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Impact of extremely low-frequency magnetic fields on neuroinflammation and synaptic protein development in prenatal and postnatal rat brains

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Brain development during prenatal and postnatal periods is critical, and external stressors such as electromagnetic fields can significantly influence this process. Although there are numerous studies on this topic, our understanding of how electromagnetic fields affect the central nervous system remains limited. In this study, we investigated the effects of extremely low-frequency magnetic fields (ELF-MF) on the developing brains of Sprague-Dawley rats. The rats were exposed to 50 Hz, 500 μT ELF-MF during prenatal, postnatal, or both periods. Using ELISA, we assessed inflammatory markers and synaptic protein levels in two brain regions. Combined prenatal and postnatal exposure to ELF-MF significantly increased IL-17A levels in the hippocampus and cortex and elevated IFN-γ levels in the cortex. However, there was no change in IL-4 levels. Additionally, in the combined prenatal and postnatal exposure group, ELF-MF significantly reduced PSD-95 levels in both the cortex and hippocampus, and Syn1 levels in the hippocampus. Our results suggest that ELF-MF may trigger inflammation in the brains of young rats, potentially impairing synaptic transmission, particularly in the hippocampus where reduced Syn1 may limit presynaptic neurotransmitter release. This study provides new insights into the impact of ELF-MF on brain development and underscores the need for further research in this field.

Keywords: ELF-MF, IL-17A, IFN-γ, Developing Brain, Neuroinflammation

Brain development is a complex and critical process that begins in the prenatal period and continues until puberty, influenced by various physical and environmental factors[1,2]. During this time, neural progenitor cells play a vital role in the molecular and cellular differentiation necessary for proper brain formation. In the early stages of embryonic development, particularly during the first two weeks, there is a high proliferation of stem cells, including embryonic neuronal stem cells, which are essential for the formation of the fetal nervous system[3].

The differentiation of these stem cells into neuronal and glial cells is a crucial step in neurogenesis, with each stage being fundamental to the overall development and health of the nervous system. Disruptions during these stages can lead to neuroinflammation and subsequent cell death, highlighting the importance of each step in developmental neurogenesis[4,5].

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Electromagnetic fields (EMFs) are environmental stressors of increasing concern due to their ubiquitous presence in modern life. Power-line freuency fields (50/60 Hz), known as extremely low-frequency magnetic fields (ELF-MF), are among the most widespread electromagnetic exposures in modern life[6].

Classified as a possible human carcinogen (Group 2B) by the International Agency for Research on Cancer (IARC)[7], 50 Hz ELF-MF are subject to occupational exposure limits recommended by International Commission on Non-Ionizing Radiation Protection (ICNIRP) and endorsed by the WHO[8,9].

The potential health risks associated with ELF-MF exposure first came to light following an epidemiological study that linked it to childhood leukemia[10].

This study prompted numerous in vivo and in vitro experiments to further investigate the effects of ELF-MF[11-13]. However, the mechanisms underlying these effects remain poorly understood, with research producing contradictory results[13]. Beyond cancer risk, there is growing interest in how ELF-MF exposure might affect neurodevelopment and cognitive function[14].

Neural progenitor cell differentiation into astrocytes and oligodendrocytes is highly sensitive to environmental stressors such as EMFs1[5], and disruptions during this process can have lasting consequences for brain development and function.

ELF-MF exposure during the embryonic stage alters transcription of apoptosis-related genes in embryonic stem cell–derived neurons, underscoring their vulnerability to electromagnetic stress[16-18]. Moreover, ELF-MF exposure during embryonic development has been associated with growth retardation and an increased risk of congenital anomalies, suggesting potential toxic effects on the developing fetus[19].

Several animal studies have demonstrated that exposure to 50 Hz ELF-MF can negatively affect hippocampal neuronal structures and related cognitive functions, such as recognition memory and synaptic plasticity[20,21]. Additionally, ELF-MF exposure has been linked to an increased incidence of brain tumors[22] and a decrease in neuron numbers within the hippocampus of the central nervous system (CNS) in children[23,15]. Prenatal ELF-MF exposure has been linked to cognitive and memory impairments in offspring, potentially disrupting hippocampal-dependent functions during critical developmental windows[21,24,25]. Rodents exposed in utero to ELF-MF have shown deficits in spatial memory and reduced hippocampal neuron density, potentially due to impaired synaptic plasticity and long-term potentiation mechanisms[26].

Additionally, ELF-MF exposure has been associated with increased permeability of the blood–brain barrier (BBB), especially under vulnerable physiological conditions like diabetes, where leakage of albumin-bound dyes into brain tissue has been observed[27]. Moreover, ELF-MF exposure has been shown to alter voltage-gated sodium and potassium channel currents in hippocampal CA1 pyramidal neurons, potentially disrupting ionic homeostasis and contributing to altered neural function[28].

Understanding how ELF-MF exposure interacts with the developing immune and synaptic systems requires the careful selection of biologically meaningful markers. Given the sensitive nature of neural cells, this study investigated by analyzing the effects of continuous exposure to extremely low-frequency magnetic fields (50 Hz, 500 μT). The magnetic flux density of 500 μT was selected to establish a controlled high-level experimental exposure model during sensitive developmental windows and to allow comparison with previous experimental ELF-MF studies investigating biological, inflammatory, and neurodevelopmental outcomes. This intensity is higher than typical residential or environmental ELF-MF exposure levels and exceeds the ICNIRP reference level for general public exposure at 50 Hz; however, it remains below the ICNIRP occupational reference level for 50 Hz magnetic field exposure. Therefore, 500 μT was not intended to represent ordinary daily environmental exposure, but rather to evaluate biological responses under sustained high-intensity exposure conditions that may be relevant to certain occupational or technical environments. The exposure was produced by a calibrated Merritt coil system during critical developmental periods: prenatal (gestational days 0–21) and postnatal (PND 0–21).

Interleukin-4 (IL-4), Interleukin-17A (IL-17A) and interferon-gamma (IFN-γ) were selected as representatives of the T helper 1 (Th1), T helper 17 (Th17), and T helper 2 (Th2) pathways, given their established roles in neuroinflammation and ELF-MF–related immune responses[29-31]. Postsynaptic density protein-95 (PSD-95) and Synapsin 1 (Syn1) were included as synaptic markers for postsynaptic integrity and presynaptic function, both sensitive to neuroinflammatory and electromagnetic stress[32,33]. Together, this panel enables a focused evaluation of ELF-MF–induced neuroinflammatory and synaptic changes in the developing brain.

