Phototherapy in the blue range of visible spectrum: the possibilities of optimization of the functional state of the cardiorespiratory system in humans under extreme conditions

Abstract— It was recently shown that perception of the blue part of visible spectrum is mediated by melanopsins localized not only in the retina, but also in cells of the vascular wall. We have studied changes in the human cardiorespiratory system under the influence of light with a wavelength of 470 ± 10 nm in normal life and under extreme conditions of high-latitude marine expeditions (2017 and 2019). Using the method of spiroarteriocardiorythmography (SACR), we recorded parameters of the cardiorespiratory system at rest and under conditions of stress tests; the time of recording was 2 min in all cases. The changes in the studied indicators over and under conditions of stress tests; the time of recording was statistically significant effect of photostimulation on individual groups. However, recent studies have shown that melanopsins, the non-visual pigments most sensitive to the blue range of visible spectrum, are located not only in the retina, but also in the cells of the skin and vascular wall [4]. It was proven that blue light phototherapy not only modulates circadian rhythms and affects the skin [3], but also can accelerate bone regeneration processes [16] and modulate the vascular tone [15]. The vasodilating effects can be a result of direct effect on the contractile elements of vascular smooth muscle cells [2] and also can be mediated by the release of the major endothelial vasodilator NO [4].

In this context, phototherapy in the blue range of the visible spectrum can be effective for improving human performance, e.g. in sports, due to the impact on the cardiorespiratory system.

Our aim was to study changes in the cardiorespiratory system induced by exposure to light with a wavelength of 470 ± 10 nm under extreme conditions of high-latitude marine expeditions.

II. MATERIALS AND METHODS

A. Organization

We performed three experimental series (Table 1):

1. In Moscow, where the participants of the control and experimental groups live and work constantly. The participants did not change their lifestyle throughout the experiment.

2. During a marine expedition in 2017 from the port of Murmansk to Franz Josef Land archipelago (N81°, E55°) aboard Alter Ego yacht within the framework of the "Open Ocean: Arctic Archipelagos-2017. Two captains" project (https://vk.com/topic-123498870_35819244). The participants were divided into the control and experimental groups.

All participants in all series of the experiment signed informed consent form. Compliance with international and Russian laws on the legal and ethical principles of scientific researches with human participation was confirmed by the decision of the Ethics Committee of the Institute of General Pathology and Pathophysiology, 02.09.2019.

C. Methods

Blue light phototherapy was performed using autonomous light-emitting bracelets (BASI; registration certificate No. FSR 2012/13206) (Fig. 1). The bracelet was worn in such a way that led lamps were located on the wrist in the area of superficial veins, which allowed exposure of the blood vessels to electromagnetic radiation. Phototherapy was performed daily (two 12-min sessions) in the mornings from 8:00 to 9:00. The total radiation energy was 58 J. The participants included in the control group did not use the bracelets.

In each series, the state of the cardiorespiratory system in all participants was assessed by spiroarteriocardiohrythmography (SACR) at the beginning and at the end of the experiment. For participants of high-latitude sea expeditions, this examination was performed before the exit and before returning to the Murmansk port.

The following parameters were recorded by SACR:
- minimum, maximum, and mean systolic and diastolic finger blood pressure (ADSmax, ADSmin, ADS, ADD max, ADDmin, ADD), systolic and diastolic BP range (ADSRange, ADDRrange), pulse BP (ADpuls);
- spectral parameters of systolic and diastolic digital BP variability (TPS, LFS, HFS, TPD, LFD, HFD);
- spontaneous baroreflex sensitivity measured and calculated as the Alpha Index [13] (BRS, Alpha Index);
- parameters of cardiac performance (Stroke Volume, Cardiac Output);
- respiratory cardiac performance during the physiological load, spirometric indicators (Tidal Volume, Lung Capacity).

In the beginning and at the end of the experiment, 3 consecutive 2-min registrations were performed for each participant in the sitting position:
- at rest,
- with spirometric mask on under conditions of free breathing,
- with spirometric mask on under conditions of controlled breathing (6 cycles per minute).

The free-breathing mode with mask simulates mild hypoxia and hypercapnia [11] and was developed for the SACR instrument with consideration of its design features. The test with controlled breathing (6 cycles per minute) is a common test for detecting changes in activity of the autonomic nervous system [8], in particular, disorders of autonomic regulation of the cardiovascular system in diabetic neuropathy [1]. In addition, this test is used for BRS assessment [12].

D. Statistics

As the distribution for some data arrays did not fit the normal law (according to the Shapiro–Wilk test), nonparametric algorithms were used to evaluate the differences between the groups by individual parameters: Wilcoxon paired test for related variables and Mann–Whitney test for independent samples. The results in the tables are presented as the median and interquartile range. Statistical significance of general changes in the functional state of the cardiorespiratory system (for all indicators of SACR) was assessed by the results of discriminant analysis (direct step-by-step algorithm). Statistical significance of the actual discriminant functions was assessed using the canonical analysis. The calculations were performed using Statistica 7.0 software.

