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Rose of Jericho Counters Extremely Low Frequency Electromagnetic Fields Dependent Cognitive and Behavioral Changes in Rats

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ABSTRACT

The substantial increase in human exposure to extremely low-frequency electromagnetic fields (ELF-EMFs) from mobile phones, domestic appliances, and power lines has raised concerns about their potential impact on cognitive functions. While some studies report cognitive improvements linked to ELF-EMFs via mechanisms such as increased neurogenesis and neurotrophic factor activity, others document negative outcomes like oxidative stress, DNA damage, anxiety-like behaviors, and cognitive impairment. This study evaluates the therapeutic potential of the Rose of Jericho on the cognitive and neuromotor functions in rats exposed to ELF-EMF. Thirty male Wistar rats were randomly divided into three groups: control, ELF-EMF exposed, and ELF-EMF exposed treated with Rose of Jericho. Rats were subjected to a 7-day ELF-EMF exposure protocol (50 Hz, 1 mT) and evaluated using the Morris Water Maze (MWM) for spatial memory, Elevated Plus Maze (EPM) for anxiety behavior, and Rotarod test for motor coordination. ELF-EMF exposure led to significant cognitive and behavioral impairments, including prolonged test duration in MWM, increased anxiety-like behavior in EPM, and reduced motor performance. Treatment with Rose of Jericho significantly reversed these effects, improving spatial memory, reducing anxiety, and improving motor coordination. Exposure to ELF-EMF impairs spatial memory, behavior, and motor coordination in rats. Rose of Jericho exhibits neuroprotective effects and may serve as a potential therapeutic agent against ELF-EMF-induced dysfunction. Further studies are warranted to confirm these findings and explore underlying mechanisms.

Keywords: Rose of Jericho, extremely low frequency, electromagnetic fields, memory, learning, cognition, behavior, motor coordination, stress.

INTRODUCTION

The use of mobile phones has increased tremendously during last two decades. This has caused a multifold increase in human exposure to radiation emitted from mobile phones. In addition to mobile phones, other hand-held devices such as tablets and domestic appliances such as microwave ovens are additional[1]. The exposure falls in the category of extremely low-frequency electromagnetic fields (ELF-EMFs), typically ranging from 3 to 300 Hz. In addition to mobile phones and domestic appliances, these ELF-EMFs are emitted from power as well. Some hand-held devices have been documented to be emitting magnetic fields up to 70.03 µT during active use[2]. Given the abundant nature of these exposures, exploring their potential cognitive effects has become a crucial public health concern[3].

The physical and cognitive effects of high voltage power lines have already been documented in monkeys[4]. Research studies particularly focusing on ELF-EMF have reported both positive and negative influences on neurocognitive performance. Exposure to ELF-EMF has been reported to enhance hippocampal neurogenesis and cognitive functions, potentially through the upregulation of neurotrophic factors like brain-derived neurotrophic factor (BDNF) and activation of the Notch signaling pathway in a rat model of brain ischemia[3-5]. However, alterations in physiological processes such as increased oxidative stress, DNA damage, and disruptions in calcium homeostasis have also been documented, potentially leading to impairment of cognitive processes[6]. Animal studies have shown that ELF-EMF exposure can result in anxiety-like behaviors and deficits in spatial learning and memory[7]. Based on this rather conflicting situation, it is apparent that a significant knowledge gap persists regarding the impact of ELF-EMF exposure on human cognition, especially in the long-term. The reported studies differ greatly in their methodologies, exposure durations, and field intensities, which may account for inconsistent results[8]. For these

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reasons, the formulation of clear public health guidelines has been halted[9].

Use of medicinal plants in reversing cognitive decline in many situations is gaining attention in contemporary neuroscience research. Many phytochemicals with antioxidant and anti-inflammatory properties have shown promising results in reversal of oxidative stress-induced cognitive impairment in various animal models[10,11]. The constituents of these phytochemicals such as polyphenolic compounds, flavonoids, and antioxidants are thought to be responsible for their neuroprotective potential[12,13]. Among these, the Rose of Jericho (Anastatica hierochuntica) (RoJ) is traditionally used in herbal medicine for its health benefits, including antioxidant and anti-inflammatory effects. RoJ has shown some promise in reversing cognitive decline in sleep deprived rodents[14]. However, its potential role in protecting against cognitive and motor dysfunctions induced by environmental stressors such as ELF-EMFs has not been thoroughly investigated.

