Correction of Microcirculatory Disturbances with Terahertz Electromagnetic Radiation at Nitric Oxide Frequencies in Albino Rats under Conditions of Acute Stress

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Terahertz electromagnetic irradiation at frequencies corresponding to NO molecular emission and absorption spectrum 150.176-150.664 GHz corrects disturbances in peripheral circulation typical of acute stress reaction in rats during acute immobilization stress.

Key Words: *microcirculation; peripheral perfusion; terahertz radiation*

Changes in regional (coronary, cerebral, renal) blood flow and systemic hemodynamics, including circulatory failure, are associated with microcirculation disturbances [15]. In some cases, it provokes complications of some cardiovascular disease [10].

Microvasculature blood flow is regulated by active and passive mechanisms [8,12]. Vascualr endothelium plays a key role in active regulation of microcirculatory blood flow [6,8]. Among numerous vasoactive compounds produced by endothelial cells, NO, a potent vasodilator and antiaggregant, plays a specific role [6,9, 13]. NO molecular emission and absorption spectrum lays in terahertz frequency band (THF) [1,14]. Electromagnetic radiation of very high and terahertz frequencies are used for non-drug physiological regulation [3].

Here we studied the effects of electromagnetic radiation at the frequencies of NO emission and absorption spectrum 150.176-150.664 GHz on peripheral perfusion in albino rats under conditions of acute immobilization stress (AS).

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MATERIALS AND METHODS

Experiments were carried out on 45 albino mongrel male rats weighing 180-220 g. All animals were kept under the same conditions. Animal experiments were performed in accordance to Principles of the Declaration of Helsinki.

The animals were divided into 3 groups, 15 animals in each: group 1 (control) consisted of intact animals; group 2 (reference) included male rats with modeled AS; group 3 (experimental) comprised stressed animals exposed to THF irradiation.

Rigid fixation in the supine position for 3 h was used for modeling AS [4,7].

The animals were irradiated using a KVCh-NO apparatus developed by Medical-Technical Association KVCh (Moscow, Russia) in collaboration with NPP-Istok (Fryazino, Russia) and TsNIIIA (Saratov, Russia) [2]. Skin surface (3 cm^2) above the xiphoid process of the sternum was irradiated. The radiator was positioned at a distance of 1.5 cm above the skin. The radiation power was 0.7 mW and power density 0.2 mW/cm^2 (for skin area of 3 cm^2). Radiation dose was determined by power density and total time of irradiation. Single irradiation of animals in AS state was carried out for 30 min.

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Laser Doppler flowmetry (LDF) was performed using laser blood flow analyzer LAKK-02 version 2 (Lazma) and LDF 2.20.0.507WL software. Transducer of laser blood flow analyzer was fixed on the dorsal surface of the right paw using atraumatic patch.

Analysis of LDF-gram and interpretation of the results were carried out according to commonly accepted methods [8].

Statistical treatment was started with testing of hypothesis on the type of data distribution (Shapiro–Wilks test). Since majority of experimental data did not comply with normal distribution law, Mann–Whitney *U* test was used for comparisons.

RESULTS

In male rats exposed to AS, perfusion parameters were significantly decreased (compared to the control), which attested to microcirculatory blood flow impairment (Table 1). Moreover, male rats in AS also demonstrated significant decrease in flux and coefficient of variation (Table 1), which reflects decreased modulation of microciculatory blood flow and inhibition of active mechanisms for microcirculation regulation (endothelial secretion and vasomotor mechanisms of microcirculation regulation).

The amplitude-frequency analysis of LDF-grams demonstrated significantly reduced amplitude of endothelial oscillations in male rats subjected to AS (Table 1), which suggested reduced basal NO production by the endothelium. These animals also demonstrated statistically significant decrease in vasomotor oscillations, which attested to increased peripheral resistance. We observed no statistically significant changes in the amplitude of breathing oscillations in male rats in AS, but the amplitude of pulse (cardiac) oscillations was significantly reduced, which attested to decreased arterial blood influx to microvessels.

Thus, peripheral perfusion was disturbed in male rats in AS, which manifested in reduced mean perfusion parameter, inhibition of active mechanisms for microcirculatory blood flow regulation, reduced basal and induced vasodilating activity of microvascular endothelium (reduced basal NO secretion), rise of peripheral resistance, and afferent vessel constriction.

