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Hemodynamic changes caused by exposure of animals with acute immobilization stress to continuous terahertz radiation

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Abatract: Experimental simulation of hemodynamic disorders during acute immobilization stress has shown that exposure to continuous terahertz radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) for 5, 15 and 30 minutes allows to revert post-stress hemodynamic changes in great vessels. This allows using terahertz electromagnetic radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) to treat hemodynamic disorders accompanying some of pathologic diseases.

Keywords: Hemodynamics, Linear Blood Flow Rate, Terahertz Waves, Nitrogen Oxide, Atmospheric Oxygen

1. Introduction

Hemodynamic disorders can be treated by a wide range of vasodilating agents. However, the optimal results are rather hard to achieve: there is always a risk of undesirable adverse effects and counter indications limiting application of these agents.

That's why, nowadays, development of new drug-free methods of hemodynamic disorder treatment is a subject of intense study. One of such methods is application of low-intensive millimeter and submillimeter radiation [1,2,3,4].

In recent years, a new branch of information therapy has emerged – terahertz therapy [5]. Terahertz frequency band makes for an interesting research subject because molecular absorption and emission spectra (MAES) of various cell metabolites (NO, CO, active forms of oxygen etc.) belong to this band [6].

Of the above mentioned test subjects for electromagnetic radiation effect study, the most interesting are frequencies of absorption and emission spectra of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) as there is evidence of positive effect of the said frequencies energy deposition on rheological properties of blood and platelet functional activity [7,8], blood clotting and fibrinolytic activity [8], blood gas and electrolyte concentration [10], lipid peroxidation and antioxidative activity [11,12], functional status of thyroid body [13], primary indices of metabolic status [14], concentration of adrenocorticotropic hormone in blood [15], receptor system of formed blood elements [16], state of vascular endothelium [17] and microcirculation [18].

The lack of data on physiological effects of exposure of albino rats to electromagnetic terahertz radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) during their immobilization stress leading to disrupted blood flow velocity served as a primary reason for studying various modes of terahertz radiation with the said frequencies.

Thus, the purpose of this work is to study the effects of exposure of albino rats to continuous terahertz radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) during their immobilization stress on their blood flow rate.

2. Materials and Methods

In order to a find a solution to the aforementioned problem, a group of 120 male non-pedigree albino rats with average weight of 180 – 220 g was chosen as a test subject. Simulation of hemodynamic disorders was achieved by incurring active immobilization stress.

The animals were exposed to electromagnetic terahertz radiation equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz). The exposure was done using Orbita, an extremely-high frequency (EHF) therapy apparatus [19,20]. The animals with acute immobilization stress received a single dose of radiation for 5, 15 and 30 minutes.

Blood flow analysis within abdominal aorta and femoral artery was performed using MM-D-F portable microprocessor-based Doppler ultrasonograph ("Minimax", Russia) [21] and Doppler ultrasonic transducer with 10 MHz working frequency used for ultrasound probing. During the analysis, the following parameters were registered: average linear blood flow velocity (Vam), average linear systolic blood flow velocity (Vas), average linear diastolic blood flow velocity (Vad) and pressure differential (PG).

The studied animals was divided into 5 groups of 15 rats each: 1st group – control group (noninvolved animals), 2nd group – comparison group (animals with acute immobilization stress), 3rd, 4th and 5th groups were comprised of animals exposed to terahertz radiation equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) for 5, 15 and 30 minutes (respectively) while 6th, 7th and 8th were comprised of animals exposed to terahertz radiation equal to absorption and emission frequencies of atmospheric oxygen (129.0 ± 0.75 GHz) for 5, 15 and 30 minutes (respectively).

The obtained data were processed with generally accepted parametric and nonparametric methods of statistical analysis using Statistica for Windows v.6.0 software. As Gaussian law was found to be not applicable to majority of obtained data, Mann-Whitney U test was used for value comparison instead and Fischer's z test and certainty factor p were calculated on the basis of Mann-Whitney U test value.