This study aims to address this knowledge gap by evaluating the cognitive effects of ELF-EMF exposure in a controlled rodent model, focusing on spatial learning and memory assessed through the Morris Water Maze (MWM) test. Our results add significant knowledge to the ongoing debate about the safety and potential risks or benefits associated with ELF-EMF exposure. We published before about the therapeutic effect of natural products on cognitive function and behavior[14,15]. Herin, we further explore the possible therapeutic role of the Rose of Jericho in a rat model of ELF-EMF induced memory, learning, behavioral and neuromotor dysfunction.

MATERIALS AND METHODS

Ethical considerations: The study protocol was approved by the Research and Ethics Committee of the Arabian Gulf University (approval number: E23-PI-1-23) and adhered to the internationally recognized Guiding Principles for the Care and Use of Laboratory Animals [16]. All experimental procedures were performed by personnel trained and certified in laboratory animal handling. Upon completion of the study, euthanasia of all animals was carried out using carbon dioxide (CO_2) inhalation.

Experimental settings and animals: The experiments of this study were performed between January 01, 2024, and June 30, 2024, at the Animal House Unit of the College of Medicine and Health Sciences, Arabian Gulf University, Kingdom of Bahrain. Thirty male Wistar albino rats, each weighing 150-200 grams, were used. The rats were allowed to acclimatize for 10 days before starting the experiments. Rats were kept in an air-conditioned room (temperature 22±0.5˚C) with a 12-hour light/dark cycle and had access to standard laboratory chow and water and libitum.

Study groups: Rats were randomly assigned to three experimental groups (10 in each group) as follows: control (C) group (sham-exposed rats were subjected to the same experimental protocol as the ELF-EMF exposed ones except that the source of the electromagnetic field was inactivated), ELF-EMF exposed (ELF-EMF) group (rats followed a 7-day exposure to ELF-EMF protocol and received a daily morning single dose of 1 ml distilled water via oral gavage), and ELF-EMF RoJ-treated (ELF-EMF +RoJ) group (rats followed a 7-day exposure to ELF-EMF protocol and received 1 ml RoJ (5% extract, Dreams Oil Presses, Jeddah, SA) as single daily dose (250 mg/kg) via oral gavage[14,17]). All treatments were administered in the morning between 8 and 10 am.

Electromagnetic fields: Electromagnetic field exposure was generated using a Helmholtz coil system consisting of two coils, each 40 cm in diameter with 154 turns, positioned 20 cm apart. The experimental cage was centrally placed within this configuration. The coils were connected to a standard signal generator ensuring consistent voltage and frequency output. A 50 Hz sinusoidal current was applied to produce a relatively uniform alternating magnetic field with a mean intensity of 1 mT, verified using a PHYWE Digital Tesla Meter (PHYWE Systeme GmbH & Co. KG, Germany) with micro-Tesla sensitivity. The orientation of the magnetic field lines aligned with the horizontal component of the Earth's geomagnetic field. Background magnetic field levels at 50 Hz were maintained below 1 nT, as measured by a Multidetector II device (Gewerbegebiet Aaronia AG, Germany), also with a detection sensitivity of 1 nT[18,19].

Blinding of outcome assessors: To reduce potential bias and enhance the reliability of the findings, outcome assessors were blinded to group allocations throughout the study. Additionally, comprehensive measures were implemented to minimize animal stress during the sleep deprivation protocol and behavioral assessments.

Assessment of spatial memory and learning: Spatial learning and memory were evaluated using the Morris Water Maze (MWM) test following established protocols[14,15,20]. In this assay, rats were placed in an opaque water-filled pool and tasked with locating a submerged escape platform. After a five-day training period conducted post-acclimatization and prior to the sleep deprivation phase, animals demonstrated improved navigation, reflected in reduced swim distances, and increased speed. Key performance metrics recorded included total test duration (seconds), average swim speed (cm/sec), and total distance traveled (cm).

Assessment of anxiety-related behavior: Anxiety-related behavior was evaluated using the Elevated Plus Maze (EPM) test, following previously established methodologies[14,15,21]. The EPM consists of two open arms and two closed arms arranged in a plus-shaped configuration. Behavioral indicators of anxiety included the duration spent in open versus closed arms (in seconds) and the number of entries into the open arms. Prior to the experimental assessment, rats underwent a five-day training period following the acclimatization phase to ensure familiarity with the apparatus.

