MEDICAL SCIENCE MONITOR
BASIC RESEARCH

ANIMAL STUDIES

eISSN 2325-4416
© Med Sci Monit Basic Res, 2013; 19: 141-145
DOI: 10.12659/MSMBR.883907

Received: 2012.11.27
Accepted: 2013.02.23
Published: 2013.05.10

What is the impact of electromagnetic waves on epileptic seizures?

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Source of support: Self financing

Background: The effects of electromagnetic waves (EMWs) on humans and their relationship with various disorders have been investigated. We aimed to investigate the effects of exposure to different frequencies of EMWs in various durations in a mouse epilepsy model induced by pentylenetetrazole (PTZ).

Material/Methods: A total of 180 4-week-old male mice weighing 25–30 g were used in this study. Each experimental group consisted of 10 mice. They were exposed to 900, 700, 500, 300, and 100 MHz EMWs for 20 hours, 12 hours and 2 hours. Following electromagnetic radiation exposure, 60 mg/kg of PTZ was injected intraperitoneally to all mice. Each control was also injected with PTZ without any exposure to EMW. The latency of initial seizure and most severe seizure onset were compared with controls.

Results: The shortest initial seizure latency was noted in the 12-hour group, followed by the 700 MHz. The mean initial seizure latencies in the 2-hour EMW exposed group was significantly shorter compared to that in the 12- and 20-hour groups. There was no significant difference between 12- and 20-hour EMW exposed groups. There was a significant difference between control and 2- and 10-hour EMW exposed groups. No statistically significant differences were noted in mean latencies of the most severe seizure latency, following 20-, 12-, and 2-hour EMW exposed groups and control groups.

Conclusions: Our findings suggest that acute exposure to EMW may facilitate epileptic seizures, which may be independent of EMW exposure time. This information might be important for patients with epilepsy. Further studies are needed.

Key words: epilepsy • pentylenetetrazole • mice • electromagnetic waves

Full-text PDF: http://www.medscimonit.com/download/index/idArt/883907

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Background

The effects of electromagnetic waves (EMWs) on humans and the relationship of EMSs with various disorders have been investigated [1]. As a result of advances in technology, people are constantly exposed to EMW. Alternating electric currents, computer screens, radio, television, cell phones, and radar devices are examples of sources of electromagnetic fields. All of these EMW sources operate at different frequencies. Several studies have suggested serious negative effects of EMWs on health [2–4].

We aimed to investigate the effects of different frequencies of EMWs at various durations on time of seizure onset (seizure latency) and the most severe seizure latency in a mouse model of epilepsy induced by pentylenetetrazole (PTZ) and to compare these results with controls.

Material and Methods

Study groups

The study was approved by our local Animal Ethics Committee. It was conducted on 180 4-week-old male albino mice weighing 25–30 g. Experiments were started after 10 A.M. Animals were kept at 24±1°C in a 12–12 hour light-dark cycle and were provided with water and food before and during the study.

Six experimental groups were established, including controls. Each group consisted of 10 mice. They were exposed to 900, 700, 500, 300 and 100 MHz EMW for 20, 12, and 2 hours. Following the exposure, 60 mg/kg of PTZ was injected intraperitoneally (IP) into all mice. PTZ was injected into the controls after the same periods without exposure to EMWs. All mice were then monitored and seizures were scored. Time to the first myoclonic jerk was recorded as initial seizure latency. Seizure severity was scored on a scale from 0 to 6.

Generation of EMWs

An antenna was used to generate EMWs. The antenna intercepts the EMWs and converts them into electrical currents. A 0.5-mm diameter transmitter dipole antenna with electromagnetic field frequencies of 900, 700, 500, 300, 100 MHz was fabricated for use in this experimental study [5]. Electromagnetic wave frequency was measured by a spectrum analyzer and frequency meter before the dipole antenna generated electromagnetic waves.

Administration of pentylenetetrazole (PTZ)

PTZ is a convulsant drug used in experimental epileptic seizure models, which causes convulsions similar to absence and myoclonic type seizures in humans when administered subcutaneously, intravenously, or intraperitoneally in mice and rats [6]. PTZ acts by binding to the GABA-A/benzodiazepine receptor complex and blocks the GABA-gated chloride channels. Drugs effective against PTZ model exert their anticonvulsant effects through their effects on T-type Ca^{+2} currents and GABA-A [**7**]. In this study, PTZ was administered at a dose of 60 mg/kg IP in mice.

