Electromagnetic Field Changes Emotional-Motivated Behavior in Genetically Epilepsy-Prone Rats

Nato Bukia*, Giorgi Kekelia, Marina Butskhrikidze, Lamara Machavariani, Militsa Svanidze.

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia
Email: nata_buk@yahoo.com

Abstract. In recent years, electro-magnetic field (EMF) exposure is tested as a tool for diagnosis and treatment of the wide range of neurological and psychological disorders (including epilepsy). In the present study, we examined the effects of acoustic range EMF on emotional-motivated behavior in genetically epilepsy-prone rats (GEPRs) of Krushinsky-Molodkina strain in Open field test.

Methods. For this reason, generator of EMF with original coil design was used. The optimal parameters of EMF, which partially or fully inhibited the behavioral manifestation of seizure were established during pilot experiments. These were 10-15 kHz, 1-1,5 milliTesla, duration 20 min.

Before and after EMF exposure in open field test, parameters of emotional-motivated behavior - entering the center, numbers of crossed squares, head raise, vertical stands, the frequency and duration of grooming, number of fecal boluses and urination were registered; Data reliability was assessed by using parametric and non-parametric techniques, with the use of one- and two-way layout of factorial analysis.

Results and Discussion.

On the background of a 5-days exposure of electric-magnetic field (EMF) the number of crossed squares (from 100±8 to 120±12, $p \leqslant 0.01$), hole reflex (from 17±2 to 24±3, $p \leqslant 0.01$) and head lifts (from 11 ±2 to 14±4, $p \leqslant 0.05$) were increased. The number of vertical stands (16±2 to 12±1 $P \leqslant 0.05$), duration (from 21 ±2 to 15±4, $p \leqslant 0.05$) and the number of grooming episodes (from 75 ±7 to 45±6 $P \leqslant 0.01$), as well as the number of fecal boluses and the frequency of urination were decreased.

These findings suggest that acoustic range magnetic field decreases anxiety degree and consequently, enhances locomotor and exploratory activity of the GEPRs.

A 5-days exposure EMF to inbred white rats did not change significantly locomotion/exploratory activity in open field test.

Conclusion.

Acoustic range EMF can be applied for suppression of behavioral manifestation of seizure. These data support a potential role of EMF exposure in changing emotion regulation of anxiety, but the mechanisms of such influence are not known. Proposed biological mechanisms in anti-seizure and anxiolytic effects of EMF exposure in GEPRs might include normalization of neuroendocrine, neurotransmitter, and/or neurotrophic factors.

Keywords: Electromagnetic field; seizure; rats; general behavior

1 Introduction

The exposition by electro-magnetic field (EMF) is a noninvasive treatment method. It is used as a complementary to the drugs, for treating different neurodegenerative diseases (Parkinson's disease, schizophrenia, depression, tinnitus, etc.) (4, 8, 9). EMF can also be used as a separate treatment therapy (14). Transcranially applied weak fields generated by Direct Current (DC) and Alternating Current (AC) have a wide variety of effects that are potentially important for using the therapy. Furthermore, repetitive transcranial magnetic stimulation (rTMS) is seen as a safe treatment method, without enduring side effects: no long-term neurological, cognitive or cardiovascular side effects have been reported (18,19). EMF appears to be biologically active, penetrating into the living tissue without any impediment (14). However, it is unclear how the low-frequency EMF can block seizure activity.

The audiogenic seizure model is one of several experimental models used in the study of epilepsy and the identification of the underlying mechanisms for genetically epilepsy-prone rats (GEPRs). They manifest short lasting seizure activity in neonatal age, and fully fledged seizure activity after hierarchical implication of brainstem structures (16), in which seizures are initiated largely through the midbrain inferior colliculus, but may also involve additional subcortical and forebrain structures (6,10,11). In response to a strong sound (the bell -90-dB, during 60 sec), GEPRs display either fear reaction accompanied by facial muscle clonus (group a) or fear reactions with elevated motor act responses (wild running, jumps), which are accompanied with tonic-clonic behavioral seizures (group b). The present study was conducted on animals of group b.

In earlier investigations, we attempted to identify the optimal parameters of repeated EMF, which can fully or partially depress seizure behavioral manifestations in GEPRs. For repetitive (a 5-days) EMF, we used the following parameters: (10-15 kHz, 1-1.5 milliTesla, duration 20 min).

The goal of this study was to explore the impact of above mentioned low-frequency repeated EMF exposure on epilepsy and on emotional motivated behavior of GEPRs and albino rats using Open Field Test.

2 Method

2.1 Subjects

Experiments were conducted on male GEPRs of Krushinsky-Molodkina (KM) strain (n=14) and inbred white rats (n=14), weighing 200-250 g. Animals were housed in laboratory cages with food and water *ad libitum*. Behavioral testing was performed during 5 min, at the same time between 11.00 am to 13.00 pm.

