdy et al., 1993).

There are electrical currents and internal electrical fields within all living organisms involved in complex physiological control mechanisms, such as cellular death and activity and the development and repair of tissues. The synthetic properties of their effects on biological systems have also been investigated. Based on research, EMF (Kazemi et al., 2022a; Kazemi et al., 2022b; Kazemi et al., 2018) initially causes dizziness, tinnitus, weakness, fatigue, blurred vision, and sleepiness during work, as well as the emergence of unknown diseases, changes in blood composition, impairment in neuromuscular system, genetic transformation, and a higher incidence of cancers such as lymphoma, leukemia, brain tumors, salivary gland cancer, and fertility disorder in men and women (Kazemi et al., 2018; Tekieh et al., 2017; Walkiewicz et al., 2016).

EMF changes the normal secretion of neuroendocrine hormones, including melatonin, adrenocorticotropic hormones (ACTH), cortisol, and epinephrine, which can cause behavioral and cognitive impairment in a person. EMF affects the secretion of protein and amine hormones by activating the mechanisms of G receptor proteins and membrane enzymes (phospholipase C or adenylyl cyclase). It increases the production of the cAMP or diacylglycerol, as well as the activity of protein kinase A or protein kinase C, which then causes the phosphorylation of proteins with serine or threonine, changing the transcription of genes (Capone et al., 2014; Capone et al., 2017; Duan et al., 2014; Walkiewicz et al., 2016). The ACTH peptide hormone is secreted from the anterior pituitary gland and positively affects the cortical part of the adrenal gland. This hormone also increases the secretion of cortisol and aldosterone. The ACTH level drops by raising cortisol levels and vice versa. In fact, the ACTH hormone regulates hormones in the cortical and central part of the adrenal gland (Consales et al., 2018; D'Angelo et al., 2015; Rauš Balind et al., 2016).

Glucocorticoid receptor (GR) is an active transcription factor of flowing glucocorticoids and interferes with their effects on various bodily functions. These receptors play an essential role in neurons and glands. Gene expression of *GR* receptors plays a vital role in learning and memory, especially in hippocampal cells. The stress system activates the *GR* receptors and thus restores memory to the hippocampus of the rat. The expression of *GR* receptors in the peripheral blood lymphocytes is a good marker of the expression of these *GR* receptors in the hippocampal and prefrontal neurons and other neurons in the nervous system (Salehi & Hamzehloueian, 2017).

The importance of learning and how to enhance and improve this crucial cognitive process lies in promoting human performance. Learning is one of the most critical activities of the brain, which causes a relatively stable change in the person's feelings, thoughts, and behaviors based on previously recorded memories (Aliyari et al., 2018; Devesa et al., 2016b; Esmaeilzadeh Kanafgourabi et al., 2023). Learning can be defined with two bases: Memory and attention (Aliyari et al., 2015; Gruart et al., 2015).

Learning and memory require communication between different areas of the brain, especially the hippocampal regions (the main position of memory formation), the prefrontal cortex (the main position of focus and thought), the cerebellum (position of voluntary movement of the body) and visual paths (Aliyari et al., 2022; Bisoglio et al., 2014). The cerebellum regulates the body's movements, learning, and thought. Stimulants within the neural fibers are transferred from the cerebellum to the rest of the brain, including the sensory cortex and visual system. These actions help maintain balance, converting thought to action and coordinating movements (Llinas & Negrello, 2015). According to studies, the cerebellum also plays a vital role in attention and spatial understanding (Llinas & Negrello, 2015; Schreglmann et al., 2018; Striemer et al., 2015). On the other hand, injury to the cerebellum impairs the coordination of the sensory and motor parts of the brain and disrupts the learning outcomes (De Zeeuw & Ten Brinke, 2015; Sokolov et al., 2017).

This study aimed to investigate the effects of an HV tower field on cognitive and behavioral functions of the brain, including learning and visual memory in a male rhesus monkey.

2. Materials and Methods

Study animals

The researchers have studied the human and Macaca monkeys' genes and found that 93% of gene sequences in humans and monkeys are common. Macaca monkey is the closest to humans in cognitive aspect after the chimpanzee (Aliyari et al., 2022; Van Schaik, 2016). Accordingly, this study was performed on the Macaca monkey.

Two adult male rhesus monkeys (one as a control and another as a test) (Kazemi et al., 2021; Kazemi et al., 2022b; Kazemi et al., 2018; Tekieh et al., 2017), aged 4-5 years with an average weight of 4 kg were included after being acclaimed with the environment (12 months). The animal room was standard in terms of light, temper-

Figure 1. The monkey's cage under a uniform electrical field of 3 kV/m

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ature, and humidity and had a condition of 12 hours of light and 12 hours of dark (Kazemi et al., 2022a; Kazemi et al., 2018; Tekieh et al., 2017).

Protocols and simulation of high-voltage field

According to the protocol, after the pretest period, a monkey was exposed to a simulated HV electrical field of 3 kV/m, 4 hours a day for 1 month, and the other monkey was kept in an environment without the field as a control sample (Aliyari et al., 2022).

The applied HV EMF was 3 kV/m (simulated effects of exposure to a 400-kV, 50-Hz transmission line on the human) that was simulated in the experimental environment of the Amirkabir University of Technology (Tehran Polytechnic), the High Voltage Laboratory, Tehran City, Iran. A crane placed two metal plates (2×2 m), one below the monkey's cage and the other above. The distance between the two plates was 2 m, and a voltage of 6 kV was applied to them to create a uniform field of 3 kV/m on the monkey's cage (teflon) (1×1×1 m) (Figure 1) (Aliyari et al., 2022).

Biological test

Before and after applying the field, behavioral studies were performed on test and control monkeys. The monkey should be fast for 17 hours to do behavioral tests. An amount of 10 mL of blood was taken from each monkey's femoral area for biological tests. Then, 5 mL was used to measure and compare the changes in serum hormonal concentrations using the special ACHD primates' kit, prepared by the MyBiosource Company, USA, and ELISA device. Another 5 mL was used to assess the N-methyl-D-aspartate (NMDA) receptor gene's expression from peripheral blood lymphocyte cells by the reverse transcription polymerase chain reaction (RT-PCR) method. Lymphocyte isolation was performed using a Ficoll solution and a centrifuge device. Hormonal concentration was measured in three steps (before applying the field, after that, and at the recovery stage) (Aliyari et al., 2022).

The volumetric measurements of magnetic resonance imaging (MRI) of cerebellar anatomy in samples were performed before applying the field and then by DICOM LiteBox software (Lichstein et al., 2018).

