

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

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Abstract: 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 adrenocorticotrophic 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 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 were 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 above-mentioned 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 terahertz 150,176 – 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
					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
					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
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
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					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
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
					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
					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 terahertz 150,176 – 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
			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
Vas, cm/s	21,17 (19,6;22,74)	24,30 (23,52;28,23) Z ₁ =3,86 p ₁ =0,000115			

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 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	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 =3,45746 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 Ca²⁺ 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 (adrenocorticotrophic hormone, adrenocorticotrophic 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 adrenocorticotrophic 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 E₂ and I₂ [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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