3. Results

According to test results, acute immobilization stress leads to statistically-valid (in comparison to control group) changes of hemodynamic parameters including increase of average linear, average linear systolic and average linear diastolic blood flow velocities as well as pressure differential. I.e., in abdominal aorta linear blood flow velocity increased by 26%, systolic blood flow velocity – by 15%, diastolic blood flow velocity – by 75% and pressure gradient – by 34%, while in femoral artery, linear blood flow velocity increased by 50%, systolic blood flow velocity – by 23%, diastolic blood flow velocity – by 25% and pressure gradient – by 67%.

Maximal efficiency of continuous exposure of male rats with acute immobilization stress to terahertz radiation equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) was found to be achieved after 5 minutes exposure to terahertz waves. In this case, exposure of male rats with acute immobilization stress to terahertz radiation led to complete recovery from any systematic hemodynamic disorders of abdominal aorta and femoral artery which was evidenced by absence of statistically-valid differences in such hemodynamic parameters as average linear, average linear systolic and average linear diastolic blood flow velocities as well as pressure differential of animals from the studied group in comparison to animals from control group. Continuous exposure of male rats with acute immobilization stress to terahertz radiation for 15 and 30 minutes also led to complete recovery from any systematic hemodynamic disorders in both of the abovementioned great vessels (Table 1,2).

Table 1. *Hemodynamic parameters of abdominal aorta blood flow in control groups rats, rats with acute immobilization stress, and rats exposed to terahertz150,176 – 150,664 GHz radiation under immobilization stress.*

Group parameters	Control group	Immobilization stress	Time of radiation exposition under stress		
			5 minutes	**15 minutes**	**30 minutes**
Vam, cm/s	15,2 (14,04;15,8)	17,7 (17,17;20,6) Z_1=4,33 p_1=0,000015	16,19 (15,37;17,64) Z_1=1,60 p_1=0,110288 Z_2=2,88 p_2=0,003943	15,09 (14,25;15,86) Z_1=0,06 p_1=0,950390; Z_2=4,58; p_2=0,000005; Z_3=1,76 p_3=0,077932	14,77 (14,16;15,74) Z_1=0,39 p_1=0,693551 Z_2=4,67 p_2=0,000003 Z_3=2,01 p_3=0,442543 Z_4=0,44 p_4=0,663186

Vas, cm/s	34,5 (32,93;37,64)	40,56 (35,28;43,91) Z_1=2,65 p_1=0,007941	34,45 (30,58; 38,12) Z_1=0,10 p_1=0,917411 Z_2=2,30 p_1=0,021334	34,60 (31,36;36,07) Z_1=0,62 p_1=0,533833 Z_2=2,79 p_2=0,005114 Z_3=0,48 p_3=0,633364	34,34 (31,36;38,42) Z_1=0,48 p_1=0,633364 Z_2=2,92 p_2=0,003454 Z_3=0,37 p_3=0,708923 Z_4=0,06 p_4=0,950390
Vad, cm/s	3,13 (0,78;4,7)	3,92 (3,13;6,27) Z_1=2,07 p_1=0,038089	2,45 (0,78; 3,92) Z_1=0,37 p_1=0,708923 Z_2=2,57 p_2=0,010122	1,46 (0,00;3,13) Z_1=1,61 p_1=0,105740 Z_2=3,38 p_2=0,000724 Z_3=1,49 p_3=0,135383	2,50 (1,56;3,92) Z_1=0,35 p_1=0,724416 Z_2=2,51 p_2=0,012093 Z_3=0,29 p_3=0,771551 Z_4=1,68 p_4=0,092885
PG, mmHg	0,46 (0,4;0,54)	0,64 (0,49;0,73) Z_1=2,63 p_1=0,008443	0,46 (0,36; 0,57) Z_1=0,12 p_1=0,900972 Z_2=2,36 p_2=0,018067	0,45 (0,38;0,49) Z_1=0,87 p_1=0,383733 Z_2=2,86 p_2=0,04210 Z_3=0,73 p_3=0,467921	0,48 (0,38;0,57) Z_1=0,37 p_1=0,708923 Z_2=2,73 p_2=0,006190 Z_3=0,33 p_3=0,740022 Z_4=0,35 p_4=0,724416

The data present as median and intercvartiles –Me (Q1-Q3). p1 is p-level of difference from control group. p2 is p-level of difference from group with acute immobilization stress.