Primer sequences of glucocorticoid receptor (GR) were as follows:

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Figure 2. A plexiglass transparent container designed to perform a visual learning test and the cage prepared by teflon

Forward primer: AGGAAAAGCCATTGTCAAGAGG;

Reverse primer: CCTCTACAGGACAAACTGATAG.

PCR *GR* receptors assays

The second part of the blood samples was used for cellular and molecular assays. To this end, after collecting the blood samples, blood lymphocytes were initially isolated using the Ficoll solution in a centrifuge at 1500 rpm for 5 minutes, followed by another 15 minutes at 2500 rpm. The isolated lymphocytes were tested to determine the expression of GR-receptor genes using the PCR technique. To assess the impact of the expression of visual learning and visual memory of glucocorticoid receptor (*GR*) genes involved in mature and immature monkeys, the semi-quantitative reverse transcriptase-PCR (semi-RT-PCR) was utilized. As described earlier, the peripheral blood sample was collected from each animal at a related time, and the total mRNA was purified using the RNX-Plus kit (CinnaGen Co. Iran) following the manufacturer's guidelines. The quantity and quality of each isolated RNA were evaluated using the NanoDrop spectrophotometer (Thermos, USA) and agarose gel electrophoresis, respectively. After that, a Bioneer kit (Takara, Japan) was applied to synthesize cDNA from each sample. Briefly, 100 ng of each RNA sample was converted to cDNA by the master mix containing M-MLV reverse transcriptase, random hexamers, oligo (dT), and the related buffer. Finally, PCR and related specific primer sets detected the *GR2a* gene expression. The mRNA expression of β-actin was used as an internal control. All PCR reactions were performed in a thermocycler (Techne, UK) containing 1.5 µL cDNA, 0.2 mM of the deoxynucleoside triphosphates (dNTPs), 2.5 mM $MgCl_2$, 10 pmol of each primer and 1.5 U of Taq DNA polymerase (CinnaGen Co., Iran). The PCR program had a 6 min initial denaturation at 94°C, 35 cycles of 45 s at 95°C, and 45 s at 58°C. To measure the density of amplicons, each PCR product was run on 2% agarose gel electrophoresis, stained by ethidium bromide, and visualized under UV gel documentation. Finally, the density of each product band was measured using Image J software, version 1.51.

Behavioral test

Visual learning

A container was designed to measure the visual learning test. This container has a spring-hinged opening that can only be opened in one direction so that the animal should hold the lid of the container with one hand and get the reward with another hand to reap the reward inside the container (peanuts) (Figure 2). The protocol included 10 repetitions a day for a week. After the test period, it was the same except for the container door's direction (Lyons et al., 2010).

Visual memory

The visual memory behavior recorder consisted of two dishes (each one with an opening in one direction only). It was non-transparent (the reward was inside the container, invisible to the primate). Two coated containers were located on a movable base (Darusman et al., 2014;

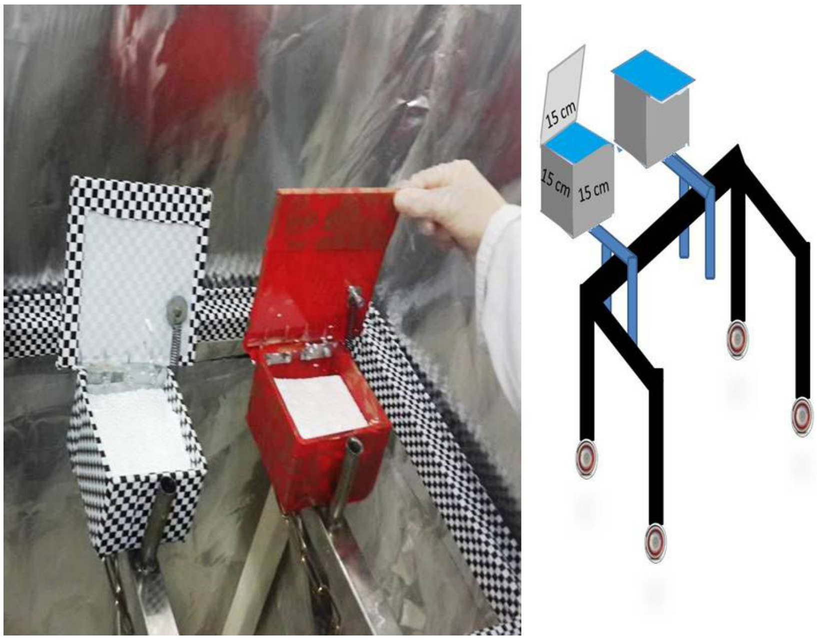

Figure 3. The visual memory behavior device shape test (delay response task)

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Tsujimoto & Postle, 2012). This test was performed in 2 phases of 30 and 60 seconds (Figure 3).

In the first phase of the test, the visual memory behavior recorder device was positioned in front of the primate eyes, the favorite reward for the animal (peanut) was placed in one of the dishes randomly, and after 30 seconds, the dishes were given to the animal. The animal was allowed to reach the reward only once. Therefore, it should pay attention and focus because it may deprive of gaining a reward if making a mistake on the first attempt. The test was performed 10 times a day.

The second phase of the test was the same as the first phase, except that the dishes were given with a 60-s delay.

The protocol of these tests was performed one month before and one month after the test, and they were compared with the control sample and each other.

3. Results

The results of the behavioral study indicated a decrease in the performance of visual learning tests in the tested monkey under an HV field compared to the pre-test period. At the same time, the control sample had no significant change (Figure 4).

In addition, the monkey under test showed reduced performance in terms of visual memory in the HV field compared to the previous condition. At the same time, there was no significant change in the control sample (Figures 5 and 6).

The results of the ACTH hormone test in the monkey under test showed a significant increase, while the control sample had no significant change. It was worth noting that within one month of recovery, this hormone was still decreasing (returning to baseline) in the test monkey (Figure 7).

The results of the *GR* receptor gene's expression in the monkey under test showed a significant reduction in the level. It must be noted that it returned to the baseline during a one-month recovery period. On the other hand, no significant changes were observed in the control sample (Figure 8).

Magnetic resonance imaging (MRI) examinations of the cerebellum have not shown any significant changes in volumetric variation in the sagittal incision (Figure 9). It is worth noting that in the clinical and histological examination of MRI for cerebellar assessment, the hemorrhage was observed in the left region of the cerebellum. However, the MRI image did not show such a complication before applying the field. The clinical examination of the tested monkey exposed to a simulated HV field revealed that the tested cerebellum had a bleeding disorder in the left cerebellar part compared with the time before the test (Figure 10).

