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Article · March 2018

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ИЗВЕСТИЯ ВЫСШИХ УЧЕБНЫХ ЗАВЕДЕНИЙ
Т. 59, № 9/2 ФИЗИКА 2016

UDC 57 591.1, 57.024, 577.1

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LABORATORY MICE ARE STRESSED AFTER EXPOSURE TO NANOSECOND REPETITIVE PULSED MICROWAVES

The state of laboratory mice was examined after direct exposure of their brain and epididymal adipose tissue to nanosecond repetitive pulsed microwaves (RPMs). It is found that single daily exposures to 4000 μ pulses for 10 days changes the corticosterone level in the mice blood serum, which can be mediated by stress effects developing in the mice. The effects depend on the pulse repetition frequency.

Keywords: *repetitive pulsed microwaves, nanosecond pulses, mice brain, epididymal adipose tissue, corticosterone.*

Introduction

Radio frequency electromagnetic radiation, including repetitive pulsed microwaves (RPMs), is a factor that may affect the endocrine status in an irradiated organism and induce stress and depression [1]. Earlier, it was suggested that whether RPMs induce a stress response in mice could be traced from corticosterone levels in their blood as a universal indicator of stress or its absence [2]. Thus, reasoning from a change in corticosterone levels in RPM-irradiated mice, one can judge the possibility of negative aftereffects [3]. Besides, the brain structures involved in behavioral adaptation to stress factors contain corticosterone-sensitive receptors [4], and the neuromodulatory effects of corticosteroid hormones provide integration of neural and hormonal mechanisms to adapt to stress [3]. The previous studies demonstrated a significant change in a series of behavioral reactions, motion activity, and mass of viscera and epididymal adipose tissue in laboratory mice after local exposure of their brain and epididymal adipose tissue to nanosecond RPMs [5]. Such changes are likely to be stressful to an animal, and direct action on adipose tissues, being an important neuroendocrine regulator [6], is bound to affect a wide range of reactions in the whole organism. White adipose tissue lies in the center of a network of autocrine, paracrine, and endocrine signaling systems, secretes a vast amount of substances of different biological actions, and can influence the functions of other organs, including the central nervous system (CNS) activity [7]. The response of adipose tissue to nanosecond RPMs can produce a respective change in the state of the whole organism. Reasoning from the foregoing, our aim was to clarify the possibility of stress induction in mice by local exposure of their brain and epididymal adipose tissue to nanosecond repetitive pulsed microwaves.

Experimental setup and measurement procedure

In our experiments, we used 40 inbred white male mice of line C57B1/6 with a weight of 25–30 g from a nursery of the State Scientific Research Institute of Pharmacology, Tomsk Scientific Center SB RAMS (Tomsk, Russia). The experiments conformed to all ethical rules and standards for treatment of animals [8]. Within 10 days, the region of the mice head and epididymal adipose tissue was daily exposed to a single irradiation with 4000 RPM pulses at a peak power density of 1500 W/cm^2 and repetition frequency of 6, 13, 16, and 22 Hz. The RPM source was a laboratory generator based on a MI-505 magnetron (carrier frequency 10 GHZ, pulse duration 100 ns). The intensity of exposure was estimated by a procedure described elsewhere [9]. The mice were divided into to groups: irradiated and sham-irradiated. To provide a local exposure, the body of the mice was covered with a radiation-absorbing material. The irradiation time was varied from 3 to 10 min depending on the pulse repetition frequency. The effect of RPM exposure was estimated from the corticosterone level in the mice blood serum. The level of corticosterone was determined by enzyme immunoassay (ELISA, DRG test system, Germany) with spectrophotometry of sample optical density at a wavelength of 450 nm (Stat Fax 303 Plus, USA). The hormone concentration was calculated from a calibration curve provided with the kit. The data were statistically processed with Statsoft STATISTICA for Windows 8.0 to calculate the arithmetic mean of the index and its error. The significance of the difference between the indicators of the irradiated and sham-irradiated animals was determined using the Mann-Whitney U-test.

Experimental results

The experiments demonstrated that 10-day nanosecond RPM irradiation of the brain and epididymal adipose tissue of mice changed the corticosterone level in their blood serum. Irradiation of both the brain and the adipose tissue at a pulse repetition frequency of 6, 13, and 16 Hz produced a statistically significant increase in the corticosterone concentration in the blood serum (Fig. 1), suggesting that RPMs promote development of stress in the mice.