Materials and Methods

Animal model

This study was approved by the Ethics Committee of Bezmialem University (Approval ID 2020/25). Sprague-Dawley rats were purchased from the Bezmialem University Experimental Research Laboratory and the experiment was carried out in the same laboratory.

The Control Group was formed and received no exposure at any period and duration, served as the sham group for the study. Combined Group was exposed both prenatally (from the first day of pregnancy to birth, i.e., the entire gestation period (21 days) and postnatally (the first 21 days after birth). Prenatal Group was exposed only prenatally, Postnatal Group only postnatally. All exposures were continuous (24 h/day) (Fig.1). Tissue collection was performed on PND21.

All animals were housed at 22°C±1 on a 12h/12h light-dark cycle and had ad libitum access to water and food. The experimental groups were formed as follows. Eight healthy female Sprague-Dawley rats aged 4 months were mated in separate cages. After confirmation of pregnancy, the pregnant dams were randomly assigned to four experimental groups, with two dams in each group: Control, Combined, Prenatal, and Postnatal groups. Thus, a total of four pregnant dams, corresponding to the Combined and Prenatal groups, were exposed to ELF-MF during gestation. The remaining four dams, corresponding to the Control and Postnatal groups, were not exposed during pregnancy. The average litter size was approximately seven to ten pups per dam. After birth, offspring were selected from the litters of the two dams assigned to each group in a balanced manner. The sample size indicated for each group refers to the number of offspring, not the number of dams. Accordingly, the offspring constituted the unit of analysis, while the dams were not included in the biochemical analyses.

Control Group (n=14): No ELF-MF exposure (sham group).

Combined Group (n=14): Exposed to ELF-MF both before birth (prenatal) and after birth (postnatal) for 21 days each (21d+21d=42 days).

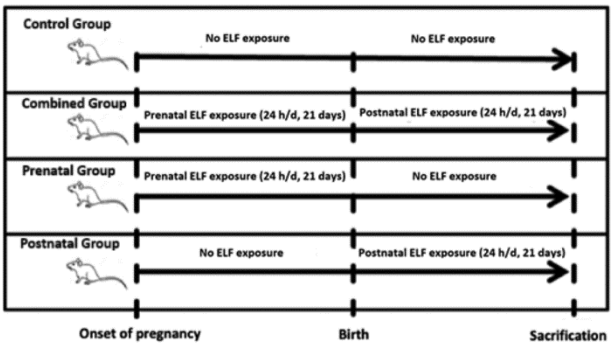

Fig. 1 — Experimental design illustrating the periods and durations of extremely low frequency magnetic field (ELF-MF) (50 Hz, 500 μT) exposure.

Prenatal Group (n=10): Exposed to ELF-MF only before birth for 21 days.

Postnatal Group (n=10): Exposed to ELF-MF only after birth for 21 days.

The number of animals in the groups differed as allowed by the ethics committee and depended on the numbers obtained from births. All offspring were sacrificed 3 weeks after birth. The mothers were not included in the study but were kept with their offspring throughout the experiment.

ELF-MF Exposure

Rats were exposed to ELF-MF using a Merritt coil system as shown in Fig. 2. The uniform magnetic field strength produced by the Merritt coil system[34,35] was confirmed using a calibrated gaussmeter and adjusted to 500 μT at the center of the exposure chamber.

The first drawing shows the height, depth and width of the Merritt coil system setup (175 cm, 125 cm, and 125 cm, respectively). Four square coils were used to generate 50 Hz, 500 μT ELF-MF. The "26/11/11/26" notation indicates the number of windings in the 1st through 4th square coils, respectively. Cages were used to house the animals in the system. Shelves used for cage placement are spaced at 47 cm – 32 cm – 47 cm from top to bottom to ensure symmetric positioning within the uniform magnetic field region.

Animals were housed in individual Plexiglas cages (42.7 × 28.7=1225 cm² floor area), with two to three animals per cage. These cages were placed on the shelves (90 × 90 cm each) of a custom-designed Merritt coil system composed of four square coils. The inner coils had 11 turns, and the outer coils had 26 turns, wound using AWG 5 enamel-coated solid copper wire (radius = 0.462 cm). A variac-controlled

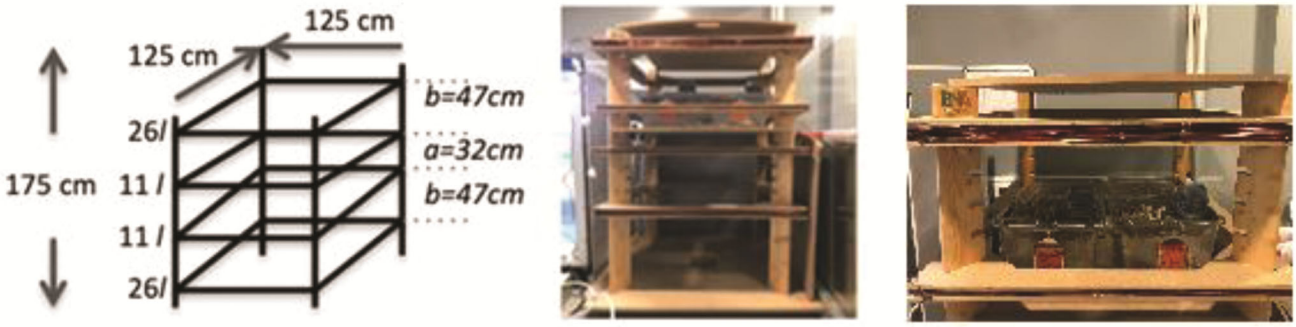

Fig. 2 — Schematic representation and actual image of the Merritt coil system used for ELF-MF exposure.

AC power supply was used to generate a continuous, sinusoidal 50 Hz magnetic field with a flux density of 500 ± 8 μT, applied 24 h/day throughout the exposure period. Exposure durations were 21 days during gestation (prenatal) and/or 21 days postnatally, depending on the group.

The magnetic field distribution was verified using a Narda EHD50D probe with 6-minute averaging, and background field measurements in the same room were 10–12 μT with the coils turned off. All animals were exposed simultaneously and housed within their own cages inside the coil system throughout the exposure period. The layout and positioning of the cages within the field are shown in Fig. 2. No increase in temperature was detected in the wires or the environment during operation. Relative humidity and ambient temperature were kept constant at 50 ± 10% and 22 ± 1°C, respectively. No other magnetic field-generating equipment was present in the exposure room, and the use of a Faraday cage was deemed unnecessary due to its ineffectiveness at shielding low-frequency magnetic fields. The induced electric field was measured as ~0.0031 V/m, remaining well below the ICNIRP basic restriction limit (0.1 V/m) for CNS exposure[8].