Table 2. *Hemodynamic parameters of femoral artery blood flow in control groups rats, rats with acute immobilization stress, and rats exposed to terahertz150,176 – 150,664 GHz radiation under immobilization stress.*

Group parameters	**Control group**	**Immobilization stress**	**Time of radiation exposition under stress**		
			5 minutes	**15 minutes**	**30 minutes**
Vam, cm/s	9,67 (8,48;10,39)	13,13 (12,01;13,91) Z_1=4,46 p_1=0,000008	9,21 (8,18;10,24) Z_1=0,48 p_1=0,633364 Z_2=4,17 p_2=0,000031	10,08 (8,61;11,96) Z_1=0,56 p_1=0,575511 Z_2=3,50 p_2=0,000457 Z_3=1,12 p_3=0,262754	9,83 (8,87;11,07) Z_1=0,62 p_1=0,533830 Z_2=4,33 p_2=0,000015 Z_3=1,02 p_3=0,309529 Z_4=0,10 p_4=0,917411
Vas, cm/s	21,17 (19,6;22,74)	24,30 (23,52;28,23) Z_1=3,86 p_1=0,000115	21,80 (18,82;25,09) Z_1=0,08 p_1=0,933886 Z_2=2,26 p_1=0,023788	22,10 (21,17;23,52) Z_1=1,76 p_1=0,077932 Z_2=2,94 p_2=0,003230 Z_3=0,87 p_3=0,383733	21,85 (20,38;22,74) Z_1=0,87 p_1=0,383733 Z_2=3,01 p_2=0,002637 Z_3=0,73 p_3=0,467921 Z_4=0,91 p_4=0,361497

Vad, cm/s	-1,57 (-2,36;0,78)	1,56 (0,78;3,92) Z_1=3,65 p_1=0,000262	-0,63 (-3,14;1,56) Z_1=0,35 p_1=0,724416 Z_2=2,90 p_2=0,003691	-0,63 (-2,36;2,35) Z_1=0,46 p_1=0,648204 Z_2=2,45 p_2=0,014397 Z_3=0,21 p_3=0,835705	-1,62 (-3,14;0,1) Z_1=0,81 p_1=0,418618 Z_2=3,96 p_2=0,000075 Z_3=1,24 p_3=0,213375 Z_4=1,02 p_4=0,309529
PG, mmHg	0,17 (0,14;0,19)	0,23 (0,21;0,33) Z_1=3,795 p_1=0,000148	0,18 (0,12;0,25) Z_1=0,06 p_1=0,950390 Z_2=2,38 p_2=0,017080	0,18 (0,17;0,21) Z_1=1,60 p_1=0,110288 Z_2=2,94 p_2=0,003230 Z_3=0,91 p_3=0,361497	0,18 (0,16;0,19) Z_1=0,68 p_1=0,493731 Z_2=3,11 p_2=0,001866 Z_3=0,71 p_3=0,480732 Z_4=0,87 p_4=0,383733

The data present as median and intercvartiles –Me (Q1-Q3). p1 is p-level of difference from control group. p2 is p-level of difference from group with acute immobilization stress.

Continuous exposure of male rats with acute immobilization stress to terahertz radiation equal to absorption and emission frequencies of atmospheric oxygen (129.0 ± 0.75 GHz) for 5 minutes leads to normalization of all studied hemodynamic parameters of abdominal aorta and femoral artery. Further increase of time of exposure to electromagnetic terahertz radiation equal to absorption and emission frequencies of atmospheric oxygen to 15 and 30 minutes does not appear to increase biological effect of terahertz radiation to hemodynamic parameters (Table 3,4).