Assessment of motor function and coordination: Motor coordination and balance were assessed using the rotarod test, as described in previous studies[14,22]. This test evaluates neuromotor performance by engaging key neural structures such as the cerebellum and sensorimotor cortex. Rats were placed on an accelerating rotating rod, and the latency to fall defined as the time (in seconds) until the animal dropped from the apparatus was recorded as an indicator of motor coordination and the effects of stress.

Statistical analysis: Data from the Morris Water Maze, Elevated Plus Maze, and rotarod tests were analyzed using Origin Pro 2023 software (OriginLab Corporation, MA, USA). Normality of the data was assessed using the Kolmogorov-Smirnov test. Statistical comparisons were conducted using one-way analysis of variance (ANOVA), followed by Tukey's post-hoc test for multiple comparisons. Assumptions of the ANOVA model included independence, normal distribution, and homogeneity of variances. A 95% confidence level was applied, and results are reported as mean ± standard error of the mean (SEM). Differences were considered statistically significant at $p \leq 0.05$.

RESULTS

Effect of RoJ on spatial memory and learning

The MWM results demonstrated that exposure to ELF-EMF significantly increased test duration (33.54 ± 5.52 sec) and decreased

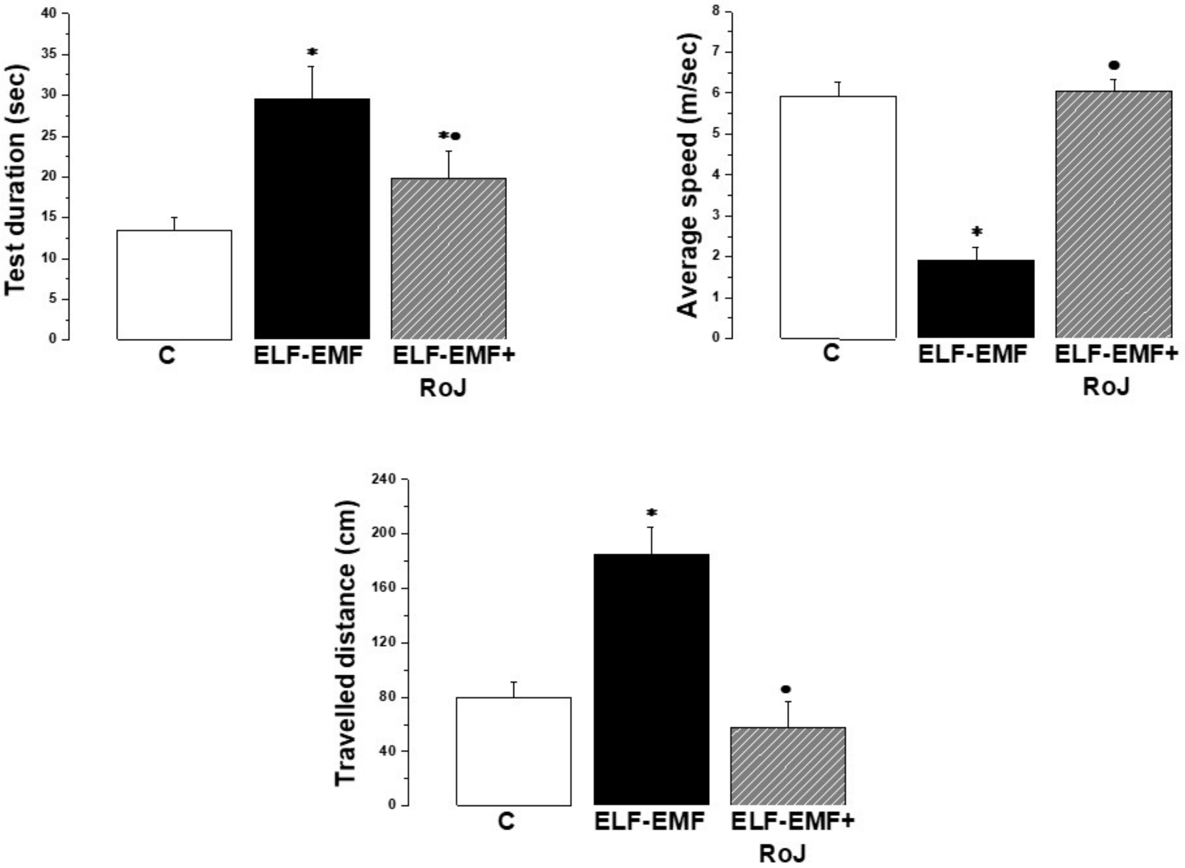

Figure 1. Treatment with Rose of Jericho improved spatial memory and learning in rats exposed to ELF-EMW performing Morris Water Maze test. [A] Test duration, [B] Average speed, [C] Travelled distance in control (C), ELF-EMW exposed (ELF-EMW), and ELF-EMW exposed treated with Rose of Jericho (ELF-EMW +RoJ) groups. Number of rats in each group was 10. P-value ≤0.05 was considered significant. * Indicates significance when compared to the C group. • Indicates significance when compared to the ELF-EMW group.