Homogenate preparation

Cerebral cortex and hippocampus were dissected from offspring brains immediately after sacrifice. Brain tissues from the Control and ELF-MF groups were rapidly removed, placed on ice, and the hippocampus and cortex were separated. Each tissue homogenate was washed in ice-cold phosphate-buffered saline to remove residual blood and weighed prior to homogenization. Tissues were minced with a scalpel on an ice-cold surface and homogenized using a motorized homogenizer in ice-cold lysis buffer (pH 7.4) at a tissue-to-buffer ratio of 1:9 (w:v). The lysis buffer contained 50 mM Tris-HCl, 150 mM NaCl, 1% Triton X-100, 0.1% SDS, and was supplemented immediately before use with a commercial protease inhibitor cocktail (Sigma-Aldrich) to prevent protein degradation. All homogenization procedures were carried out on ice to maintain protein integrity. Homogenates were centrifuged at 15,000 rpm for 15 min at 4°C, and the resulting supernatants were collected. Supernatants were either used immediately for Enzyme-Linked Immuno-Sorbent Assay (ELISA) assays or aliquoted and stored at −80°C until analysis to avoid repeated freeze–thaw cycles.

Measurement of cytokine and synaptic protein levels

IL-4, IL-17A and IFN-γ cytokine quantification analyses of the homogenates were performed using an ELISA kit (Bioassay Technology Laboratory, China) according to the manufacturer's instructions. All reagents were kept at room temperature. Homogenates, diluted standards and the detection antibody were added to the plate. Then 50 μl of Streptavidin-HRP solution was added to all the wells. After 1 h incubation at 37°C, the wells were washed and the substrate solutions (Substrate A and B) were added and plates were maintained at 37°C for 10 minutes in the dark before the addition of stop solution. The absorbance was read at 450 nm using a microplate reader. Syn1 and PSD-95 analyses of the homogenates were performed using the ELISA kit (Bioassay Technology Laboratory, China) according to the manufacturer's instructions.

Statistical Analysis

Normality of data distribution for each group was assessed using the Shapiro–Wilk and D'Agostino–Pearson tests in GraphPad Prism (v10). Datasets that did not meet normality assumptions were analyzed using the Kruskal-Wallis test followed by Dunn's multiple comparisons test, whereas datasets that passed normality were analyzed using one-way ANOVA followed by Tukey's post hoc test. All data are presented as mean ± SEM, and a significance level of $p < 0.05$ was considered statistically significant. To explore predictive links between cytokine levels (IL-17A, IFN-γ, IL-4) and synaptic protein expression (PSD-95, Syn1) in the cortex and hippocampus, we performed correlation and linear regression analyses, with cytokine levels as independent variables (X) and synaptic protein values as dependent variables (Y). We used Pearson's correlation when both variables passed normality tests and Spearman's rank correlation otherwise. Linear regression was fitted to each cytokine–protein pair, and 95% confidence intervals (CI) were reported for the slope and intercept. GraphPad Prism (v10) was used to compare regression slopes and intercepts across groups within an ANCOVA framework, and goodness of fit was expressed as R^2. Assumptions of normality and homogeneity of variance were tested prior to analysis. Data were analyzed separately for the cortex and hippocampus regions, and scatter plot graphs were used to summarize group-wise comparisons.

Results

Cytokine and Synaptic Protein Levels

IL-17A levels in the cortex were highest in Combined Group (100.71 ± 3.63 ng/L), followed by Prenatal Group (89.27 ± 2.15 ng/L), Postnatal Group (85.76 ± 4.37 ng/L), and the Control Group (82.99 ± 4.58 ng/L). Ordinary one-way ANOVA with Tukey's post hoc tests revealed a significant increase in Combined Group compared to the Control Group ($p = 0.0127$, Mean Diff: 17.73; 95% CI: 3.238 to 32.22). IL-4 levels in the cortex were relatively similar across all groups: Control Group (88.07 ± 4.90 ng/L), Prenatal Group (84.46 ± 5.17 ng/L), Combined Group (82.47 ± 3.94 ng/L), and Postnatal Group (82.41 ± 4.87 ng/L). No statistically significant differences were observed between the groups. IFN-γ levels in the cortex were highest in Combined Group (43.82 ± 2.43 ng/L), followed by Postnatal Group (35.85 ± 3.80 ng/L), Prenatal Group (34.05 ± 3.70 ng/L), and the Control Group (30.64 ± 3.32 ng/L). Group differences were analyzed using the Kruskal–Wallis test followed by Dunn's post hoc for multiple comparisons, which revealed a significant increase in Combined Group compared to the Control Group ($p = 0.028$, IQR:11.62, Dunn test).

IL-17A levels in the hippocampus were highest in Combined Group (77.50 ± 4.08 ng/L), followed by Postnatal Group (63.13 ± 4.75 ng/L), Prenatal Group (61.02 ± 4.67 ng/L), and the Control Group (62.16 ± 3.60 ng/L). Ordinary one-way ANOVA with Tukey's post hoc tests revealed a significant increase in Combined Group compared to the Control Group ($p = 0.024$; Mean Diff: 15.34; 95% CI: 0.1217 to 30.57).

IL-4 levels in the hippocampus were similar across all groups: Control Group (62.15 ± 3.22 ng/L), Prenatal Group (61.85 ± 3.65 ng/L), Postnatal Group (60.82 ± 4.00 ng/L), and Combined Group (60.18 ± 3.63 ng/L), with no statistically significant differences observed.

IFN-γ levels in the hippocampus were slightly elevated in Combined Group (44.14 ± 8.52 ng/L), compared to Prenatal Group (40.36 ± 2.51 ng/L), Postnatal Group (39.69 ± 3.00 ng/L), and the Control Group (38.98 ± 1.88 ng/L), but the differences were not statistically significant. As shown in Fig. 3, in the comparison of cytokine levels, IL-17A and IFN-γ levels were significantly increased in the cortex of the group exposed to magnetic field in the combined periods, and only IL-17A levels were significantly higher in the hippocampus compared to the Control Group.

Data are presented as mean ± SEM, with all ELISA measurements performed in duplicate. Normality was assessed using the Shapiro Wilk test. Datasets that did not meet normality assumptions IFN-γ in the cortex and IL-4 in the hippocampus were analyzed using the Kruskal–Wallis test, followed by Dunn's multiple comparisons test. All remaining datasets met normality criteria and were analyzed using one-way ANOVA, followed by Tukey's post hoc test.