III. RESULTS AND DISCUSSION

First, it should be noted that registration of the cardiorespiratory system parameters under conditions of free breathing with and without the mask detected no statistically significant effect of blue light phototherapy in all experimental series. However, registration of the cardiorespiratory system parameters during the test with controlled breathing at a rate of 6 cycles per minute revealed statistically significant effect of photostimulation on individual parameters in all 3 series of our experiment (Table 2); the same was shown by discriminant analysis (Table 3).

<table>
<thead>
<tr>
<th>Experiment series</th>
<th>Duration</th>
<th>Participants (n, m/f), mean age (M±SE, years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moscow</td>
<td>40 days</td>
<td>Control group: 6 (3/3), 55.6±1.8; Experimental group: 5 (3/2), 55.7±2.9</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2017)</td>
<td>27 days</td>
<td>Control group: 4 (3/1), 41.2±5.6; Experimental group: 5 (5/0), 45.0±4.1</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2019)</td>
<td>26 days</td>
<td>Control group: 4 (4/0), 44.6±4.6; Experimental group: 6 (6/0), 48.7±3.8</td>
</tr>
</tbody>
</table>

Fig. 1. Device for phototherapy (bracelet with laser sources) on an arctic expedition.

TABLE I. DESCRIPTION OF EXPERIMENT SERIES AND SAMPLES
TABLE II.  CHANGES IN SACR PARAMETERS RECORDED UNDER CONDITIONS OF CONTROLLED BREATHING (6 CYCLES PER MINUTE) DURING THE EXPERIMENT (IN % IN COMPARISON WITH THE INITIAL VALUES). ONLY THE MOST SIGNIFICANT RESULTS ARE PRESENTED. THE STATISTICAL SIGNIFICANCE OF DIFFERENCES FROM THE INITIAL VALUES WITHIN EACH GROUP (PAIRED WILCOXON TEST) IS PRESENTED IN THE CORRESPONDING CELLS; SIGNIFICANCE OF DIFFERENCES BETWEEN THE CONTROL AND EXPERIMENTAL GROUPS (MANN-WHITNEY TEST) IS PRESENTED IN THE RIGHT COLUMN.

<table>
<thead>
<tr>
<th>Experiment series</th>
<th>Parameters</th>
<th>Control group $M_e (Q_1; Q_3)$</th>
<th>Experimental group $M_e (Q_1; Q_3)$</th>
<th>$Z$ (M-U)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moscow</td>
<td>Alpha Index</td>
<td>8.4 [16.9; 18.8] $p = 0.600$</td>
<td>-20.5 [40.5; -17.7] $p = 0.115$</td>
<td>2.008</td>
<td>0.045</td>
</tr>
<tr>
<td></td>
<td>ADpulse</td>
<td>13.3 [8.5; 61.8] $p = 0.046$</td>
<td>-4.6 [-9.6; 1.3] $p = 0.915$</td>
<td>1.643</td>
<td>0.100</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2017)</td>
<td>ADSmax</td>
<td>-24.2 [-35.6; -23.9] $p = 0.067$</td>
<td>-12.8 [-15.2; -4.6] $p = 0.138$</td>
<td>-2.449</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>ADSmin</td>
<td>-32.9 [-38.8; -29.3] $p = 0.067$</td>
<td>-6.6 [-8.9; -3.2] $p = 0.043$</td>
<td>-2.449</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>ADDrange</td>
<td>-34.8 [-51.6; -15.2] $p = 0.067$</td>
<td>5.4 [-10.3; 20.8] $p = 0.892$</td>
<td>-1.715</td>
<td>0.086</td>
</tr>
<tr>
<td></td>
<td>ADD</td>
<td>-26.1 [-28.6; -18.2] $p = 0.585$</td>
<td>16.2 [-16.0; 62.3] $p = 0.043$</td>
<td>1.715</td>
<td>0.086</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2019)</td>
<td>LF/HF</td>
<td>-2.8 [-13.6; 49.2] $p = 0.099$</td>
<td>-24.3 [-26.4; -15.4] $p = 0.043$</td>
<td>1.960</td>
<td>0.050</td>
</tr>
<tr>
<td></td>
<td>RRmin</td>
<td>-6.6 [-17.3; -4.7] $p = 0.067$</td>
<td>7.3 [-11.7; 21.5] $p = 0.418$</td>
<td>-1.706</td>
<td>0.088</td>
</tr>
<tr>
<td></td>
<td>HF%</td>
<td>29.6 [16.1; 48.8] $p = 0.067$</td>
<td>-25.3 [-46.9; -3.1] $p = 0.043$</td>
<td>2.558</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>LF/HF</td>
<td>-29.5 [-64.8; -17.3] $p = 0.067$</td>
<td>29.1 [17.7; 66.4] $p = 0.043$</td>
<td>-2.558</td>
<td>0.011</td>
</tr>
</tbody>
</table>

TABLE III.  RESULTS OF A DISCRIMINANT ANALYSIS OF THE DEGREE OF CHANGE IN THE INDICATORS OF THE CARDIO-RESPIRATORY SYSTEM DURING THE EXPERIMENT.