2.2 Experimental Paradigm

At the beginning of experiments, both control (Inbred, white male and GEP) rats were placed into the open field for testing the parameters of behavioral activity. After that, rats were placed into coil for EMF exposure with defined parameters of EMF for a 20-min session. 10 min after the EMF session, the animals were re-tested for general behavior in the open field for 5 min. The GEPRs (with or without EMF exposure) were given audiogenic stimuli, for 60 secs, before and after testing in open field for monitoring behavioral correlates of seizure activity.

2.3 EMF Exposure

For EMF exposure (carried for five consecutive days), we used the coil designed at Tbilisi Technical University, Georgia. Parameters of magnetic field (stimulus frequency, its intensity and train duration), which partially or fully depressed behavior manifestation of seizure activity, were established during pilot experiments. For repetitive (a 5-days) EMF exposure, we used the following parameters: 10-15 kHz, 1-1,5 milliTesla, duration 20 min.

2.4 The Open Field Test

Emotional-motivational status of the rats was tested in Open Field. This is a chamber of 80 cm in diameter surrounded by 30 cm walls. The floor of the chamber was divided into 32 squares and lighted up with 200 W lamp. To minimize initial procedure-related anxiety, rats were adapted to the open field during 5 min for 3 days prior to experiments. The rats were video-recorded for initial 5 minutes after the placement into the Open Field, for three consecutive days (the same time of day). We registered the following parameters: entering the center, numbers of crossed squares, head raising, vertical stands, the cumulative duration of grooming and number of bouts (grooming episodes), number of fecal boluses and urination. After each trial, the chamber was cleaned with 30 % ethanol solution.

2.5 Data Analysis.

We determined the parameters of locomotor and emotional-motivated activity in Open field (see above).

2.6 Statistics

Data obtained were processed using adequate statistical program. Data reliability was assessed using parametric and non-parametric techniques, with the use of two-way layout of factorial analysis.

3 Results and Discussion

3.1 EMF Affected Locomotor and Emotional-Motivated Activity of GEPRs and Inbred, White Rats

Testing the animals' general behavior in the Open Field allowed us to judge about the rats' locomotor and exploratory activity as well as the level of the rats' emotional status/fear. More specifically, increases in the number of crossed squares, vertical stands, entering the center and the duration of the time spent in the center were signs of increased locomotor activity and decreased fear (5, 13).

Grooming is an important and evolutionarily ancient behavior. Beyond the primary purpose of hygiene and caring for the body surface, grooming serves a variety of other functions, including stimulation of the skin, thermoregulation, chemo-communication, social interaction, de-arousal, and stress reduction (2, 3, 15). Regulation of grooming behavior is mediated by multiple brain regions (especially the basal ganglia and hypothalamus) (3,15), as well as by various endogenous agents neuromediators (17). Grooming is increased in a stress condition and, therefore, it is logical to expect that the prolongation of total grooming duration be considered as a sign of activation of the mechanisms involved into adaptation to stress (7).

Following EMF exposure in control rats, we observed an increase in locomotor activity. Specifically, the rats manifested significant increases in the number of crossed squares (from 85±8 to 119±12, $p \leqslant 0.01$), hole reflex (from 11±2 to 18±3, $p \leqslant 0.01$) and head lifts (from 14 ±2 to 21±4, $p \leqslant 0.05$). The number of vertical stands decreased from 21±4 to 13±2 ($P \leqslant 0.01$). The number of grooming episodes decreased from 17±3 to 8±2 ($P \leqslant 0.05$). The total duration of these episodes decreased from 68±12 sec to 35±7 sec ($P \leqslant 0.05$).

These findings suggest that EMF exposure causes anxiolytic effect, which helps the animal to cope with a stress condition. In our experiments, the exposure of EMF decreased the number of fecal boluses ($P \leqslant 0.05$). The frequency of urination did not change significantly (see Fig. 1).

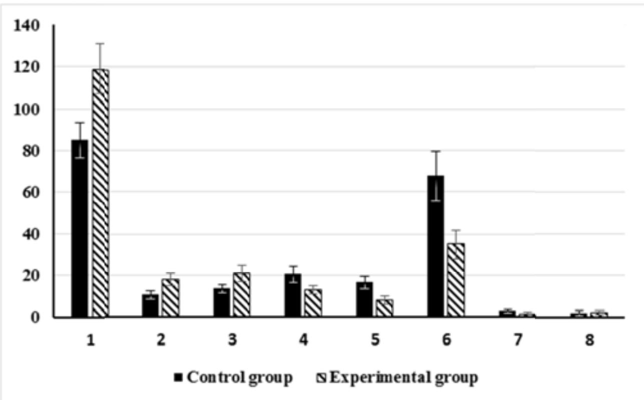

Figure.1. The effect of acoustic range magnetic field on the locomotor and exploratory activity of inbred rats in the Open Field. Black columns – white, inbred rats (control group). Patterned columns – white, inbred rats with MS (Experimental group). 1. Numbers of crossed squires, 2. Hole reflex, 3. Head lifts, 4. Vertical stands, 5. Number of grooming episodes, 6. Duration of grooming, 7. Number of fecal boluses; 8. Urination.