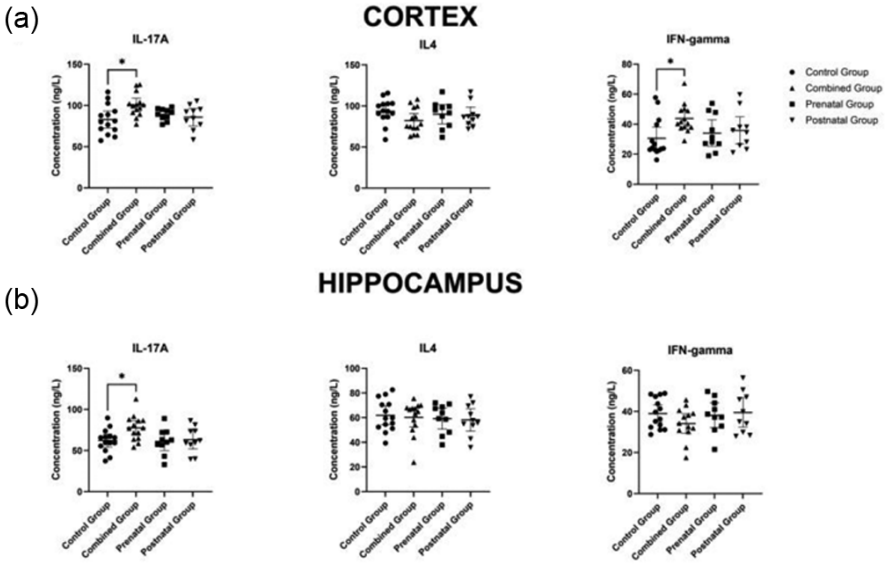

Fig. 3 — Effects of ELF-MF exposure on IL-17A, IL-4 and IFN-γ concentrations (ng/L) in the cortex; (a) and hippocampus, (b) of rat offspring. Combined: prenatal + postnatal ELF-MF (n = 14), Prenatal: prenatal ELF-MF (n = 10), Postnatal: postnatal ELF-MF (n = 10), and Control (sham) group (n = 14).

Syn1 and PSD-95 concentration graphs for the hippocampus region are presented in Fig. 4. Syn1 levels in the hippocampus were highest in the Control Group (1.41 ± 0.05 ng/L), followed by Prenatal Group (1.28 ± 0.07 ng/L), Postnatal Group (1.26 ± 0.08 ng/L), and Combined Group (1.16 ± 0.05 ng/L). Ordinary one-way ANOVA with Tukey's post hoc tests revealed a significant reduction in Combined Group compared to the Control Group ($p = 0.035$; Mean Diff: -0.2502; 95% CI: -0.4687 to -0.03160). PSD-95 levels in the hippocampus were highest in the Control Group (1.92 ± 0.17 ng/L), followed by Postnatal Group (1.81 ± 0.15 ng/L), Prenatal Group (1.74 ± 0.16 ng/L), and Combined Group (1.29 ± 0.10 ng/L). Group differences were analyzed using the Kruskal–Wallis test followed by Dunn's post hoc test for multiple comparisons, tests revealed a significant reduction in Combined Group compared to the Control Group ($p = 0.037$, IQR=1.29). As shown in Fig. 4, in the comparison of synaptic protein levels, Syn1 and PSD-95 levels were significantly decreased in the hippocampus of the group exposed to the magnetic field during combined period compared to the Control Group.

Syn1 and PSD-95 concentration graphs for the cortex region are presented in Fig. 5. Syn1 levels in the cortex were highest in the Control Group (1.20 ± 0.08 ng/L), followed by Postnatal Group (1.16 ± 0.09 ng/L), Prenatal Group (1.16 ± 0.07 ng/L), and Combined Group (1.15 ± 0.04 ng/L). The differences between groups were not statistically significant. PSD-95 levels in the cortex were highest in the Control Group (2.37 ± 0.24 ng/L), followed by Prenatal Group (1.84 ± 0.27 ng/L), Postnatal Group (1.79 ± 0.26 ng/L), and Combined Group (1.40 ± 0.15 ng/L). Dunn post hoc tests revealed a significant decrease in Combined Group compared to the Control Group ($p = 0.025$: IQR: 1.067). As shown in the bar graph in Fig. 5, Syn1 levels in the cortex did not differ significantly between groups, whereas PSD-95 levels were significantly reduced in combined compared to the Control Group.

To explore predictive relationships between inflammatory mediators and synaptic proteins, we conducted linear regression analyses in the cortex and hippocampus. In the cortex (Fig. 6A), IL-17A levels positively correlated with PSD-95 expression in Combined Group. The regression slope was significant ($\beta = 0.0241$, 95% CI 0.0039–0.0444, $R^2 = 0.359$, $p = 0.0235$). This means higher IL-17A concentrations predicted increased PSD-95 levels. In the hippocampus (Fig. 6B), IFN-γ levels showed a significant negative correlation with Syn1 in Prenatal Group ($\beta = –0.0133$, 95% CI –0.0243 to –0.0023, $R^2 = 0.491$, $p = 0.0240$). In other words, increased IFN-γ and decreased Syn1 expression are correlated. Also, in the hippocampus (Fig. 6C), IL-4 showed a significant negative relationship with Syn1 in Prenatal Group ($\beta = –0.0142$, 95% CI –0.0254 to –0.0030, $R^2 = 0.519$, $p = 0.0189$). This indicates that higher IL-4 levels predicted decreased Syn1 expression.

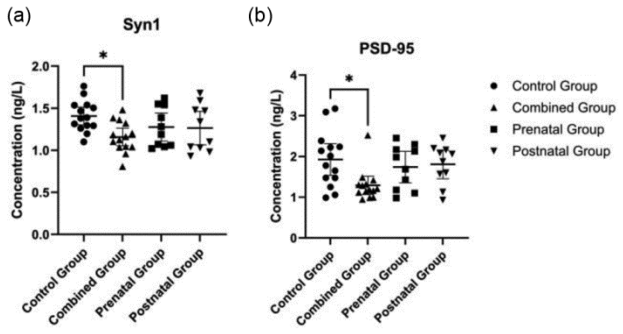

Fig. 4 — Effects of ELF-MF exposure on Syn1 and PSD-95 concentrations (ng/L) in the hippocampus of rat offspring from four groups: Combined Group (prenatal + postnatal ELF-MF) (n=14), Prenatal Group (prenatal ELF-MF) (n=10), Postnatal Group (postnatal ELF-MF) (n=10), and Control Group (sham control) (n=14). Data are presented as mean ± SEM, with all ELISA measurements performed in duplicate. **A)** Syn1 levels were significantly reduced in the hippocampus of Combined Group compared to the Control Group ($p = 0.035$). **B)** PSD-95 levels were also significantly decreased in the hippocampus of Combined Group compared to the Control Group ($p = 0.037$). * $p < 0.05$ compared with the Control Group.