In male rats exposed to THF-irradiation at NO emission and absorption frequencies 150.176-150.664 GHz, perfusion index was restored and did not significantly differ from the control (Table 1). Statistically significant increase in flux and coefficient of variation was observed in group 3 in comparison with group 2. In addition, a trend toward an increase in flux value and, particularly, in coefficient of variation was noted in animals of this group in comparison with the control, which indicated more pronounced modulation of microvessel blood flow and mechanisms of its regulation.

Amplitude-frequency analysis of LDF-grams showed that THF-irradiation significantly increased the amplitude of endothelial and vasomotor oscillations in male rats subjected to AS in comparison with group 2 (Table 1). It reflects the increase in vasodilating activity of the endothelium (activation of basal NO production) and decrease in peripheral resistance. The amplitude of pulse (cardiac) oscillations also increased, which attested to increased arterial blood inflow to the microcirculation bed. All parameters of amplitude-frequency analysis of LDF-grams in this group did not significantly differ from the control.

The observed changes were not associated with heating effect of electromagnetic radiation, because radiation power used in the experiment was low (0.7 mW and 0.2 mW/cm^2 power density for skin area of 3 cm^2). Moreover, it is known that at a radiation power of 1-10 mW and lower, the increase in the temperature of irradiated living object does not exceed 0.1^{o}C [5]. A possible mechanism for realization of the effect of THF-radiation is resonance interaction with endogenous NO system [7] resulting in increased basal NO production. Analysis of interactions of resonance and antiresonance or near-resonance frequencies with biological objects suggests that deviation from resonance frequency results in rapid reduction of positive biological effect, and sometimes negatively affects the organism [11]. Comparison of the efficiency of electromagnetic irradiation with NO frequencies 150.176-150.664 GHz and with frequencies of 42.2 GHz and 53.5 GHz for correction of increased platelet functional activity showed that electromagnetic irradiation at frequencies of 42.2 GHz and 53.5 GHz produced lower antiaggregant effect [5], which was probably associated with insufficient stimulation of NO production [2].

Thus, electromagnetic irradiation at teraherz frequency band with NO emission and absorption frequencies 150.176-150.664 GHz appears to be an effective method for correction of microvascular blood flow and can be used in clinical practice.

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TABLE 1. Microvascular Blood Flow Parameters in Animals under Conditions of AS and under the Effect of THF-Irradiation with NO Emission and Absorption Frequencies 150.176-150.664 GHz

Parameter	Group		
	1	2	3
Perfusion index, perf. units	11.28 (9.91; 13.34)	8.22 (7.20; 8.44) Z_1=2.76 p_1=0.005811	11.02 (9.65; 11.84) Z_1=1.18 p_1=0.238647 Z_2=2.18 p_2=0.029097
Flux, perf. units	1.02 (0.75; 1.26)	0.56 (0.41; 0.72) Z_1=3.24 p_1=0.001215	1.23 (0.96; 1.73) Z_1=1.33 p_1=0.183147 Z_2=3.73 p_2=0.000190
Coefficient of variation, %	8.6 (7.17; 10.87)	6.69 (5.28; 9.78) Z_1=2.05 p_1=0.040057	12.85 (8.43; 16.31) Z_1=1.79 p_1=0.073553 Z_2=3.01 p_2=0.002601
Maximum amplitude of endothelial oscillations, perf. units	2.08 (1.65; 2.81)	1.14 (0.72; 1.68) Z_1=3.38 p_1=0.000724	2.35 (1.95; 3.39) Z_1=1.11 p_1=0.265747 Z_2=3.84 p_2=0.000123
Maximal amplitude of vasomotor oscillations, perf. units	1.33 (1.16; 1.87)	1.01 (0.57; 1.33) Z_1=2.74 p_1=0.006190	1.54 (1.24; 2.31) Z_1=0.96 p_1=0.336976 Z_2=2.88 p_2=0.003971
Maximum amplitude of respiratory oscillations, perf. units	0.34 (0.25; 0.46)	0.21 (0.17; 0.35) Z_1=1.68 p_1=0.092985	0.38 (0.30; 0.64) Z_1=1.16 p_1=0.247455 Z_2=2.51 p_2=0.012091
Maximum amplitude of pulse oscillations, perf. units	0.14 (0.11; 0.29)	0.10 (0.06; 0.17) Z_1=2.14 p_1=0.032670	0.20 (0.12; 0.25) Z_1=0.41 p_1=0.678425 Z_2=2.33 p_2=0.019548

Note. Mean values (Me, median) and lower and upper quartiles (25%; 75%) are presented. Z_1, p_1: in comparison with group 1; Z_2, p_2: in comparison with group 2.

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