average speed (2.32 ± 0.41 sec) compared to corresponding values in the C group (13.57 ± 1.31 sec and 5.73 ± 0.12 sec respectively). Treatment with RoJ improved test performance in ELF-EMF exposed rats as evident by reducing test duration (7.38 ± 1.69 sec) and increasing speed (7.91 ± 0.71 sec) which was significantly different when compared to the corresponding values in the C and ELF-EMF groups ($p < 0.05$). Additionally, the ELF-EMF+RoJ group showed significant reduction in total distance traveled (59.56 ± 18.83 cm) when compared to the C and ELF-EMF groups (79.51 ± 11.72 and 184.91 ± 19.71 cm respectively) (Figure 1).

Effect of RoJ on behavior

As shown in figure 2, the EPM test results revealed significant behavioral differences across the study groups. Rats in the C group spent an average of 60.81± 13.85 sec in the open arms, while their counterparts in the ELF-EMF group spent significantly less time (16.24± 5.09 sec, $p \leq 0.05$). Rats in the ELF-EMF+RoJ group spent significantly longer time in the open arms when compared to the rats in the ELF-EMF group (65.83± 25.41 sec, $p \leq 0.05$). Understandably, control rats spent less time in the closed arms, when compared to the ELF-EMF rats (239.21± 13.85 vs 283.87± 15.49 sec respectively, $p \leq 0.05$). Treatment with RoJ significantly decreased the time spent in the closed arms when compared to the ELF-EMF group (224.82± 25.31 sec, $p \leq 0.05$). The number of entries dropped from 16.43± 1.58 in the C group to 5.21± 1.51 in the ELF-EMF group ($p \leq 0.05$), while it increased significantly in the ELF-EMF+RoJ group (25.23 ± 2.92 entries) when compared to the to both the C and ELF-EMF groups ($p \leq 0.05$).

Effect of RoJ on motor coordination

The Rotarod test results showed significant differences in motor coordination among the studies groups. The latency to fall in the C group was 246.86 ± 37.34 sec, which was significantly longer than the corresponding value in the ELF-EMF group (85.41 ± 26.93 sec, $p \leq 0.05$). Rats in the ELF-EMF+RoJ group showed significant improvement as evident by a longer latency to fall when compared to both the C and ELF-EMF groups (141.47 ± 18.29 sec, $p \leq 0.05$) (Figure 3).

DISCUSSION

Using a rodent model, this the present study investigated the cognitive and behavioral impairments induced by extremely low-frequency magnetic field (ELF-MF) exposure and the potential therapeutic effects of *Rose of Jericho* (RoJ) extract in reversing these deficits. Our findings align with previous studies that have reported ELF-MF-induced anxiety-like behaviors, motor impairments, and cognitive deficits[23]. Notably, RoJ supplementation demonstrated significant neuroprotective effects across all behavioral paradigms, suggesting its potential as a therapeutic agent against ELF-MF-induced neurotoxicity.