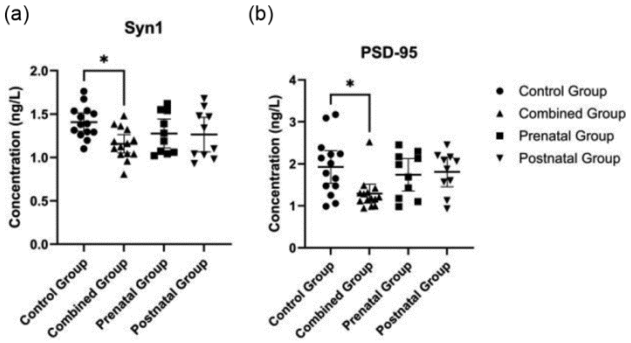

Fig. 5 — Effects of ELF-MF exposure on Syn1 and PSD-95 concentrations (ng/L) in the cortex of rat offspring from four groups: Combined Group (prenatal + postnatal ELF-MF) (n=14), Prenatal Group (prenatal ELF-MF) (n=10), Postnatal Group (postnatal ELF-MF) (n=10), and Control Group (sham control) (n=14). Data are presented as mean ± SEM, and with all ELISA measurements performed in duplicate. **A)** Syn1 levels in the cortex did not show a significant difference between groups. **B)** PSD-95 levels were significantly decreased in the cortex of combined compared to the Control Group ($p = 0.025$). * $p < 0.05$

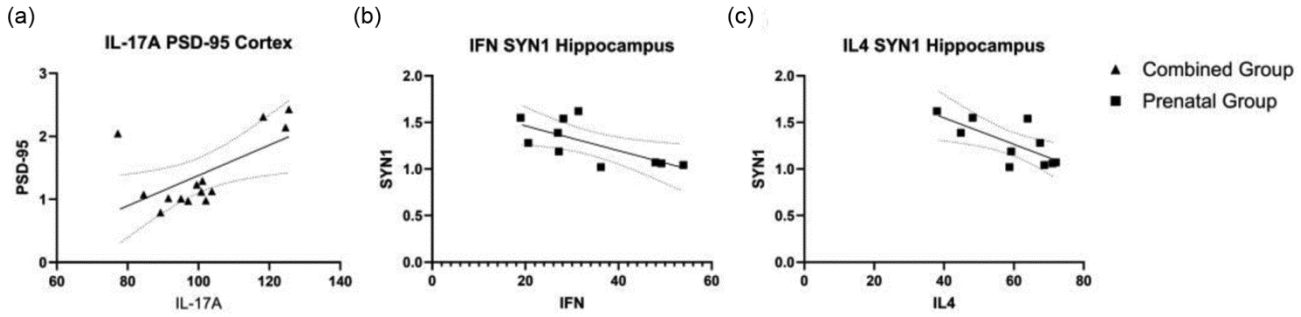

Fig. 6 — Regression analyses of cytokine levels and synaptic protein expression in cortex and hippocampus. A) In the cortex, IL-17A levels were significantly associated with PSD-95 expression, with higher IL-17A predicting increased PSD-95. B) In the hippocampus, IFN-γ levels showed a negative relationship with Syn1 levels, which reached statistical significance. C) In the hippocampus, IL-4 levels were significantly and inversely associated with Syn1 indicating that higher IL-4 predicted reduced Syn1 expression. Each dot represents data from an individual animal. Solid lines indicate best-fit linear regression; dotted lines represent 95% confidence intervals of the regression.

Overall, these analyses show that cytokine–synaptic protein interactions vary by region and group. Positive associations occur in the cortex, while negative ones occur in the hippocampus with increased inflammatory signaling. Although IL-4 levels did not differ between groups, exploratory regression suggested that within Prenatal Group higher IL-4 values were associated with lower Syn1 indicating that even subtle shifts in cytokine balance may affect presynaptic proteins.

Discussion

This study investigated the neurological effects of continuous exposure to ELF-MF at 500 μT and 50 Hz during the developmental stages of Sprague Dawley rats. Our objective was to establish a controlled high-level experimental exposure model by applying a homogeneous, sinusoidal magnetic field during critical periods of brain development: prenatal and early postnatal. Unlike previous studies that primarily focus on postnatal or adult periods[13,14], our experimental design enabled us to assess the combined effects of both prenatal and postnatal ELF-MF exposure on cytokine levels and synaptic proteins in the cortex and hippocampus[36]. One notable finding in our study was that only the group exposed to ELF-MF both before and after birth (Combined Group) showed significant changes in inflammatory and synaptic markers. In contrast, exposure during prenatal (Prenatal Group) or postnatal (Postnatal Group) period did not have similar effects. This suggests that the timing and total amount of exposure are both crucial in determining how susceptible the brain is to ELF-MF during development[36].

In the combined exposure group, we detected a significant increase in IL-17A levels in both the cortex and hippocampus, alongside a slight rise in IFN-γ levels, particularly in the cortex. The increase in IFN-γ in the hippocampus did not reach statistical significance. These results may suggest a shift toward Th17- and Th1-related inflammatory signaling in the developing brain. IL-17A is known to play a crucial role in central nervous system inflammation, disrupting BBB integrity and affecting cortical lamination[18,36-39]. In models of maternal immune activation, elevated IL-17A has been linked to increased microglial clustering, accelerated phagocytosis of progenitor cells, and lasting behavioral changes in cortical circuits. Our findings suggest that ELF-MF may foster a Th17-dominated inflammatory environment during critical neurodevelopmental periods[37,39]. Our findings resonate with earlier research revealing ELF-MF's impact on the Th1/Th17 response. Öztürk *et al.*[31], uncovered that prenatal and postnatal ELF-MF exposure increased IL-17A and IFN-γ levels in rats, while IL-4 levels stayed the same. In line with this, Salehi *et al.*[29], and Sobhanifard et al.[30], demonstrated ELF-MF's role in reshaping the cytokine profile, favoring a Th1/Th17 rather than Th2 response. This immune transformation has been consistently linked to neurodevelopmental disorders, cognitive decline, and behavioral changes [21,23,24].