Table 3. *Hemodynamic parameters of abdominal aorta blood flow in control groups rats, rats with acute immobilization stress, and rats exposed to terahertz 129.0 – 0.75 GHz radiation under immobilization stress.*

Parameters	**Control group**	**Immobilization stress**	**Time of radiation exposition under stress**		
			5 minutes	**15 minutes**	**30 minutes**
Vam, cm/s	15,2 (14,04-15,8)	17,7 (17,17-20,6) Z_1=4,33446 p_1=0,000015	15,07 (12,93-15,29) Z_1=0,154672 p_1=0,87708 Z_2=4,025768 p_2=0,000001	15,53 (13,93-15,98) Z_1=1,80775 p_1=0,070646 Z_2=4,70016 p_2=0,000003	15,57 (14,39-15,86) Z_1=1,74574 p_1=0,080857 Z_2=4,058853 p_2=0,000049
Vas, cm/s	34,5 (32,93-35,64)	40,56 (35,28-43,91) Z_1=-2,6546 p_1=0,007941	32,72 (31,36-37,52) Z_1=1,361114 p_1=0,173479 Z_2=3,511056 p_2=0,000446	35,51 (32,15-36,85) Z_1=0,66887 p_1=0,503580 Z_2=3,109337 p_2=0,001875	34,9 (31,36-37,64) Z_1=1,361145 p_1=0,071416 Z_2=3,666061 p_2=0,000246
Vad, cm/s	3,13 (0,78-4,7)	3,92 (3,13-6,27) Z_1=-2,0739 p_1=9,038089	2,35 (0,79-3,13) Z_1=1,562188 p_1=0,118245 Z_2=3,743064 p_2=0,000182	2,31 (0,79-2,35) Z_1=0,054237 p_1=0,95675 Z_2=2,07897 p_2=0,037626	2,35 (0,78-3,92) Z_1=0,63283 p_1=0,526844 Z_2=2,531328 p_2=0,011364
PG, mmHg	0,46 (0,4-0,54)	0,64 (0,57-0,73) Z_1=-2,63386 p_1=0,008443	0,52 (0,38-0,6) Z_1=1,05177 p_1=0,292906 Z_2=3,232646 p_2=0,001227	0,48 (0,38-0,6) Z_1=0,37963 p_1=0,704222 Z_2=2,964716 p_2=0,00303	0,4 (0,36-0,54) Z_1=1,96396 p_1=0,079535 Z_2=3,513308 p_2=0,000443

The data present as median and intercvartiles –Me (Q1-Q3). p1 is p-level of difference from control group. p2 is p-level of difference from group with acute immobilization stress.

Table 4. *Hemodynamic parameters of femoral artery blood flow in control groups rats, rats with acute immobilization stress, and rats exposed to terahertz129.0 – 0.75 GHz radiation under immobilization stress.*

Parameters	Control group	Immobilization stress	Time of radiation exposition under stress		
			5 minutes	15 minutes	30 minutes
Vam, cm/s	9,67 (8,48-10,39)	13,13 (12,01-13,91) Z_1=4,45889 p_1=0,000008	9,32 (9,08-9,76) Z_1=1,11400 p_1=0,265280 Z_2=3,20983 p_2=0,001328	9,36 (9,08-9,84) Z_1=1,24434 p_1=0,213375 Z_2=3,46342 p_2=0,000533	9,5 (9,12-9,84) Z_1=1,01621 p_1=0,309529 Z_2=2,5509 p_2=0,010745
Vas, cm/s	21,17 (19,6-22,74)	24,30 (23,52-28,23) Z_1=3,85746 p_1=0,000115	22,06 (21,17-22,74) Z_1=1,03848 p_1=0,299050 Z_2=3,37977 p_2=0,000726	22,82 (21,17-23,52) Z_1=1,63838 p_1=0,101343 Z_2=1,80430 p_2=0,071186	22,34 (21,17-23,52) Z_1=0,954 p_1=0,340087 Z_2=2,44721 p_2=0,014397
Vad, cm/s	-1,57 (-2,36-0,78)	1,56 (0,78-3,92) Z_1=3,65007 p_1=0,000262	-1,7 (-2,36-0,79) Z_1=0,45315 p_1=0,650439 Z_2=3,34200 p_2=0,000832	-1,56 (-2,36-0,79) Z_1=0,477 p_1=0,633364 Z_2=2,46795 p_2=0,01359	-1,79 (-2,75-0,79) Z_1=1,63838 p_1=0,101343 Z_2=2,38499 p_2=0,01708
PG, mmHg	0,17 (0,14-0,19)	0,23 (0,21-0,33) Z_1=3,79524 p_1=0,000148	0,18 (0,17-0,19) Z_1=0,92519 p_1=0,354869 Z_2=3,39865 p_2=0,000677	0,19 (0,17-0,21) Z_1=1,61764 p_1=0,105740 Z_2=1,82503 p_2=0,067997	0,18 (0,17-0,21) Z_1=0,82956 p_1=0,406787 Z_2=2,57104 p_2=0,010122