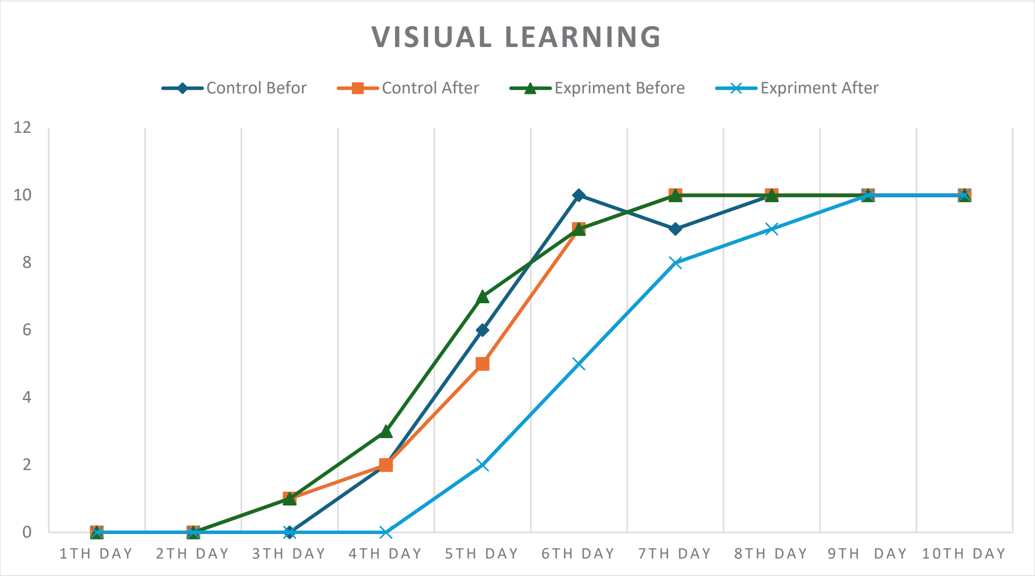

Figure 4. The visual learning test

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4. Discussion

Hazardous environmental factors threaten the ecosystem and living things, especially human beings (Aliyari et al., 2019a). One of these damaging environmental factors is the electromagnetic fields produced by high-voltage towers. In other words, industrialization and expansion of electrical lines and the proximity of HV towers with residential buildings have increased the risks of EMF exposure (Aliyari et al., 2019a; Aliyari et al., 2019b). Based on the research, high-voltage fields are not only influencing the health and lifestyle of people but also cause cognitive and behavioral changes in animals and humans (Aliyari et al., 2019b; Aliyari et al., 2019a; Gajšek et al., 2016; Aliyari et al., 2022).

One of today's research challenges is the value of learning, this cognitive function, in promoting and improving human performance (Akcaoglu, 2014; Aliyari et al., 2020; Li et al., 2020). Learning is one of the most important neurological activities that include a relatively stable change in the senses, thoughts, and behavior of an individual, made in a person based on the previously

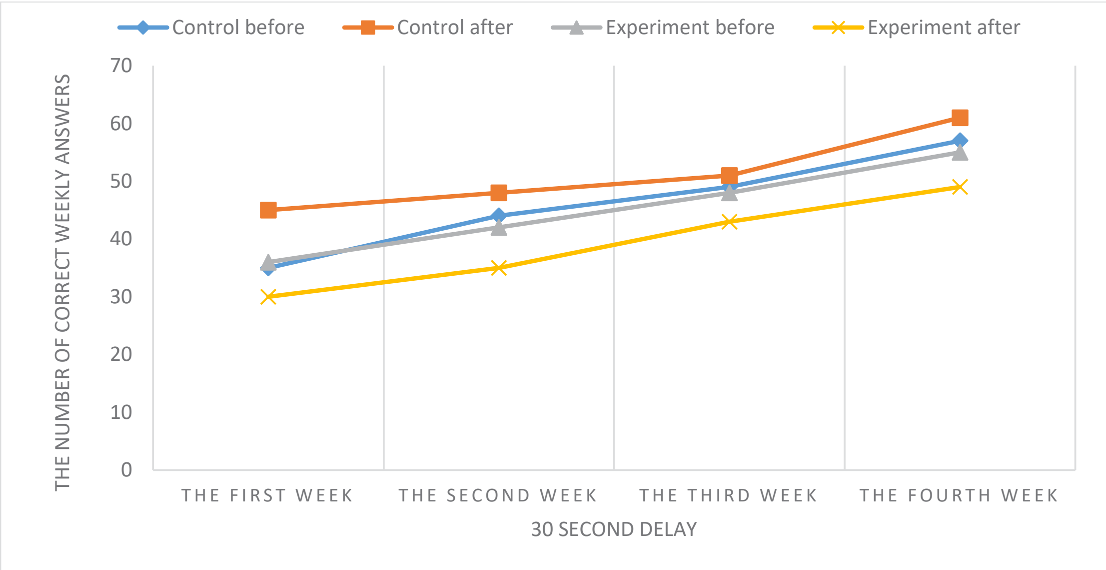

Figure 5. The visual memory test at a delay of 30 seconds

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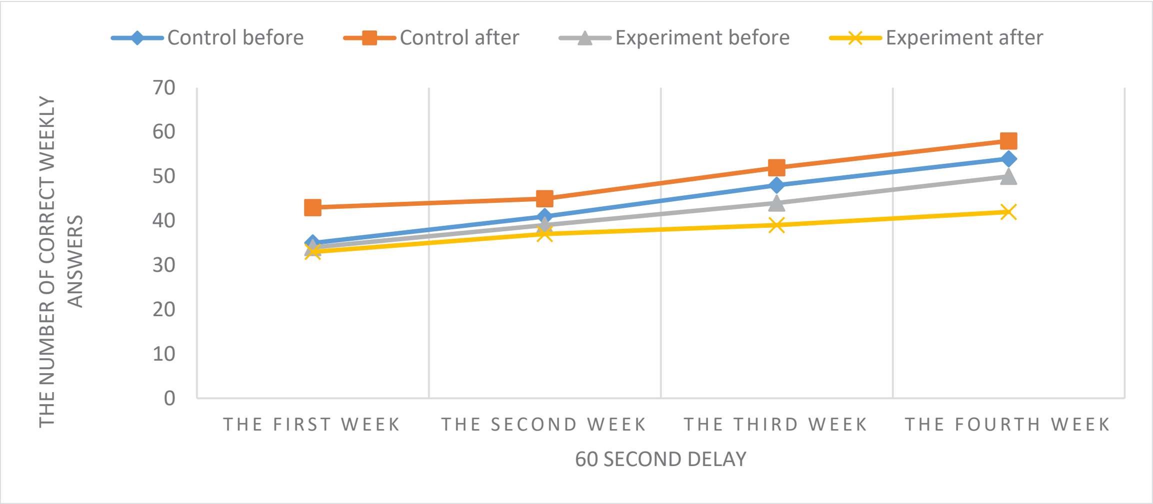

Figure 6. The visual memory test at a delay of 60 seconds

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recorded memory (Aliyari et al., 2019b; Devesa et al., 2016a).