<table>
<thead>
<tr>
<th>Experiment series</th>
<th>Discriminant Function Analysis Summary</th>
<th>Variants in model</th>
<th>Chi-Square Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moscow</td>
<td>$\lambda_w = 0.238$ $F (3, 7) = 7.438$ $p = 0.014$</td>
<td>Alpha Index 0.866 $p = 0.004$</td>
<td>$R = 0.872$ $\lambda_w = 0.239$ $\chi^2 (3) = 10.741$ $p = 0.013$</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2017)</td>
<td>$\lambda_w = 0.002$ $F (6, 2) = 146.336$ $p = 0.007$</td>
<td>ADSmnin 0.537 $p = 0.003$</td>
<td>$R = 0.998$ $\lambda_w = 0.002$ $\chi^2 (6) = 24.347$ $p = 0.001$</td>
</tr>
<tr>
<td>Marine expedition to Franz Josef Land (2019)</td>
<td>$\lambda_w = 0.011$ $F (7, 2) = 26.101$ $p = 0.037$</td>
<td>RRmin 0.292 $p = 0.018$</td>
<td>$R = 0.994$ $\lambda_w = 0.011$ $\chi^2 (7) = 20.365$ $p = 0.004$</td>
</tr>
</tbody>
</table>
As is seen from Table 2, the differences between the control and the experimental groups under normal conditions (in Moscow) were found only in the dynamics of alpha index, but in none of the studied groups, the changes in this parameter during the experiment attained the level of statistical significance. Nevertheless, this parameter, as well as the measured parameter BRS were included in the discriminant function (Table 3) along with the level of statistical significance. Nevertheless, this changes in this parameter during the experiment attained of alpha index, but in none of the studied groups, the influence of psychological factors on the state of the cardiovascular system

Under extreme conditions of Arctic expedition in 2017, intergroup differences were revealed for SBPmax, SBPmin, and sBP: during the expedition, these indicators in the experimental group decreased to a lesser extent than in the control group. The decrease in dBP in the experimental group was also less pronounced (though statistically significant) than in the control and was accompanied by an increase in dBPRange. In general, these changes can be interpreted as an increase in the stability (adaptability) of the cardiovascular system in participants of the experimental group.

We also revealed a decrease in the relative power of the LF range in the sBP variability spectrum (LFS%). Physiological significance of the latter indicator is poorly understood, but there is a point of view that, by analogy with the interpretation of the HRV spectrum, this range reflects sympathetic and baroreflex influences on the cardiovascular system [13, 14]. In this context, the decrease in LFS% can be an analog to BRS decrease detected from the Moscow series. The discriminant function model in this series includes BP indicators (SBPmin and dBP) and indicators reflecting autonomic BP regulation (HFS). It is important to note that under extreme conditions of Arctic expedition, the discriminant function included HR indexes (HR, RRmax) and its regulation (TP).

Analysis of the results of the Arctic expedition 2019 confirmed the involvement of BRS, HR, BP, and indexes reflecting their autonomic regulation in changes of the functional state of the participants. However, the list of changed indicators and discriminant functions did not completely coincide, probably due to small number of the participants in all groups in all series of the experiment.

In addition, limited yacht crew does not allow realization of a more convincing design of the experiment including the placebo group. Therefore, we cannot exclude the influence of psychological factors on the state of the experimental group. Moreover, we found a tendency to health improvement in participants of Arctic expedition 2017 [6], while psychological studies in individuals wearing BASI revealed the stimulating effect of blue light on psychophysiological parameters [5].

IV. CONCLUSION

Our results suggest principal possibility of the influence of photostimulation in the blue range of the visible spectrum on the cardiorespiratory system in humans. The results of such therapy do not reflect the indicators recorded at rest, but improve the adaptive capacity of the body under conditions of increased physical and psychoemotional stress. However, this possibility requires more profound studies.

ACKNOWLEDGMENT

The authors are grateful to M. V. Gavrilov, Ph.D., the scientific director of the projects "Open Ocean: Arctic Archipelagos 2017. Two captains" and "Open Ocean: Arctic Archipelagos 2019. Barents" for research coordination.

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