Our study's lack of increased IL-4 in the cortex further underscores that the inflammatory response did not shift toward a Th2-related profile, indicating a persistent Th1/Th17-skewed immune profile rather than a Th2 response. The combined elevation of IL-17A and IFN-γ in the cortex may exacerbate

neuroinflammation by enhancing microglial activation. IL-17A is known to stimulate microglia[36,40], while IFN-γ directs them towards a neurotoxic phenotype through iNOS production, increased nitric oxide, and oxidative stress[41-43]. The more pronounced increase in IFN-γ in the cortex compared to the hippocampus suggests regional differences in glial cell responses to environmental stimuli[40,42]. This type of regional variability may help explain why specific brain regions exhibit greater susceptibility to inflammation. Evidence from both animal and human studies indicates that exposure to ELF-MF affects the permeability of the BBB and influence on oxidative stress, and the activation of peripheral cytokines. The BBB immaturity during prenatal and early postnatal periods may increase its vulnerability to elevated cytokine levels impacting brain tissue[39,44,45]. IL-17A has been shown to facilitate immune cell migration into the brain by compromising tight junctions[38,39]. A study on power plant workers reported that ELF-MF exposure increases circulating levels of proinflammatory markers such as IL-1β and IL-6[46,47]. In line with this, Korenevskiy and colleagues[48,49] observed that long-term occupational exposure to 50 Hz electromagnetic fields is linked to elevated free radical generation, oxidative stress, and impaired immune function. Together, these data place our findings within a broader context of ELF-MF–related biological vulnerability.

Alongside inflammatory changes, we noted significant disruptions in synaptic proteins. Combined prenatal and postnatal ELF-MF exposure (Combined Group) was associated with decreased PSD-95 levels in the cortex and hippocampus and reduced Syn1 levels in the hippocampus. PSD-95 is a crucial scaffolding protein in the postsynaptic density that stabilizes glutamatergic synapses[33,50]. Lower levels of this protein have been associated with impaired dendritic spine maturation, altered plasticity, and diminished cognitive performance[51,52]. Syn1 regulates presynaptic vesicle dynamics, and its reduction may hinder neurotransmitter release[32,42,53]. Taken together, our findings suggest that ELF-MF may affect both pre- and postsynaptic components of synaptic structure.

The interplay between neuroinflammation and synaptic dysfunction has been highlighted in a growing body of work. IL-17A and IFN-γ, for example, can influence synaptic protein expression through NF-κB–dependent and calcium-regulated signaling pathways[42,43,54]. Several studies have also reported that ELF-MF exposure interferes with neuronal calcium balance[25,55], a change that may heighten the impact of inflammatory mediators. In this context, elevated IL-17A and IFN-γ together with altered calcium homeostasis might contribute to synaptic alterations, although in our sample IL-17A levels showed a positive association with PSD-95 in the cortex, suggesting a more complex relationship. The positive association between IL-17A and PSD-95 within the Combined Group may reflect a context-dependent role of IL-17A at the synaptic level rather than straightforward pro-inflammatory suppression. However, causal inference is not possible from these correlational data, and this finding warrants further investigation[36,42,56].

However, this study has some limitations. First, cytokine and synaptic protein levels were measured exclusively by ELISA. Although ELISA provides quantitative information on protein concentrations, it does not allow confirmation of protein expression patterns or regional/cellular localization within brain tissue. Therefore, future studies incorporating complementary approaches such as Western blotting, immunohistochemistry, or immunofluorescence would provide further validation of these findings at both the protein expression and spatial distribution levels. Furthermore, while the elevated IL-17A and IFN-γ levels suggest involvement of Th1/Th17-mediated neuroinflammatory signaling, the measurement of only three cytokines constitutes a limitation, and the present findings therefore reflect a partial view of the inflammatory response. Broader cytokine panels or multiplex approaches in future studies would be necessary to more comprehensively characterize the neuroinflammatory milieu and strengthen mechanistic interpretations. In addition, although the observed reductions in PSD-95 and Syn1 may indicate alterations in synaptic protein regulation, this study did not include behavioral testing, electrophysiological recordings, or direct functional assessments of synaptic transmission. Therefore, conclusions regarding cognitive function or synaptic activity should be interpreted with caution. It should be noted that new projects addressing these limitations, including broader cytokine profiling, complementary protein expression analyses, and behavioral and electrophysiological assessments, are currently ongoing in our laboratory. Future studies

combining molecular analyses with behavioral and electrophysiological approaches are needed to determine the functional consequences of ELF-MF exposure during brain development.

Conclusion

In conclusion, our data show that continuous exposure to 50 Hz, 500 μT ELF-MF during prenatal and postnatal periods leads to higher IL-17A levels in the cortex and hippocampus, higher IFN-γ levels in the cortex, and decreased PSD-95 levels in both the cortex and hippocampus, together with reduced Syn1 levels in the hippocampus. These changes indicate that ELF-MF may promote a pro-inflammatory environment in the developing brain and negatively affect synaptic function by disrupting brain development. The most significant changes occur when exposure spans both developmental periods, revealing the cumulative impact of prolonged exposure. The increases in IL-17A in both the cortex and hippocampus and in IFN-γ in the cortex, with no change in IL-4, suggest a shift toward a Th1/Th17 immune profile. This shift may weaken synaptic structure and presynaptic vesicle regulation in early development due to the decrease in PSD-95 structure and Syn1 levels in the hippocampus.

Although our exposure model represents higher magnetic field levels, closer to former occupational exposure limits than to typical environmental doses, the findings suggest that strong or prolonged ELF-MF exposure may pose a risk to neurodevelopmental processes. As stated before, until we have a clearer understanding of how developmental stages influence sensitivity to ELF-MF, it may be prudent to limit high-level exposure during pregnancy and early childhood. A better grasp of potential regional differences in brain susceptibility will contribute to more reliable public health recommendations in the future. As research in this area progresses, identifying the periods when the developing brain is most vulnerable will allow exposure guidelines to be shaped with greater confidence.

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Conflict of interest

The authors report no conflict of interest.

References

1 Odacı E, Ünal D, Mercantepe T, Topal Z, Hancı H, Türedi S, Erol HS, Mungan S, Kaya H & Çolakoğlu S, The pathological effects of prenatal exposure to a 900-MHz electromagnetic field on the 21-day-old male rat kidney, *Biotech Histochem*, 90 (2015) 93.

2 Miguel PM, Pereira LO, Silveira PP & Meaney MJ, Early environmental influences on the development of children's brain structure and function, *Dev Med Child Neurol*, 61 (2019) 1127.

3 Franco SJ, Gil-Sanz C, Martinez-Garay I, Espinosa A, Harkins-Perry SR, Ramos C & Müller U, Fate-restricted neural progenitors in the mammalian cerebral cortex, *Science*, 337 (2012) 746.

4 Götz M & Huttner WB, The cell biology of neurogenesis, *Nat Rev Mol Cell Biol*, 6 (2005) 777.

5 Ruan X, Kang B, Qi C, Lin W, Wang J & Zhang X, Progenitor cell diversity in the developing mouse neocortex, *Proc Natl Acad Sci USA*, 118 (2021) e2018866118.