The study results indicate that the tested monkey showed significant changes in cognitive and behavioral elements as exposed to HV fields (Aliyari et al., 2019b). Regarding the behavioral characteristics, the tested monkey was intelligent, with high attention, stirring, and vitality, and active before the test, but there were significant changes after the test period (Aliyari et al., 2019b). After the test, the monkey turned into an unresponsive, lethargic, inactive, jadish, and depressed one, even with a weight loss of about 1 kg. The results of the cognitive tests indicated a reduced number of correct responses to the tests after the study period. The bases of learning, attention, and concentration were gradually diminished in the tested monkey at the time of placement under the field, and the animal's visual learning decreased. Research has shown that learning and memorizing is the basis of memory (Basar, 2004; Clark & Mayer, 2016). The tested monkey's cognitive elements of attention, learning, and memorizing were impaired, resulting in decreased visual memory (Aliyari et al., 2019b; Kazemi et al., 2021).

Hormonal studies in the tested monkey indicated an increase in the ACTH level after the test. ACTH hormone acts as a regulator of cortisol hormones, which

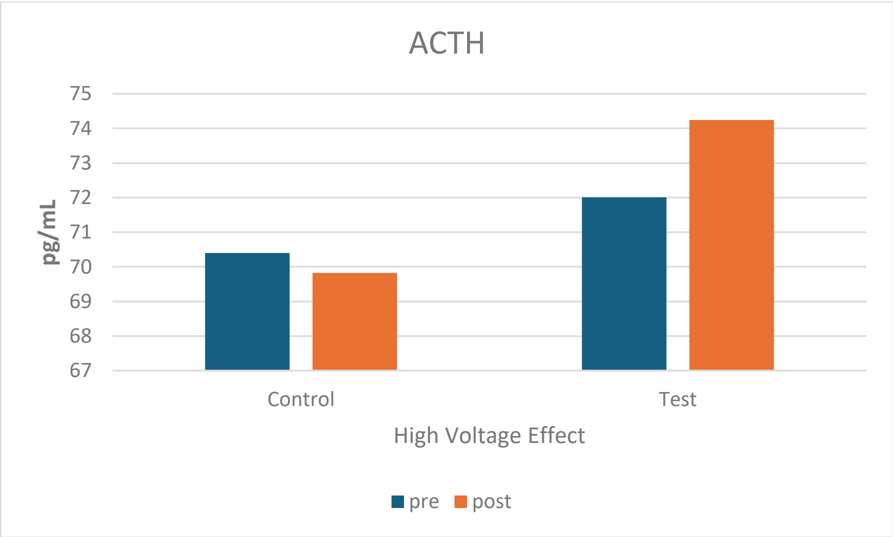

Figure 7. The ACTH changes in the control and test sample before and after applying the field

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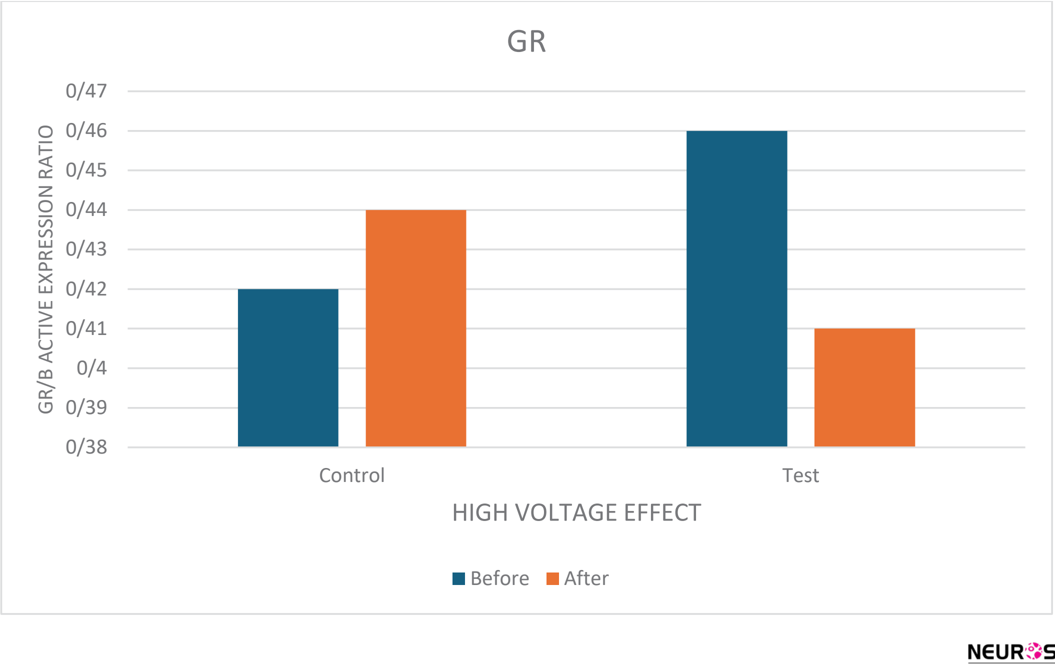

Figure 8. The changes in *GR* receptor gene's expression in the test and control samples before and after applying the field

plays an important role in cognitive indices like memory and learning in the central nervous system (Kazemi et al., 2021; Kazemi et al., 2022b; Kazemi et al., 2018; Aliyari et al., 2022). Increasing the ACTH hormone reduces the release of cortisol hormone from the cornea of the adrenal gland (Rauš Balind et al., 2016). Abnormal changes in cortisol hormone secretion result in mental disorders in an individual (Deary et al., 2009; Logsdon et al., 2002; Phirom et al., 2020; Aliyari et al., 2022). Electromagnetic fields cause abnormal changes in cortisol secretion and increase the activity of the stress and oxidative pathway to produce free radicals, leading to neurological diseases by interfering with the normal functioning of neurons (Aliyari et al., 2022; Consales et al., 2012; Liburdy et al., 1993). An increase in ACTH by boosting the activity of membrane receptors of G proteins by means of increasing cAMP and calcium ions as a secondary messenger increases the activity of protein kinase A and genomic changes in neurons (Wyszkowska et al., 2016). The study's results indicated an increase in ACTH, which can reduce normal cortisol levels. These changes could disrupt the tested monkey's cognitive elements, so it can be argued that cortisol hormone changes play an important role in impairing learning and memory. It also contributes to inactivity and depression in the tested monkey. Cortisol, on the other hand, plays an essential role in expressing the *GR* receptor gene. The *GR* and NMDA receptors (which play an important role in memory and learning processes) are scattered throughout the central nervous system (Kazemi et al., 2018; Aliyari et al., 2022). The highest concentration of *GR* and NMDA receptor genes in the central nervous system is seen in the hippocampus, prefrontal, amygdala, and cerebellum (De Zeeuw & Ten Brinke, 2015; Duan et al., 2014; Llinas & Negrello, 2015; Sokolov et al., 2017). These two receptor gene expressions play an important role in the memory and learning of humans and primates. The study's results showed that the expression of the *GR* receptor gene in the tested monkey was reduced (Aliyari et al., 2019b). The decrease in the expression of the *GR* receptor gene has also an important role in reducing learning and memory (Oitzl et al., 1998). However, there were no significant changes in the control sample regarding the above-mentioned cases (cognitive, behavioral, genomic, and hormonal factors).