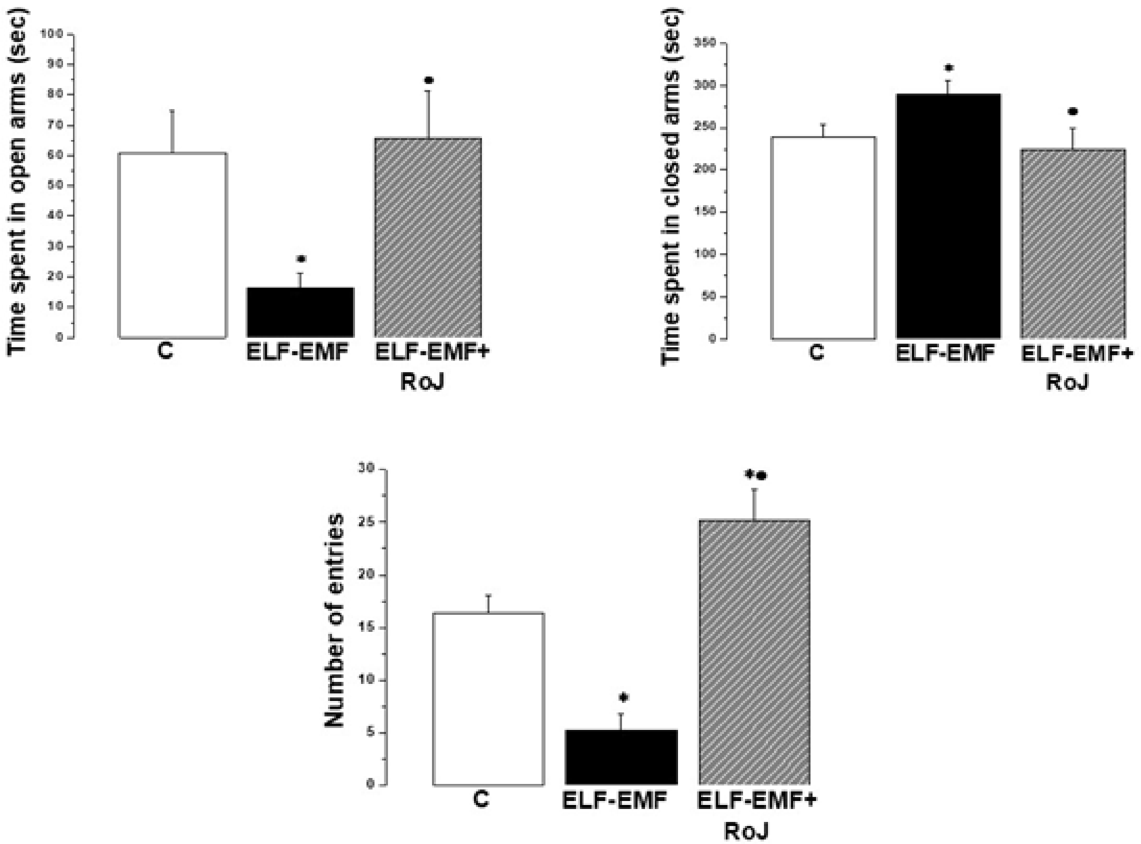

Figure 2. Treatment with Rose of Jericho decreased anxiety in rats exposed to ELF-EMW in Elevated Plus Maze test. [A] Time spent in open arms, [B] Time spent in closed arms, [C] Number of entries in control (C), ELF-EMW exposed (ELF-EMW), and ELF-EMW exposed treated with Rose of Jericho (ELF-EMW +RoJ) groups. Number of rats in each group was 10. P-value ≤0.05 was considered significant. * Indicates significance when compared to the C group. • Indicates significance when compared to the ELF-EMW group.

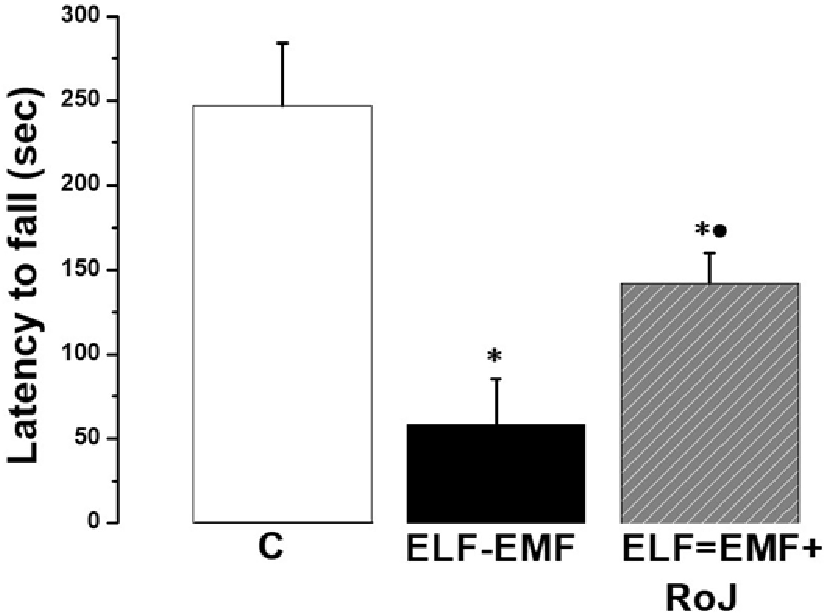

Figure 3. Rotarod test results show improvement of motor coordination in rats exposed to ELF-EMW rats treated with Rose of Jericho. Latency to fall in control (C), ELF-EMW exposed (ELF-EMW), and ELF-EMW exposed treated with Rose of Jericho (ELF-EMW +RoJ) groups. Number of rats in each group was 10. P-value ≤0.05 was considered significant. * Indicates significance when compared to the C group. • Indicates significance when compared to the SD group.