6 Hadzibegovic S, Nicole O, Andelkovic V, Poulletier de Gannes F, Hurtier A, Lagroye I & Bontempi B, Examining the effects of extremely low-frequency magnetic fields on cognitive functions and functional brain markers in aged mice, *Sci Rep*, 15 (2025) 8365.

7 International Agency for Research on Cancer (IARC) Working Group on the Evaluation of Carcinogenic Risks to Humans, Non-ionizing radiation, Part 1: Static and extremely low-frequency (ELF) electric and magnetic fields. *IARC Monogr Eval Carcinog Risks Hum*, 80 (2002) 1.

8 International Commission on Non-Ionizing Radiation Protection (ICNIRP), ICNIRP guidelines for limiting exposure to time-varying electric and magnetic fields (1 Hz–100 kHz). *Health Phys*, 99 (2010) 818.

9 Lou X, Jia S, Li R, Gao P & Zhang Y, Occupational exposure to 50 Hz magnetic fields does not alter responses of inflammatory genes and activation of splenic lymphocytes in mice, *Int J Occup Med Environ Health*, 29 (2016) 277.

10 Wertheimer N & Leeper N, Electrical wiring configurations and childhood cancer, *Am J Epidemiol*, 109 (1979) 273.

11 Tian H, Zhu H, Gao C, Shi M, Yang D, Jin M, Wang F and Sui X, System-level biological effects of extremely low-frequency electromagnetic fields: an in vivo experimental review, *Front. Neurosci*. 17 (2023) 1247021.

12 Sandoval-Diez N, Loizeau N, Huss A, Röösli M & Vienneau D, Long-term residential magnetic field exposure and neurodegenerative disease mortality: An 18-year nationwide cohort study in Switzerland, *Environ Int,* 208 (2026) 110145.

13 Klimek A & Rogalska J, Extremely low-frequency magnetic field as a stress factor—Really detrimental? Insight into literature from the last decade, *Brain Sci*, 11 (2021) 174.

14 Dong L, Xia P, Tian L, Tian C, Zhao W, Zhao L, Duan J, Zhao Y & Zheng Y, A review of aspects of synaptic plasticity in hippocampus via extremely low-frequency magnetic fields, *Bioelectromagnetics*, 44 (2023) 63.

15 Kaplan S, Deniz OG, Önger ME, Türkmen AP, Yurt KK, Aydın I, Altunkaynak BZ & Davis D, Electromagnetic field and brain development, *J Chem Neuroanat*, 75 (2016) 52.

16 Nikolova T, Czyz J, Rolletschek A, Blyszczuk P, Fuchs J, Jovtchev G, Schuderer J, Kuster N & Wobus AM, Electromagnetic fields affect transcript levels of apoptosis-

related genes in embryonic stem cell-derived neural progenitor cells, *FASEB J*, 19 (2005) 1686.
17 Giorgi G & Del Re B, Epigenetic dysregulation in various types of cells exposed to extremely low-frequency magnetic fields, *Cell Tissue Res*, 386 (2021) 1.
18 Abtin S, Seyedaghamiri F, Aalidaeijavadi Z, Farrokhi AM, Moshrefi F, Ziveh T, Zibaii MI, Aliakbarian H, Rezaei-Tavirani M & Haghparast A, A review on the consequences of molecular and genomic alterations following exposure to electromagnetic fields: Remodeling of neuronal network and cognitive changes, *Brain Res Bull*, 217 (2024) 111090.
19 Moon JH, Health effects of electromagnetic fields on children, *Clin Exp Pediatr*, 63 (2020) 422.
20 Sakhaie MH, Soleimani M, Pourheydar B, Majd Z, Atefimanesh P, Asl SS & Mehdizadeh M, Effects of extremely low-frequency electromagnetic fields on neurogenesis and cognitive behavior in an experimental model of hippocampal injury, *Behav Neurol*, 2017 (2017) 9194261.
21 Zhao QR, Lu JM, Yao JJ & Mei YA, Neuritin reverses deficits in murine novel object associative recognition memory caused by exposure to extremely low-frequency (50 Hz) electromagnetic fields, *Sci Rep*, 5 (2015) 11768.
22 Seomun G, Lee J & Park J, Exposure to extremely low-frequency magnetic fields and childhood cancer: A systematic review and meta-analysis, *PLoS One*, 16 (2021) e0251628.
23 Podda MV, Leone L, Barbati SA, Mastrodonato A, Li Puma DD, Piacentini R & Grassi C, Extremely low-frequency electromagnetic fields enhance the survival of newborn neurons in the mouse hippocampus, *Eur J Neurosci*, 39 (2013) 893.
24 Kashani ZA, Pakzad R, Rashidi Fakari F, Haghparast MS, Abdi F, Kiani Z, Talebi A & Moradi Haghgoo S, Electromagnetic fields exposure on fetal and childhood abnormalities: Systematic review and meta-analysis, *Open Med*, 18 (2023) 20230697.
25 Wang X, Ye Y, Zuo H & Li Y, Neurobiological effects and mechanisms of magnetic fields: A review from 2000 to 2023, *BMC Public Health*, 24 (2024) 3094.
26 Zheng Y, Zhao L, Dong L, Tian C, Xia P & Jin Z, The time-dependence of three different modes of ELF-EMF stimulation on LTP at Schaffer collateral-CA1 synapses, *Bioelectromagnetics*, 42 (2021) 538.
27 Oztas B, Kalkan T & Tuncel H. Influence of 50 Hz frequency sinusoidal magnetic field on the blood-brain barrier permeability of diabetic rats. *Bioelectromagnetics*, 25 (2004) 400–402. doi:10.1002/bem.20030.
28 Zheng Y, Xia P, Dong L, Tian L & Xiong C, Effects of modulation on sodium and potassium channel currents by extremely low frequency electromagnetic fields stimulation on hippocampal CA1 pyramidal cells, *Electromagn Biol Med*, 40 (2021) 274.
29 Salehi I, Ghazikhanlou-Sani K & Zamani A, Exposure of rats to extremely low-frequency electromagnetic fields alters cytokines production, *Electromagn Biol Med*, 32 (2013) 1.
30 Sobhanifard M, Eftekharian MM, Solgi G, Khamaneh AM, Gholami M, Nejad AK, Moini A & Zamani A, Effect of extremely low frequency electromagnetic fields on expression of T-bet and GATA-3 genes and serum interferon-γ and interleukin-4, *J Interferon Cytokine Res*, 39 (2019) 122.
31 Öztürk H, Saribal D, Gelmez YM, Deniz G, Yılmaz A, Kirectepe Aydın A & Ercan AM, Extremely low frequency electromagnetic fields exposure during the prenatal and postnatal periods alters pro-inflammatory cytokines levels by gender, *Electromagn Biol Med*, 41 (2022) 163.
32 Mirza FJ & Zahid S, The role of synapsins in neurological disorders, *Neurosci Bull*, 34 (2018) 349.
33 Borczyk M, Śliwińska MA, Caly A, Bernas T & Radwanska K, Neuronal plasticity affects correlation between the size of dendritic spine and its postsynaptic density, *Sci Rep*, 9 (2019) 1693.
34 Merritt R, Purcell C & Stroink G, Uniform magnetic field produced by three, four, and five square coils, *Rev Sci Instrum*, 54 (1983) 879.
35 Nishimura I, Oshima A, Shibuya K & Negishi T, Lack of teratological effects in rats exposed to 20 or 60 kHz magnetic fields, *Birth Defects Res B Dev Reprod Toxicol*, 92 (2011) 469.
36 Kubo A, Kamiya S, Sanaka S, Nakamura K, Kishi K & Sasaki T, How does maternal immune activity affect fetal survival and brain development? The critical roles of IL-17A and microglia, *Neuroglia*, 6 (2025) 45.
37 Papageorgiou IE, Lewen A, Galow LV, Cesetti T, Scheffel J, Regen T, Hanisch UK & Kann O, TLR4-activated microglia require IFN-γ to induce severe neuronal dysfunction and death in situ, *Proc Natl Acad Sci USA*, 113 (2016) 212.
38 Yu Y, Weiss RM & Wei SG, Interleukin-17A contributes to blood–brain barrier disruption of hypothalamic paraventricular nucleus in rats with myocardial infarction, *J Am Heart Assoc*, 13 (2024) e032533.
39 Fujitani M, Miyajima H, Otani Y & Liu X, Maternal and adult interleukin-17A exposure and autism spectrum disorder, *Front Psychiatry*, 13 (2022) 836181.
40 Sasaki T, Tome S & Takei Y, Intraventricular IL-17A administration activates microglia and alters their localization in the mouse embryo cerebral cortex, *Mol Brain*, 13 (2020) 93.
41 Liu Z, Qiu AW, Huang Y, Yang Y, Chen JN & Gu TT, IL-17A exacerbates neuroinflammation and neurodegeneration by activating microglia in rodent models of Parkinson's disease, *Brain Behav Immun*, 81 (2019) 630.
42 Basurco L, Abellanas MA, Ayerra L, Conde E, Vinueza-Gavilanes R, Luquin E, Vales A, Vilas A, San Martin-Uriz P, Tamayo I, Alonso MM, Hernaez M, Gonzalez-Aseguinolaza G, Clavero P, Mengual E, Arrasate M, Hervás-Stubbs S & Aymerich MS, Microglia and astrocyte activation is region-dependent in the α-synuclein mouse model of Parkinson's disease, *Glia*, 71 (2023) 571.
43 Mao H, Zhao X & Sun SC, NF-κB in inflammation and cancer, *Cell Mol Immunol* (2025).
44 McAdams RM & Juul SE, The role of cytokines and inflammatory cells in perinatal brain injury, *Neurol Res Int*, 2012 (2012) 561494.
45 Zhao Q, Dai W, Chen HY, Jacobs RE, Zlokovic BV, Lund BT, Montagne A & Bonnin A, Prenatal disruption of bloodbrain barrier formation via cyclooxygenase activation leads to lifelong brain inflammation, *Proc Natl Acad Sci USA*, 119 (2022) e2113310119.