Anatomical investigation of the brain by the MRI is a common and non-invasive technique neurologists might use to investigate neurological disorders, including Alzheimer (Harach et al., 2015; Hunter et al., 2012). Anatomical examination of the cerebellum by MRI in the tested monkey showed no significant changes in the cerebellum. This volumetric study was measured using the DICOM LiteBox software. However, the clinical examination of the tested monkey exposed to a simulated HV field showed that the tested cerebellum had bleeding in the left cerebellar part compared with the time before the test (Le Bihan, 2014; Zeng, 2017). This complication was confirmed by a radiologist, Dr Hossein Ghanaati of

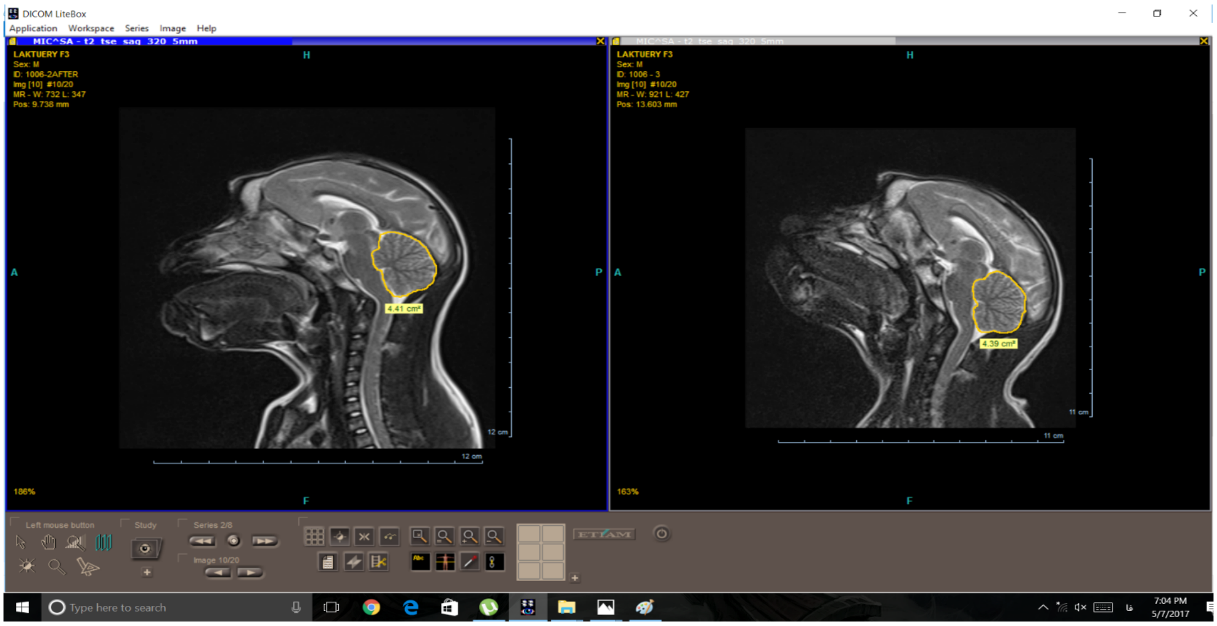

Figure 9. The anatomical size of the cerebellum computed with the DICOM LiteBox software with MRI images of the test sample

Tehran University, and could be another reason for the decreased learning and memory of the tested monkey.

5. Conclusion

According to the cognitive tests (visual learning and visual memory), the tested monkey showed decreased correct functioning under a simulated HV field. This disorder was assessed by the ACTH hormonal study and its increase in the tested sample. Also, with a reduction in the expression of the *GR* receptor gene and its essential role in learning and memory, this disorder in the tested monkey receives another confirmation. Finally, anatomical examination of the test sample revealed no changes

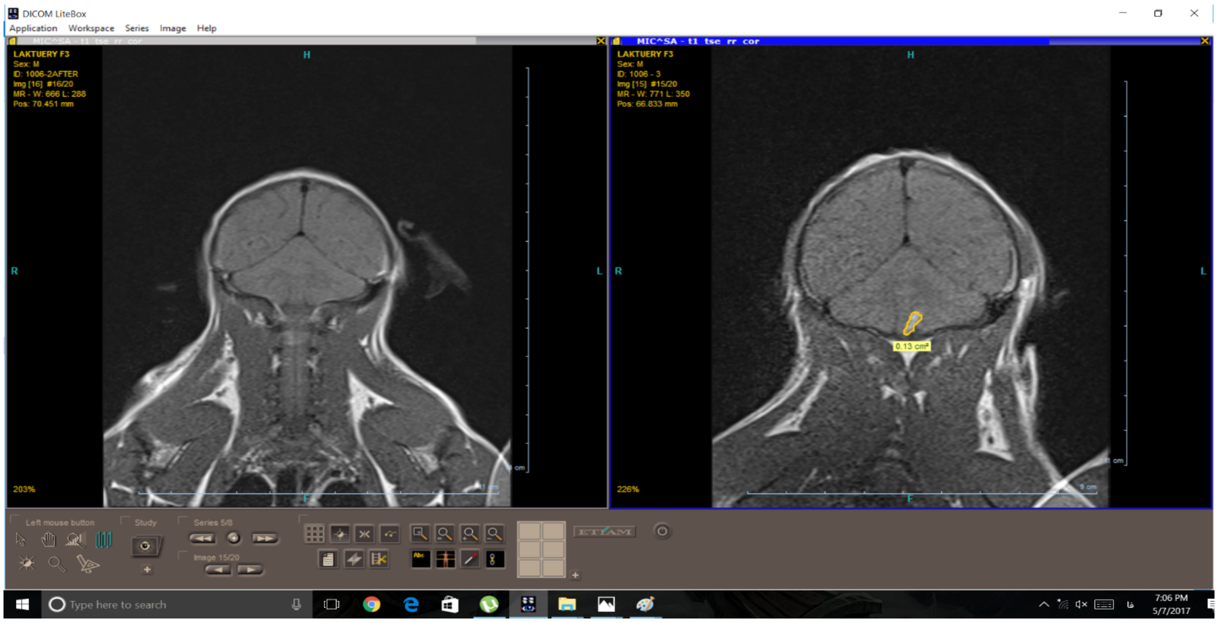

Figure 10. The incidence of hemorrhagic lesions in the cerebellum section of the tested monkey after the test period

Note: The right photo was taken after the test period.

in the volume of the cerebellum, but the hemorrhage in the cerebellum was observed in the clinical examination, which can cause cognitive impairment (learning and visual memory).