Evaluation of seizures

After 20-hours, 12-hours and 2-hours groups of mice were exposed to 900, 700, 500, 300, and 100 MHz electromagnetic wave fields respectively, 60 mg/kg of PTZ was injected intraperitoneally. The control groups were also injected with 60 mg/kg of PTZ. All mice were monitored for 20 minutes. The seizure score was recorded according to the following scale; 0: No response, 1: Ear and facial twitching, 2. Mild myoclonic jerks of the limbs, 3: Severe myoclonic jerks of the limbs and rearing, 4: Forelimb convulsions, 5: Increase in general muscle tone in combination with rearing and falls, and 6: Status epilepticus and death [8].

Time to onset of initial myoclonic jerk was defined as first seizure onset latency. Mice were kept in a bell glass for 20 minutes following PTZ injection and the highest score (most severe seizure onset latency) was recorded [9].

Statistical analysis

SPSS 13.0 for Windows software was used for analysis. Groups were compared using one-way ANOVA, Kruskal Wallis test and chi-square tests.

Results

The shortest initial seizure latency was noted at 500 MHz ($p<0.05$) and the longest at 300 MHz ($p<0.05$) in the 2-hour group. The shortest initial seizure latency was noted at 700 MHz ($p<0.05$) and the longest in the control group, followed by 100 MHz ($p<0.05$) in the 12-hour group. The shortest initial seizure latency was noted at 300 MHz ($p<0.05$) and the longest in the 500 MHz ($p<0.05$) in the 20-hour group.

The shortest initial seizure latency was noted in the 12-hour group, followed by 700 MHz and the longest in the 20-hour group, followed by the 500 MHz. Mean initial seizure latencies of EMW-exposed groups were; 2 hour-group: 18.5 s, 12-hour group: 22.3 s, and 20-hour group: 27.2 s. The mean initial seizure latencies of the 2-hour EMW exposed group was significantly shorter compared to that in the 12- and 20-hour groups ($p<0.05$). There was no significant difference between 12- and 20-hour EMW exposed groups ($p>0.05$). There was a significant difference between the control group and the 2- and 10-hour

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Table 1. Comparison of the initial seizure latencies (sec) without EMW exposure and with 900, 700, 500, 300, 100 MHz EMW exposure in the 2, 12 and 20-hours experimental groups and controls.

Exposure Duration (hours)	Latency in 900 MHz (mean second ±SD)	Latency in 700 MHz (mean second ±SD)	Latency in 500 MHz (mean second ±SD)	Latency in 300 MHz (mean second ±SD)	Latency in 100 MHz (mean second ±SD)	Seizure latency in Controls (sec) ±SD)
2	25.9±15.3	15.2±11.5	11.9±7.3*	27.2±15.1*	12.6±7.4	19.8±7.8
12	22.4±20.4	9.5±12.9*	26.5±29.7	14.4±18.7	38.8±23.7	39.4±26.3*
20	11.5±11.2	44.5±17	57±28*	9.9±5.4*	13.1±18.8	22.4±20.4

*The shortest and the longest latencies.

Table 2. Comparison of the latency of the most severe seizure (sec) following 900, 700, 500, 300, 100 MHz EMW exposure in the 2, 12, 20 hours experimental groups and controls.

Duration of EMW exposure (hours)	Latency in 900 MHz (mean second ± SD)	Latency in 700 MHz (mean second ± SD)	Latency in 500 MHz (mean second ± SD)	Latency in 300 MHz (mean second ± SD)	Latency in 100 MHz (mean second ± SD)	Seizure latency in Controls (sec)
2	317.7±218.2	263±225.2	219.2±98.7	299.9±272.7	292.2±118.8	172.9±137.3
12	385.3±312.12	317.7±298.6	403.8±351.2	161.6±96.2	314.7±311.5	331.5±361.6
20	321.2±185.9	189.4±174.9	250.2±221.06	288.7±230.10	261.1±234.32	313.8±214.31

EMW exposed groups, and no significant difference between controls and the 12-hour EMW exposed group (Table 1). No statistically significant difference was noted in the mean latencies of the most severe seizure latency following 20-, 12-, 2-hour groups and the control groups (Table 2).

Discussion

There are several published studies on the effect of EMWs on tumors [10,11], but there has not yet been a detailed study on EMWs and epilepsy. We investigated different frequencies of EMW on seizures in this comparative experimental epilepsy model. Five different frequencies (100, 300, 500, 700, 900 MHz) of EMWs were applied for 3 different time periods (2, 12, and 20 hours).