The EMF exposure resulted in enhanced locomotor and exploratory activity of GEPRs. The number of crossed squares (from 100±8 to 120±12, $p \leqslant 0.01$), hole reflex (from 17±2 to 24±3, $p \leqslant 0.01$) and head lifts (from 11 ±2 to 14±4, $p \leqslant 0.05$) were increased. The number of vertical stands (16±2 to 12±1 $P \leqslant$

0.05), total duration (from 21 ±2 to 15±4, p⩽0.05) and the number of grooming episodes (from 75 ±7 to 45±6 P⩽0.01), as well as the number of fecal boluses and the frequency of urination were decreased (see Fig. 2).

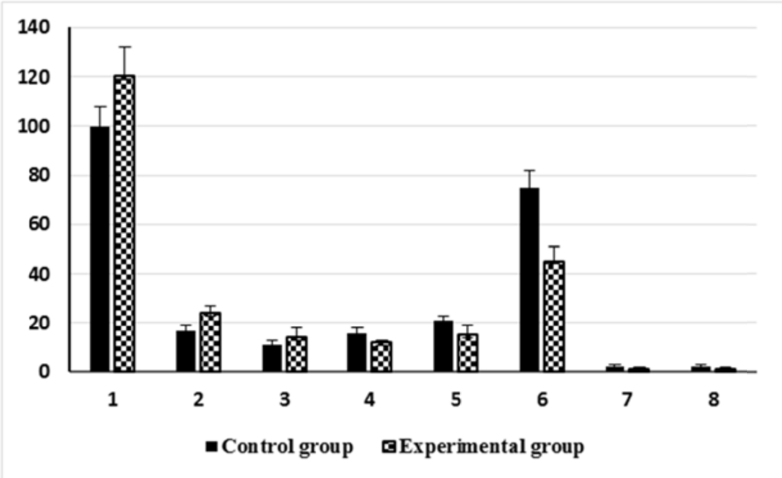

Figure 2. The effect of acoustic range magnetic field on locomotor and exploratory activity of GEPRs in open field test. Black columns – GEPRs (control group). Patterned columns – GEPRs with EMF exposure (Experimental group). 1. Number of crossed squires, 2. Hole reflex, 3. Head lifts, 4. Vertical stands, 5. Number of grooming episodes, 6. Duration of grooming, 7. Number of fecal boluses; 8. Urination.

The number of crossed squares was more in GEPRs compared to control ones and they exhibited persistent anxiety-like behaviors. Acoustic range EMF decreases the anxiety degree and, consequently, enhances locomotor and exploratory activity, hole reflex and head lifts not only in GEPRs, but also in inbred white rats in Open Field test. Decreased total grooming duration and grooming episodes in animals with EMF exposure also indicates a decrease in negative emotional tension. As a result, we see decreased number of fecal boluses and the frequency of urination.

4 Summary and Conclusion

Findings in the present study suggest that low frequency (acoustic range) EMF is a noninvasive procedure that allows to depress (fully or partially) the seizure activity, developed in response to audiogenic stimuli in GEPRs. This method might be applied for epilepsy treatment. The exposure of acoustic range EMF decreases the level of anxiety/fear reaction in the rats of both groups. These data support a potential role of EMF exposure in changing emotional tension of anxiety, but the ways in which the EMF exerts this influence are not known.

We tried to understand the possible mechanisms by which EMF exposure, with the mentioned field parameters, is capable positively affect the GEPRs. The first possible cause of the above-mentioned positive influence may be the frequency (acoustic) range of impact, and second is a fact that the source of the acoustic waves is the EMF. The modulation of brain function is carried out in several ways: by magnetic, electric and acoustic stimulation.

Brain structures are subjected not only to direct transcranial stimulation, but they also receive changed afferent signals from the whole body. The artificially created EMF may change the tonic activity of the cells located in the local area of EMF action (whole body) and, as a result of it, this stimulation would be the cause for changes in the mode of neural impulses formation. The multi-modal sensory afferent pathways from different parts of the body pass through the central nuclei and change the neuronal activity of the cortex. For example, EMF can modulate the ponto -geniculo-occipital (PGO) waves, which has a possible inhibitory effect on EEG seizure activity (6). Increased number of PGO spikes in animals exposed to auditory stimulation is attributed to the anatomical proximity of the structures involved in acoustic signal processing. Besides, acoustic stimulation could promote the release of acetylcholine in the brainstem structures, which are involved in initiation of PGO waves. Perhaps, these influences are mediated by changes in the membrane ion-channel permeability (1, 12). In addition, we suggest that EMF exposure on the brain results changes in electric and current density fields, accompanied by modification of synaptic activity, modes of synchronous bursts of neuronal populations, ion dynamics and other phenomena. Finally, it will be manifested on the behavioral and cognitive level.

Thus, proposed biological mechanisms in anxiolytic effects of EMF exposure in GEPRs might include normalization of neuroendocrine, neurotransmitter, and/or neurotrophic factors.

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