According to the results of this study, the HV field towers pose serious cognitive hazards for residents around the power lines, which require further research in this context.

Ethical Considerations

Compliance with ethical guidelines

All ethical standards were observed following international law regarding the transportation, location, and method of keeping animals and the study was approved by the (Baqiyatallah Medical University, Medical Ethics Committee (No.: 112-1394).

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Authors' contributions

All authors contributed equally in preparing all parts of the research.

Conflict of interest

The authors declared no conflict of interest.

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Reference

Akcaoglu, M. (2014). Learning problem-solving through making games at the game design and learning summer program. *Educational Technology Research and Development, 62*(5), 583-600. [DOI:10.1007/s11423-014-9347-4]

Aliyari, H., Hosseinian, S. H., Menhaj, M. B., & Sahraei, H. (2019). Analysis of the effects of high-voltage transmission line on human stress and attention through electroencephalography (EEG). *Iranian Journal of Science and Technology, Transactions of Electrical Engineering, 43*(1), 211-218. [DOI:10.1007/s40998-018-0151-8]

Aliyari, H., Hosseinian, S., Sahraei, H., & Menhaj, M. (2019). Effect of proximity to high-voltage fields: Results of the neural network model and experimental model with macaques. *International Journal of Environmental Science and Technology, 16*(8), 4315-4326. [DOI:10.1007/s13762-018-1830-8]

Aliyari, H., Kazemi, M., Sahraei, H., Daliri, M. R., Minaei-Bidgoli, B., & Golabi, S. (2019). [Enhancement of cognitive index with computer game using brain signals and hormonal analysis: Randomized controlled trial (Persian)]. *Journal of Research in Rehabilitation Sciences, 15*(3), 144-151. [DOI:10.22122/JRRS.V15I3.3457]

Aliyari, H., Kazemi, M., Tekieh, E., Salehi, M., Sahraei, H., & Daliri, M. R., et al. (2015). The effects of fifa 2015 computer games on changes in cognitive, hormonal and brain waves functions of young men volunteers. *Basic and Clinical Neuroscience, 6*(3), 193–201.

Aliyari, H., Sahraei, H., Daliri, M. R., Minaei-Bidgoli, B., Kazemi, M., & Agaei, H., et al. (2018). The beneficial or harmful effects of computer game stress on cognitive functions of players. *Basic and Clinical Neuroscience, 9*(3), 177–186. [DOI:10.29252/nirp.bcn.9.3.177]

Aliyari, H., Sahraei, H., Erfani, M., Tekieh, E., Salehi, M., & Kazemi, M., et al. (2019). The impacts of video games on cognitive function and cortisol levels in young female volunteers. *Journal of Experimental and Clinical Neurosciences, 6*(1), 1-5. [DOI:10.13183/jecns.v6i1.87]

Aliyari, H., Sahraei, H., Golabi, S., Kazemi, M., Daliri, M. R., & Minaei-Bidgoli, B. (2021). The effect of brain teaser games on the attention of players based on hormonal and brain signals changes. *Basic and Clinical Neuroscience, 12*(5), 587–596. [DOI:10.32598/bcn.2021.724.9]

Aliyari, H., Sahraei, H., Golabi, S., Menhaj, M. B., Kazemi, M., & Hosseinian, S. H. (2022). The effect of electrical fields from high-voltage transmission line on cognitive, biological, and anatomical changes in male rhesus macaque monkeys using MRI: A case report study. *Basic and Clinical Neuroscience, 13*(4), 433–442. [DOI:10.32598/bcn.2021.1340.3]

Basar, E. (2004). *Memory and brain dynamics: Oscillations integrating attention, perception, learning, and memory*. Boca Raton: CRC press. [Link]

Bisoglio, J., Michaels, T. I., Mervis, J. E., & Ashinoff, B. K. (2014). Cognitive enhancement through action video game training: Great expectations require greater evidence. *Frontiers in Psychology, 5*, 136. [DOI:10.3389/fpsyg.2014.00136]

Capone, F., Corbetto, M., Barbato, C., Pellegrino, G., Di Pino, G., & Assenza, G. (2014). An open label, one arm, dose escalation study to evaluate the safety of extremely low frequency magnetic fields in acute ischemic stroke. *Austin Journal of Cerebrovascular Disease & Stroke, 1*(1), 1002. [Link]

Capone, F., Liberti, M., Apollonio, F., Camera, F., Setti, S., & Cadossi, R., et al. (2017). An open-label, one-arm, dose-escalation study to evaluate safety and tolerability of extremely low frequency magnetic fields in acute ischemic stroke. *Scientific Reports, 7*(1), 12145. [DOI:10.1038/s41598-017-12371-x]

Clark, R. C., & Mayer, R. E. (2016). *E-learning and the science of instruction: Proven guidelines for consumers and designers of multimedia learning*. Hoboken: Wiley. [DOI:10.1002/9781119239086]

Consales, C., Cirotti, C., Filomeni, G., Panatta, M., Butera, A., & Merla, C., et al. (2018). Fifty-hertz magnetic field affects the epigenetic modulation of the miR-34b/c in neuronal cells. *Molecular Neurobiology, 55*(7), 5698–5714. [DOI:10.1007/s12035-017-0791-0]

Consales, C., Merla, C., Marino, C., & Benassi, B. (2012). Electromagnetic fields, oxidative stress, and neurodegeneration. *International Journal of Cell Biology, 2012*, 683897. [DOI:10.1155/2012/683897]

Crespi, C. M., Vergara, X. P., Hooper, C., Oksuzyan, S., Wu, S., Cockburn, M., & Kheifets, L. (2016). Childhood leukaemia and distance from power lines in California: A population-based case-control study. *British Journal of Cancer, 115*(1), 122–128. [DOI:10.1038/bjc.2016.142]

D'Angelo, C., Costantini, E., Kamal, M. A., & Reale, M. (2015). Experimental model for ELF-EMF exposure: Concern for human health. *Saudi Journal of Biological Sciences, 22*(1), 75–84. [DOI:10.1016/j.sjbs.2014.07.006]