46 Hosseinabadi MB, Khanjani N, Samaei SE & Nazarkhani F, Effect of long-term occupational exposure to extremely low-frequency electromagnetic fields on proinflammatory cytokine and hematological parameters, *Int J Radiat Biol*, 95 (2019) 1573.

47 Tan Z, Bussies PL, Sarn NB, Irfan M, DeSilva T & Eng C, Morphological and functional differences between hippocampal and cortical microglia and its impact on neuronal over-excitation in a germline Pten mutant mouse model, *Neuroscience*, 570 (2025) 159.

48 Korenevskiy NA, Al-kasasbeh RT, Shaqadan A, Eltous Y, Alshamasin MS, Myasoedova MA, Rodionova SN & Ilyash M, Prediction of occupational diseases due to exposure to high radiation electromagnetic environment using a fuzzy logic model, *Crit Rev Biomed Eng*, 49 (2021) 41.

49 Korenevskiy NA, Al-Kasasbeh RT, Shaqadan A, Myasoedova MA, Al-Qodah Z, Rodionova SN, Eltous Y, Filist S & Ilyash M, Prediction of health impacts of exposure to electromagnetic field on the immunity system of power plants workers using fuzzy decision-making rules, *Int J Syst Assur Eng Manag*, 15 (2024) 4873.

50 Sweet ES, Tseng CY & Firestein BL, To branch or not to branch: How PSD-95 regulates dendrites and spines, *Bioarchitecture*, 1 (2011) 69.

51 Coley AA & Gao WJ, PSD-95 deficiency disrupts PFC-associated function and behavior during neurodevelopment, *Sci Rep*, 9 (2019) 9486.

52 Yusifov R, Tippmann A, Staiger JF & Löwel, Spine dynamics of PSD-95-deficient neurons in the visual cortex link silent synapses to structural cortical plasticity, *Proc Natl Acad Sci USA*, 118 (2021) e2022701118.

53 Bruentgens F, Moreno Velasquez L, Stumpf A, Parthier D, Breustedt J, Benfenati F, Milovanovic D, Schmitz D & Orlando M, The lack of synapsin alters presynaptic plasticity at hippocampal mossy fibers in male mice, *eNeuro*, 11 (2024) 23.

54 Trebak M & Kinet JP, Calcium signalling in T cells, *Nat Rev Immunol*, 19 (2019) 154.

55 Klimek A & Rogalska J, Extremely low-frequency magnetic field as a stress factor—Really detrimental? Insight into literature from the last decade, *Brain Sci*, 11 (2021) 174.

56 Yin J, Li W, Shen LP, Zhang WL, Chen JY, Zhang BB, Chen YJ, Li T, Li HZ, Gao Z, Xie ST, Zhang QP, Zhang C, Zhang XY & Zhu JN, Cerebellar microglia-derived IL-17A mitigates autism-related behavioral and synaptic deficits, *Mol Psychiatry*, 31 (2026) 3154.