The data present as median and intercvartiles –Me (Q1-Q3). p1 is p-level of difference from control group. p2 is p-level of difference from group with acute immobilization stress.

4. Results Discussion

Active forms of oxygen acts as intermediate agents for positive effect of electromagnetic terahertz radiation equal to absorption and emission frequencies of nitrogen oxide and atmospheric oxygen in cells and body fluids [22]. The said active forms are generated as a result of enzyme-caused changes in hydration of protein molecules and increase of nicotinamide adenine dinucleotide phosphate oxydase, cyclooxygenase and xanthine oxydase activity while concentration of the said enzymes is kept on stationary level. In their turn, active forms of oxygen together with Ca^{2+} stimulate soluble guanylate cyclase, accumulation of cyclic guanosine monophosphate in endothelial vessel cells and increase of NO-synthase activity which leads to increase of NO generation. This may be one of possible mechanisms of both anti-stress and vasodilating effect of terahertz radiation equal to absorption and emission frequencies of nitrogen oxide and atmospheric oxygen. Synthesized nitrogen oxide has the ability to form complex compound which can act as a sort of repository in vessel endothelium which is capable of releasing NO, if necessary [23,24].

Nitrogen oxide is a natural regulator of vascular tone, thus causing vasodilating effect [25]. Activation of NO-ergic system also restricts excessive secretion of pituitary-hypothalamic stress hormones (adrenocorticotropic hormone, adrenocorticotropic hormone releasing hormone etc.), blocks secretion of catecholamines by adrenal glands and nerve terminals [26]. Nitrogen oxide also supports stress limiting effect of GABA(gamma-aminobutyric acid)-ergic and opioidergic systems [27] by decreasing concentration of stress-inducing hormones (including adrenaline and adrenocorticotropic hormone), which leads to recovery of platelet aggregation ability disrupted by acute immobilization stress.

Mechanism of terahertz waves' activity always includes NO-synthase [28,29]. NO-synthase can influence formation of active forms of oxygen in endothelial cells by activating nicotinamide adenine dinucleotide phosphate oxydase, thus causing vascular relaxation. I.e. hydrogen peroxide causes endothelium-dependent vessel vasodilation which is mediated by prostaglandins E_2 and I_2 [30].

It is known that electromagnetic terahertz radiation equal to absorption and emission frequencies of nitrogen oxide and atmospheric oxygen can replenish decreased nitrite concentration in blood plasma during stress [31,32] which can serve as a indirect indication of normalization of nitrogen oxide generation process and provides an opportunity to normalize endothelial functions.

5. Conclusion

The results of this study has shown that according to experimental simulation of hemodynamic disorders during acute immobilization stress, exposure to continuous terahertz radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) for 5, 15 and 30 minutes allows to revert post-stress hemodynamic changes in great vessels. This allows using terahertz electromagnetic radiation with frequencies equal to absorption and emission frequencies of nitrogen oxide (150.176-150.664 GHz) and atmospheric oxygen (129.0 ± 0.75 GHz) to treat hemodynamic disorders accompanying some of pathologic diseases.

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