Darusman, H. S., Call, J., Sajuthi, D., Schapiro, S. J., Gjedde, A., & Kalliokoski, O., et al. (2014). Delayed response task performance as a function of age in cynomolgus monkeys (Macaca fascicularis). *Primates; Journal of Primatology, 55*(2), 259–267. [DOI:10.1007/s10329-013-0397-8]

De Zeeuw, C. I., & Ten Brinke, M. M. (2015). Motor learning and the cerebellum. *Cold Spring Harbor Perspectives in Biology, 7*(9), a021683. [DOI:10.1101/cshperspect.a021683]

Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., & Marioni, R. E., et al. (2009). Age-associated cognitive decline. *British Medical Bulletin, 92*, 135–152. [DOI:10.1093/bmb/ldp033]

Devesa, J., Almengló, C., & Devesa, P. (2016). Multiple effects of growth hormone in the body: Is it really the hormone for growth?. *Clinical Medicine Insights. Endocrinology and Diabetes, 9*, 47–71. [DOI:10.4137/CMED.S38201]

Devesa, J., Lema, H., Zas, E., Munín, B., Taboada, P., & Devesa, P. (2016). Learning and memory recoveries in a young girl treated with growth hormone and neurorehabilitation. *Journal of Clinical Medicine, 5*(2), 14. [DOI:10.3390/jcm5020014]

Draper, G., Vincent, T., Kroll, M. E., & Swanson, J. (2005). Childhood cancer in relation to distance from high voltage power lines in England and Wales: A case-control study. *BMJ, 330*(7503), 1290. [DOI:10.1136/bmj.330.7503.1290]

Duan, Y., Wang, Z., Zhang, H., He, Y., Fan, R., & Cheng, Y., et al. (2014). Extremely low frequency electromagnetic field exposure causes cognitive impairment associated with alteration of the glutamate level, MAPK pathway activation and decreased CREB phosphorylation in mice hippocampus: Reversal by procyanidins extracted from the lotus seedpod. *Food & Function, 5*(9), 2289–2297. [DOI:10.1039/C4FO00250D]

Esmaeilzadeh Kanafgourabi, S. N., Shabani, M., Mirchi, Z., Aliyari, H., & Mahdavi, P. (2023). The impact of ILF neurofeedback on inhibitory control in high-functioning adolescents with autism spectrum disorder: Preliminary evidence of a randomized controlled trial. *Applied Neuropsychology. Child*, 1–19. [DOI:10.1080/21622965.2023.2258247]

Gajšek, P., Ravazzani, P., Grellier, J., Samaras, T., Bakos, J., & Thuróczy, G. (2016). Review of studies concerning electromagnetic field (EMF) exposure assessment in Europe: Low frequency fields (50 Hz-100 kHz). *International Journal of Environmental Research and Public Health, 13*(9), 875. [DOI:10.3390/ijerph13090875]

García, A. M., Sisternas, A., & Hoyos, S. P. (2008). Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: A meta-analysis. *International Journal of Epidemiology, 37*(2), 329–340. [DOI:10.1093/ije/dym295]

Garip, A. I., & Akan, Z. (2010). Effect of ELF-EMF on number of apoptotic cells; correlation with reactive oxygen species and HSP. *Acta Biologica Hungarica, 61*(2), 158–167. [DOI:10.1556/ABiol.61.2010.2.4]

Goraca, A., Ciejka, E., & Piechota, A. (2010). Effects of extremely low frequency magnetic field on the parameters of oxidative stress in heart. *Journal of Physiology and Pharmacology, 61*(3), 333-338. [Link]

Gruart, A., Leal-Campanario, R., López-Ramos, J. C., & Delgado-García, J. M. (2015). Functional basis of associative learning and its relationships with long-term potentiation evoked in the involved neural circuits: Lessons from studies in behaving mammals. *Neurobiology of Learning and Memory, 124*, 3–18. [DOI:10.1016/j.nlm.2015.04.006]

Haddad, J. B., Obolensky, A. G., & Shinnick, P. (2007). The biologic effects and the therapeutic mechanism of action of electric and electromagnetic field stimulation on bone and cartilage: New findings and a review of earlier work. *Journal of Alternative and Complementary Medicine, 13*(5), 485–490. [DOI:10.1089/acm.2007.5270]

Harach, T., Marungruang, N., Dutilleul, N., Cheatham, V., Mc Coy, K., & Neher, J., et al. (2015). Reduction of alzheimer's disease beta-amyloid pathology in the absence of gut microbiota. *arXiv Preprint arXiv*, [Unpublished]. [Link]

Hardell, L., Carlberg, M., Söderqvist, F., & Hansson Mild, K. (2008). Meta-analysis of long-term mobile phone use and the association with brain tumours. *International Journal of Oncology, 32*(5), 1097–1103. [DOI:10.3892/ijo.32.5.1097]

Hardell, L., & Sage, C. (2008). Biological effects from electromagnetic field exposure and public exposure standards. *Biomedicine & Pharmacotherapy, 62*(2), 104–109. [DOI:10.1016/j.biopha.2007.12.004]

Hunter, J. M., Kwan, J., Malek-Ahmadi, M., Maarouf, C. L., Kokjohn, T. A., & Belden, C., et al. (2012). Morphological and pathological evolution of the brain microcirculation in aging and Alzheimer's disease. *Plos One, 7*(5), e36893. [DOI:10.1371/journal.pone.0036893]

Kazemi, M., Aliyari, H., Golabi, S., Tekieh, E., Tavakoli, H., & Saberi, M., et al. (2022). Improvement of cognitive indicators in male monkeys exposed to extremely low-frequency electromagnetic fields. *Archives of Razi Institute, 77*(1), 503–511. [DOI:10.22092/ari.2020.352384.1560]

Kazemi, M., Aliyari, H., Tekieh, E., Tavakoli, H., Golabi, S., & Sahraei, H., et al. (2022). The effect of 12 Hz extremely low-frequency electromagnetic field on visual memory of male macaque monkeys. *Basic and Clinical Neuroscience, 13*(1), 1–14. [DOI:10.32598/bcn.2021.724.8]

Kazemi, M., Sahraei, H., Aliyari, H., Tekieh, E., Saberi, M., & Tavacoli, H., et al. (2018). Effects of the extremely low frequency electromagnetic fields on NMDA-receptor gene expression and visual working memory in male rhesus macaques. *Basic and Clinical Neuroscience, 9*(3), 167–176. [DOI:10.29252/nirp.bcn.9.3.167]

Le Bihan, D. (2014). *Looking inside the brain: The power of neuroimaging*. Princeton: Princeton University Press. [Link]

