Extended Abstract
Volume 6:2, 2020

Mental Disorders and Treatment

Open Access

Brain Disorders: The effect of EMF on behavior manifestation of seizure activity in genetically epilepsy-prone rats- Nato Bukia- Ivane Beritashvili Center of Experimental Biomedicine

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Abstract

In the present study, we examined the effect of acoustic range of electromagnetic field (EMF) on the behavioural manifestation of seizure in genetically epilepsy-prone rats (GEPRs) of Krushinsky Molodkina strain. A five days exposure to EMF (10000 -15000 Hz frequency, 1, 5 m/Tesla, during 20 min) resulted in partial or complete suppression of behaviour activity in GEPRs. Besides, on the background of EMF the latency stage of first wild run was increased and on equivalent conditions, duration of untamed run was decreased. The anxiety degree in irradiated GEPRs versus the controls (GEPRs without magnetic stimulation) was decreased, whereas the locomotion/exploratory activity were increased. Audio genic stimuli obtained in GEPRs changed the Eco activity of sensomotoral cortex only in audiogenally kindled animals. Findings of this study suggest that the regulation of the behavioural manifestation of seizure in GEPRs doesn't involve the cortex; mainly, it's regulated by brainstem structures. The EMF can modulate Ponto-geniculo-occipital (PGO) waves. On the other hand, PGO waves have a possible inhibitory influence on EEG seizure activity. Increased number of PGO spikes in animals exposed to auditory stimulation attributed to the anatomical proximity of the structures involved in acoustic signal processing. Besides, acoustic stimulation could promote the discharge of acetylcholine within the brainstem structures involved within the initiation of PGO waves. Perhaps, these influences mediated by changing in membrane ion channel permeability, which occur under the effect of low-frequency EMF. Also, we propose that EMF exposure on brain results changes in electric and current density fields, amid modification of synaptic activity, modes of synchronous bursts of neuronal populations, ion dynamics, and other phenomena. Thus, acoustic range of EMF can apply for suppression of behavioural manifestation of seizure.

Introduction: Epilepsy is one of the most common disorders. According to the WHO (World health Organization) fact sheet, epilepsy affects about 50 million people of all ages worldwide. Despite the fact that it is possible to treat epilepsy using pharmacological substances, about 30- 40% of the patients are resistant to such treatment (WHO, media Centre 2016). In addition, a long-term consumption of the drugs negatively affects the patients' cognitive functions. The effectiveness of pharmacological agents, used for epilepsy treatment is limited due to incomplete understanding of the mechanisms involved in the pathogenesis of the disease. Therefore, a goal of modern psychiatric research is to find the new ways for anti-epilepsy therapy, which will give the opportunity to cure this group of patients. The EMF exposure is a non-invasive treatment method; it used as a complementary to the drugs, for treating different neurodegenerative diseases (Parkinson's disease, schizophrenia, depression, tinnitus, etc.). EMF exposure also can be used as a separate treatment therapy. Furthermore, repetitive TMS Trans cranial Magnetic Stimulation) is seen as a secure treatment method, without enduring side effects: no long-term neurological, cognitive, or cardiovascular side effects are reported. The EMF appears to be biologically active, penetrating into the living tissue with none impediments. However, it is unclear how the low-frequency EMF can block seizure activity. One of the basic provisions underlying the given research is the assumption that the macromolecules which constitute the living organism are subjected to the conformational fluctuations under the conditions of EMF impact. In our opinion the artificially created EMF may change the tonic activity of the cells located in the local area of its action and because of it the mode of neural impulses formation. Because of it, the tonic activity is also changed in the central nuclei, through which the various sensory afferent ways coming from the various parts of the body are passing. On the other hand, oscillations of acoustic range (which belong to low frequency oscillations) due to their activity can cause the intensification of chemical processes. Then, oscillations of this range can be used both for process stimulation, intensification and optimization and for their attenuation. It will depend on impact mode and selection of duration. Both a change in membrane ion channel permeability and oriented redistribution of radicals, liquid-crystalline macromolecular structures, metalloproteinase

(haemoglobin, vitamins) and molecular water fragments may occur under influence of low frequency magnetic fields

The goal of this study was to explore the potential mechanisms underlying the impact of EMF exposure on the epilepsy. In GEPRs and inbred white rats, we examined the effect of EMF exposure on ECoG activity in sensomotoral cortex. We attempted identify the optimal parameters of repeated EMF exposure, which fully or partially depress the ECoG and behavioural seizure manifestations.

Methods

Subjects and Surgical Procedures: Experiments were conducted on male white, inbred rats and GEP of Krushinsky-Molodkina (KM) strain rats (n=14). This strain of rats manifests short lasting seizure activity in neonatal age and fully-fledged seizure activity after hierarchical implication of brainstem structures. 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 behavioural seizures (group b). The present study was conducted on animals of group b. Under ketamine (5-10 mg/kg intraperitoneally) Anesthesia, the rats were implanted with stainless bipolar electrodes (8IE3633SPCXE ELEC 0.05-125 MM SS Plastics One) into sensomotoral area of neocortex.

Experimental Paradigm: At the beginning of experiments, both control (Inbred, white male rats n=7) and experimental (GEPRs n=14) rats were placed into coil for EMF exposure with defined parameters of magnetic field (see below) for a 20-min session. 10 min after the session of EMF exposure, the animals were re-tested. The GEPRs (with or without exposure) were given audio genic stimuli, for 60 secs, before and after testing in open field for monitoring behaviour correlates of seizure activity.

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 ECoG and behaviour manifestation of seizure activity, were established during pilot experiments. For repetitive (5-days) EMF exposure, we used the following parameters: (10000- 15000 Hz, 1-1.5 m/Tesla).

The Open Field Test: Emotional-motivational status of the rats was tested in a chamber of 80 cm in diameter surrounded by 30 cm height walls, Open Field. The floor of the chamber was divided into 32 squares and lighted with 200 W lamps. 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 centre, numbers of crossed squares, head raise, vertical stands, the frequency and duration of grooming, number of faecal boluses and urination. After each trial, the chamber was cleaned with 30 % ethanol solution.

Data Analysis: We determined the parameters of locomotors and emotional-motivated activity in Open field (see above), the parameters of behavioural (latency of the first wild run, duration of the first wild run, duration of pause, and duration of second wild run, duration of tonic-clonic seizure and of post-ictal activity) and ECoG seizure activity were determined as well.

Note: This work is partly presented at 5th International Conference on Brain Disorders and Therapeutics Madrid, Spain.