The shortest initial latency was observed in the 12-hour group, followed by the 700 MHz in our study. Tattersall et al. found excitability changes in rat hippocampal tissue exposed to 700 MHz radiofrequency without heating effect [12]. Our finding is compatible with results of that study.

EMWs are known to have a heating effect, which is more prominent at higher frequencies [13]. Previous studies have reported that radiofrequency leads to an increase in body core temperature [14]. It has been shown that energy absorption occurs via radiofrequency waves in target organs, the hypothalamic thermoregulatory center, and peripheral regions. Adair et al. used 450 MHz and 2450 MHz magnetic waves applied in humans, and found an increase in skin temperature [15]. Chou et al., exposed rats to 2450 MHz microwaves, and found that tail regions of the rats absorbed more energy than the head or other body regions, and that specific absorption rates (SAR) were higher in the anterior hypothalamus compared to other brain regions [16]. The role of the tail and anterior hypothalamus in the temperature regulation system should be considered during interpretation of these results. In our study, no specific body region was chosen as the target region. Whole body application of EMWs can eliminate the misinterpretation caused by regional applications. Carratala and Moya used microwaves as an indicator of febrile seizures in neonatal mice and concluded that they had no harmful effects [17]. Body temperature was not measured in the current study. Different effects of EMW exposure on seizure latency might be attributed to blood-brain barrier (BBB) damage caused by heating effect of EMWs, but this effect was reported in studies using gigahertz-levels of EMWs [18,19]. We did not perform any histological examination of BBB damage.

There have been some electroencephalography (EEG) studies of EMW exposure [20,21]. For example, awake and healthy individuals were exposed to 900 MHz EMW and no significant

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EEG changes were noted [21]. Hietanen et al. used 5 different models of cell phones and did not find any significant changes in resting EEG, but noted some EEG changes during memory tests [22]. Vorobyov et al. compared the effect of scopolamine in the electroencephalogram of rats and found that repeated low-level exposure to extremely low frequency microwaves can alter activity of the cholinergic system in the brain [23]. In our study we did not perform EEG recording.

Some studies have investigated the effects of EMWs on nervous system tissue. Carballo-Quintás et al. found c-fos and glial markers were increased by the combined stress of non-thermal irradiation and the toxic effect of picrotoxin on cerebral tissues exposed to 900 MHz [24]. In study of López-Martín et al., 900 MHz GSM radiation stimulated c-fos expression in different areas of the limbic system and triggered a marked increase in neuronal excitability in seizure-prone rats [4]. Ammari et al. showed that sub-chronic exposures to a 900 MHz EMF signal for 2 months could adversely affect rat brains (indicating potential gliosis) [25]. Also, adverse effects of free radicals on myocardium have been shown previously [26]. Tissue investigation was not performed in our study.

Servantie et al. investigated the effects of 5±1 mW/cm^2 EMW on PTZ-induced seizure latency in mice. Chronic EMW exposure of different durations were tested, and the most significant shortening in latency was noted at day 27 [27]. Although the shortest latencies were recorded in the 2-hour group in our study, obvious short latencies were also recorded in the 12- and 20-hour groups. These results suggest that the duration of EMW exposure is not the only factor affecting the occurrence of epileptic seizures.

Previous studies have shown a trigger effect of EMWs on seizure activity [4,7]. Our results also showed a trigger effect of EMWs on seizures by shortening initial seizure latency. However, there was no significant effect on most severe seizure latencies. This suggests that EMWs affect only seizure threshold, without any effect on seizure severity.

Canseven et al. did not find any effect of 50 Hz EMWs on PTZ-induced epileptic seizures [28]. Among our study groups, the shortest initial seizure latency was 9.5±12.9 seconds in the 700 MHz group at 12 hours exposure. Higher frequencies of EMW were used in our study and we found to have significant effects on initial latency of epileptic seizures. This result may indicate a relationship between the seizure threshold and higher frequencies of EMWs.

Conclusions

Our findings suggest that acute exposure to EMWs may facilitate occurrence of epileptic seizures and that this could be independent of EMW exposure time. This information might be important for patients with epilepsy. Further studies are needed to evaluate the acute effects of EMW exposure generated by cell phones and other electromagnetic devices used in everyday modern daily life.

Statement

There is no conflict of interest in this study.

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