Li, X., Niksirat, K. S., Chen, S., Weng, D., Sarcar, S., & Ren, X. (2020). The impact of a multitasking-based virtual reality motion video game on the cognitive and physical abilities of older adults. *Sustainability, 12*(21), 9106. [DOI:10.3390/su12219106]

Liburdy, R. P., Sloma, T. R., Sokolic, R., & Yaswen, P. (1993). ELF magnetic fields, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER+ breast cancer cell proliferation. *Journal of Pineal Research, 14*(2), 89–97. [DOI:10.1111/j.1600-079X.1993.tb00491.x]

Lichstein, P. M., Wilson, S. C., & Ward, W. G., Sr (2018). Compromise of radiology studies from nonstandardized viewing platforms. *Orthopedics, 41*(1), e136–e141. [DOI:10.3928/01477447-20171213-03]

Llinas, R., & Negrello, M. N. (2015). Cerebellum. *Scholarpedia, 10*(1), 4606. [DOI:10.4249/scholarpedia.4606]

Logsdon, R. G., Gibbons, L. E., McCurry, S. M., & Teri, L. (2002). Assessing quality of life in older adults with cognitive impairment. *Psychosomatic Medicine, 64*(3), 510–519. [DOI:10.1097/00006842-200205000-00016]

Lohmann, C. H., Schwartz, Z., Liu, Y., Li, Z., Simon, B. J., & Sylvia, V. L., et al. (2003). Pulsed electromagnetic fields affect phenotype and connexin 43 protein expression in MLO-Y4 osteocyte-like cells and ROS 17/2.8 osteoblast-like cells. *Journal of Orthopaedic Research, 21*(2), 326–334. [DOI:10.1016/S0736-0266(02)00137-7]

Lowenthal, R. M., Tuck, D. M., & Bray, I. C. (2007). Residential exposure to electric power transmission lines and risk of lymphoproliferative and myeloproliferative disorders: A case-control study. *Internal Medicine Journal, 37*(9), 614–619. [DOI:10.1111/j.1445-5994.2007.01389.x]

Lyons, D. M., Buckmaster, P. S., Lee, A. G., Wu, C., Mitra, R., & Duffey, L. M., et al. (2010). Stress coping stimulates hippocampal neurogenesis in adult monkeys. *Proceedings of the National Academy of Sciences of the United States of America, 107*(33), 14823–14827. [DOI:10.1073/pnas.0914568107]

Mihai, C. T., Rotinberg, P., Brinza, F., & Vochita, G. (2014). Extremely low-frequency electromagnetic fields cause DNA strand breaks in normal cells. *Journal of Environmental Health Science & Engineering, 12*(1), 15. [DOI:10.1186/2052-336X-12-15]

Oitzl, M. S., Fluttert, M., Sutanto, W., & de Kloet, E. R. (1998). Continuous blockade of brain glucocorticoid receptors facilitates spatial learning and memory in rats. *The European Journal of Neuroscience, 10*(12), 3759–3766. [DOI:10.1046/j.1460-9568.1998.00381.x]

Phirom, K., Kamnardsiri, T., & Sungkarat, S. (2020). Beneficial effects of interactive physical-cognitive game-based training on fall risk and cognitive performance of older adults. *International Journal of Environmental Research and Public Health, 17*(17), 6079. [DOI:10.3390/ijerph17176079]

Rauš Balind, S., Manojlović-Stojanoski, M., Milošević, V., Todorović, D., Nikolić, L., & Petković, B. (2016). Short- and long-term exposure to alternating magnetic field (50 Hz, 0.5 mT) affects rat pituitary ACTH cells: Stereological study. *Environmental Toxicology, 31*(4), 461–468. [DOI:10.1002/tox.22059]

Salehi, Y., & Hamzehloueian, M. (2017). The strain-promoted alkyne-nitrone and alkyne-nitrile oxide cycloaddition reactions: A theoretical study. *Tetrahedron, 73*(31), 4634-4643. [DOI:10.1016/j.tet.2017.06.038]

Schreglmann, S. R., Riederer, F., Galovic, M., Ganos, C., Kägi, G., & Waldvogel, D., et al. (2018). Movement disorders in genetically confirmed mitochondrial disease and the putative role of the cerebellum. *Movement Disorders, 33*(1), 146–155. [DOI:10.1002/mds.27174]

Sobel, E., & Davanipour, Z. (1996). Electromagnetic field exposure may cause increased production of amyloid beta and eventually lead to Alzheimer's disease. *Neurology, 47*(6), 1594–1600. [DOI:10.1212/WNL.47.6.1594]

Sokolov, A. A., Miall, R. C., & Ivry, R. B. (2017). The cerebellum: Adaptive prediction for movement and cognition. *Trends in Cognitive Sciences, 21*(5), 313–332. [DOI:10.1016/j.tics.2017.02.005]

Striemer, C. L., Chouinard, P. A., Goodale, M. A., & de Ribaupierre, S. (2015). Overlapping neural circuits for visual attention and eye movements in the human cerebellum. *Neuropsychologia, 69*, 9–21. [DOI:10.1016/j.neuropsychologia.2015.01.024]

Tekieh, E., Riahi, E., Kazemi, M., Sahraei, H., Tavakoli, H., & Aliyary, H., et al. (2017). Role of basal stress hormones and amygdala dimensions in stress coping strategies of male rhesus monkeys in response to a hazard-reward conflict. *Iranian Journal of Basic Medical Sciences, 20*(8), 951–957. [DOI:10.22038/IJBMS.2017.9120]

Tsujimoto, S., & Postle, B. R. (2012). The prefrontal cortex and oculomotor delayed response: A reconsideration of the "mnemonic scotoma". *Journal of Cognitive Neuroscience, 24*(3), 627–635. [DOI:10.1162/jocn_a_00171]

Van Schaik, C. P. (2016). *The primate origins of human nature*. Hoboken: Wiley. [Link]

Walkiewicz, A., Bulak, P., Brzezińska, M., Wnuk, E., & Bieganowski, A. (2016). Methane oxidation in heavy metal contaminated mollic gleysol under oxic and hypoxic conditions. *Environmental Pollution, 213*, 403–411. [DOI:10.1016/j.envpol.2016.02.048]

Wyszkowska, J., Shepherd, S., Sharkh, S., Jackson, C. W., & Newland, P. L. (2016). Exposure to extremely low frequency electromagnetic fields alters the behaviour, physiology and stress protein levels of desert locusts. *Scientific Reports, 6*, 36413. [DOI:10.1038/srep36413]

Zeng, G. L. (2017). *Image reconstruction: Applications in medical sciences*. Berlin: De Gruyter. [Link]