The significant reduction in open arm time and entries in the EPM among ELF-MF-exposed mice indicates heightened anxiety, consistent with previous research linking ELF-MF exposure to increased anxiety-like behaviors in rodents[24]. More time spent in closed arms further supports an anxiogenic effect of ELF-MF. This may result from ELF-MF-induced dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and increased oxidative stress, both of which are implicated in anxiety pathophysiology[25]. RoJ treatment resulted in significant reversal of the behavioral and cognitive deficit caused by ELF-MF exposure. In the EPM, RoJ not only restored time spent in open arms but also improved exploratory behaviors. This suggests a potential anxiolytic effect of RoJ, in addition to the antioxidant and anti-inflammatory effects of RoJ that have been reported to modulate neurotransmitter systems and reduce oxidative stress[14].

Motor coordination, assessed via the Rotarod test, was significantly impaired following ELF-MF exposure. Previous studies suggest that ELF-MFs may interfere with cerebellar function and neurotransmitter balance, leading to motor deficits[26]. Our findings are supported by these observations, with ELF-MF-exposed mice showing a significant reduction in latency to fall. It is interesting to note that treatment with RoJ improved motor performance in the Rotarod test, although partially. The recovery suggests that RoJ may enhance motor function through neuroprotective mechanisms, possibly by reducing the effects of ELF-MF-induced oxidative stress[26,27].

In the water maze test, ELF-MF exposure resulted in marked spatial learning and memory deficits, as evidenced by prolonged test durations, and increased total distance traveled. These findings align with earlier reports indicating that ELF-MFs can impair hippocampal-dependent cognitive functions, possibly through disruptions in synaptic plasticity and neurogenesis[19,28]. In another report, published earlier, it was also shown that the ELF MF exposure alters the synaptic plasticity in hippocampal areas in mice, thus leading to a compromise in hippocampal function[29]. The results obtained in our study validate the earlier findings. Here again, RoJ effect was notable as RoJ treated mice exhibited shorter duration and less time in swimming, showing enhanced spatial learning and memory. Apparently, the neuroprotective effects of RoJ, discussed earlier, helped reverse the deficits induced by the ELF-MF exposure.

However, these findings are in opposite to other studies that reported cognitive enhancements following ELF-EMF exposure. For example, Gao et al. (2021) reported that ELF-EMF exposure promoted hippocampal neurogenesis and improved spatial learning in rats with cerebral ischemia[4]. While this difference needs further explanation, it may be hypothesized that the brain injury model used in the above-mentioned study may have different baseline conditions altogether. In addition, it is possible that differences in exposure parameters, including field intensity, frequency, and duration, as well as variations in experimental models and cognitive assessment methods may be at play.

The underlying mechanisms through which ELF-EMFs influence cognitive functions remain complex and multifactorial. Oxidative stress, and alterations in neurotransmitter systems have all been implicated. Increased intracellular calcium levels, resulting from ELF-EMF exposure, can disrupt synaptic plasticity and lead to cognitive impairments[30,31]. Moreover, the effects of chronic exposure may be different than acute exposure. Our results contribute to this complex narrative by demonstrating that while ELF-EMF exposure can affect cognitive performance, the specific outcomes depend on various factors, including exposure conditions and biological susceptibility. These findings underline the importance of standardized research methodologies to better understand ELF-EMF effects on cognition.

CONCLUSION

This study demonstrates that exposure to 50 Hz, 1 mT ELF-EMFs can impair spatial learning and memory in rodents, indicating potential cognitive risks. These findings highlight the need for further research on underlying mechanisms and long-term effects. However, our study has certain limitations. The results are based on correlation and no causal link was established. Further studies to establish causal links are needed in future.

Authorship Contribution: Authors testify that all persons designated as authors qualify for authorship and have checked the article for plagiarism. If plagiarism is detected, all authors will be held equally responsible and will bear the resulting sanctions imposed by the journal thereafter.

Potential Conflicts of Interest: None

Competing Interest: None

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