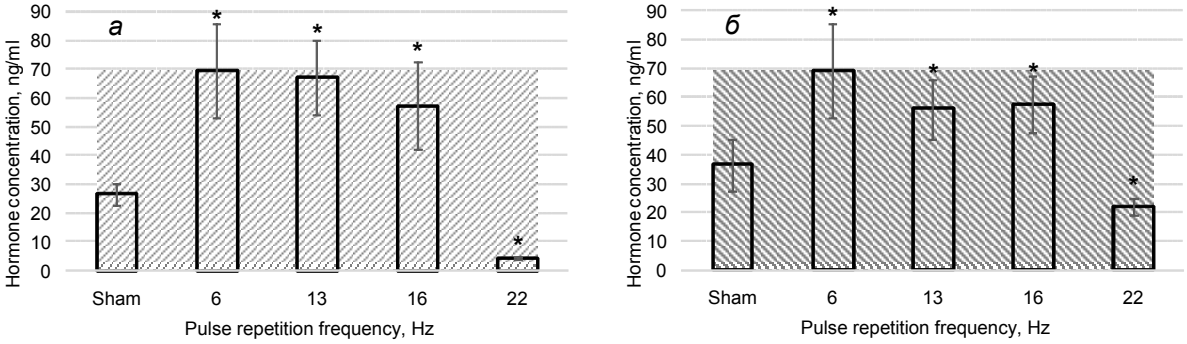

Fig. 1. Corticosterone level in the blood serum of mice after local nanosecond RPM irradiation of their brain (*a*) and epididymal adipose tissue (*b*).

However, after irradiation at a pulse repetition frequency of 22 Hz, a statistically significant decrease was observed in the corticosterone level compared to that in the sham-irradiated group (Fig. 1). This result suggests a complex and ambiguous action of RPMs on the brain and epididymal adipose tissue and on the metabolic processes controlled by them. It is not inconceivable that the decrease in the corticosterone level results from exhaustion of the hormone pool due to severe stress induced by irradiation.

Discussion

The research data and their analysis allow the conclusion that direct nanosecond RPM irradiation of the brain and epididymal adipose tissue changes the state of laboratory mice. The effects depend on the pulse repetition frequency and show up as a significant increase or decrease in the corticosterone level in the mice blood serum, which evidences the possibility of stress response to RPMs. The previous experiments on mice demonstrated that tenfold RPM irradiation of their brain decreased their food intake, mass of their body, liver, spleen, and epididymal fat as well as reduced their searching activity against enhanced passive defensiveness in an open field [5]. The results agree with our data, suggesting that depression and enhanced emotional reactivity develop in mice after tenfold irradiation, which can be mediated by developing stress [1, 3, 4].

Conventionally, it is considered that the biological efficacy of electromagnetic radiation is determined in many respects by its thermal action [10]. Microwave irradiation with a power density of tens and hundreds of milliwatt per centimeter induces biological reactions typical of thermal stress [1]. However, the microwave interaction with a biological medium is likely not limited to thermal effects alone [11]. The brain and adipose tissue of mice were irradiated with a peak power density of 1500 W/cm^2, which corresponds to an average of 1.2 mW/cm^2. Because biological effects are determined by absorbed energy, we calculated the specific absorption rate. The average absorption rate was about 15 W/kg. The degree of heating of brain and adipose tissues was no greater than 0.8 °C, which favors the existence of nonthermal mechanisms of biological effects [12]. It is known that the response of adipocytes to temperature is significant only after their overheating by 6.0–7.0° [13]. The RPM influence on brain is likely to be more complex than the mere reactions to increased temperature. According to research data [14], of all CNS structures, it is the brain which is most sensitive and reactive to thermal action. Electromagnetically induced temperature shifts by tenths of a degree are a sufficient thermal stimulus. For this reason, the disturbance of thermal homeostasis can be considered as a cause of changes in the functioning of the CNS and of the whole organism and as a cause of stress, too. At the same time, the nonlinear dependence of RPM effects on the pulse repetition frequency and on the specific absorption rate is indicative of nonthermal action of radiation. The RPM pulses have high amplitudes responsible for a strong electric field (10^5 V/m). Possibly, because of this, nonthermal effects show up either as

electroporation of cell membranes or as direct action of the electric field on extended charged intracellular complexes (cytoskeleton elements, respiratory chain, mitochondria, etc.) [15] with subsequent responses of irradiated tissues. However, reasoning from the foregoing, it is not inconceivable that there is a joint effect of thermal and nonthermal mechanisms, which is bound to assist a complex and ambiguous response.

Conclusions

Thus, it can be stated that nanosecond RPMs can be unfavorable for an organism due to possible development of stress. Because attending personnel and natural complexes can be exposed to nanosecond electromagnetic radiation, it is required to know the character, degree, and specific features of possible adverse effects. Therefore, the obtained data are useful for developing or improving sanitary and ecological standards for safe use of repetitive pulsed electromagnetic radiation.

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Article submitted August 30, 2016

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