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The Special Physiological Importance of the UV-A Spectrum for Successful Phototherapy

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Abstract—This article deals with the characteristics of the functioning of the human biological clock and the possibilities of its correction by light fluxes with different spectral characteristics in patients with seasonal depressions. Phototherapy as a nondrug method of treating seasonal depressive disorders has been used since the early 1980s. The investigation compares the efficiency of phototherapy with different spectral characteristics for correcting biorhythm disorders in subjects with seasonal depressions. Twenty-four patients with recurrent depressive disorders were examined in different years. In group 1, patients underwent a course of phototherapy according to the standard scheme (in the optical range); in group 2, patients underwent a course of phototherapy by the original method developed by the authors, with the light flux enriched in UV-A (360–380 nm) to model the structure of natural sunlight. The depth and rate of regression of symptoms in patients with seasonal depressions showed the higher efficiency of UV-A phototherapy compared to the phototherapy in the optical spectrum.

Keywords: optical range phototherapy, UV-A phototherapy, biological rhythms, seasonal depressions

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It is known that human biological rhythms are regulated by the system of the pineal gland and supraoptic nuclei of the hypothalamus [1]. Synchronization of the rhythms of physiological processes with one another and with environmental factors is determined by the regular alternation of night and day [2]. This correction is performed with sunlight. Light excites a special group of light-sensitive retinal cells containing the specific photopigment melanopsin [3]. These retinal cells, in turn, activate the neurons of suprachiasmatic nuclei, which excrete substances that trigger the complex cascades of intracellular molecular reactions resulting in the sleep hormone's (melatonin) inhibition and the long-term suppression of activity of the clock genes. Thus, sunlight performs the circadian adjustment of the molecular clock of the body [4]. Special studies have shown that artificial optical light is ineffective in this respect because of its spectral composition.

In the past decade, increasing attention has been focused on ecological factors in etiology and the development of mental disorders in general and affective pathology in particular. Since the early 1980s, the interest of researchers in seasonal desynchronosis has abruptly increased [5–7]; as a result, a special subtype of depression has been distinguished: the so-called seasonal affective disorder (SAD) [8]. There are different SAD variants depending on the research paradigm [9]; the most widespread of them are seasonal depressions (SDs). The common features of all types of seasonal depressions are as follows: annual episodes of hypothymia in autumn and/or winter [10], sleep disorders, reduced physical capacity for work and vitality, decreased appetite with a high carbohydrate diet, and the divergent or drifting rhythm of basal body temperature.

SD development is largely determined by the circadian instability of the photoperiod. The seasonal dependence of such psychopathological states reflects the influence of global environmental factors on biological organisms. The ratio of the hours of daylight and darkness (photoperiodism) is subjected to latitudinal and seasonal variations. A serious argument in favor of determining SD as an independent diagnostic rubric is the recently published data on the components of the genetic dependence of pathological seasonal sensitivity. Most authors studying the problem of SD associate these states with the decrease in daylight [11] and variations in the structure of natural illumination [12]. It has been shown that the chronobiological effect of light is mediated by the human eye media [13]. Convincing data have been obtained showing the differentiated effects of different spectral regions on the blockade of melatonin and the phase of biological rhythms [14, 15]. The new physiotherapeutic techniques using the therapeutic potential of the short-wave component of the visible light spectrum are actively sought [16–18].

Phototherapy (bright light therapy) is a physiotherapeutic method of correcting emotional and somatoautonomic disorders, as well as sleep disorders during SD and systemic desynchronosis of different nature [19–21]. Phototherapy (PT) as a method of treatment for depressions has been used since the 1980s [22], though the positive effect of light on the human psychoemotional state was noted long before that by many authors. Originally, bright light was used in phototherapy [23]. However, this technique did not always provide a sustained effect; thus, it was necessary to find factors determining the efficiency of phototherapy. Therefore, it was established that the effect of phototherapy was much more pronounced during seasonal disturbances of mood than during desynchronosis without distinct seasonal periodicity [24].

It is assumed that the effectiveness of light is determined by its three main characteristics: intensity, spectrum, and the hours of exposure [25]. The clinical application of PT as a chronotherapeutic method of treatment is pathogenetically substantiated [25], which implies that PT sessions should be performed in the dark (twilight) hours. The methodical aspects of using light of different intensities and in different hours have been thoroughly discussed in the literature [26]. Nevertheless, the important problem of the spectral composition of artificial light remains far from solved. In terms of employing the chronotherapeutic potential, it is promising to use therapeutic devices with both optical and ultraviolet (320–380 nm, UV-A according to [27]) spectral regions.

The objective of this study was the comparative assessment of the efficiency of phototherapy with different spectral characteristics for correcting biorhythm disorders in patients with seasonal depressions. Phototherapy was performed with the use of lamps radiating light in the optical range and by the original method developed by the authors, with the light flux enriched in long-wave ultraviolet radiation (360–780 nm, UV-A) imitating the structure of natural sunlight.

The relevance of the research is determined by the importance of studying the physiological mechanisms of biorhythm regulation, as well as by the wide spread occurrence depressive disorders, the significant side effects and serious complications of drug treatment.

METHODS

A total of 114 patients received a course of phototherapy; 24 of them (5 men and 19 women, 27 to 58 years old), with depressive states of different depths and, intensities, in different periods of time (different episodes of disease) received phototherapy in the optical range (group 1) with the use of our original technique (RU Patents no. 2295989 and no. 2319522 of March 4, 2005) with the light flux enriched in UV-A (group 2). The average age of the patients at the onset of the disease was 32 ± 5 years for men and 36 ± 8 years for women. The duration of the disease at the time of examination was 9 months to 8 years (2.7 years on average). We note that the anamnesis of all male patients showed repeated travels in the latitudinal and longitudinal directions: four subjects had worked previously or continued to work in the period of treatment on a rotational basis (with monthly flights over two to three time zones to the near-polar regions) and one subject took regular (twice a year) trans-Atlantic flights.

The work was carried out in the clinics of Samara State Medical University: Samara Psychiatric Hospital, City Psychoneurological Dispensary (Samara), and Samara Regional Clinical Hospital for War Veterans.

Patients were selected using the following characteristics (inclusion criteria): (1) the history of distinct episodes (phases) of depression lasting for no less than two weeks without psychotic symptoms in the state; (2) the possibility of nondrug treatment of patients during phototherapy; (3) the absence of contradictions to phototherapy; (4) the patient's consent to nondrug treatment by phototherapy; (5) a phototherapy course duration of no less than 25 days; (6) patients were selected on the basis of seasonal dependence and regular recurrence of affective pathology episodes (the presence in the past history) in the fall–winter period (September–December); (7) the absence of significant psychogenic factors of etiology and pathogenesis of disorders under study, the absence of manifest organic disorders of the central nervous system, alcoholism, drug addiction, and serious somatic and concomitant mental diseases.

The main comparison groups consisted of pairs of depressive episodes in 24 patients with recurrent depressive disorder (*F*33 ICD-10). More comprehensive clinical characteristics of seasonal depression patients are given in [16].

Group 1 included disease episodes when patients received a course of phototherapy according to the standard scheme [21], and group 2 included the episodes when patients received a course of phototherapy with exposure to illumination modeling the structure of natural sunlight (the spectral regions of visible and longwave ultraviolet light). The above groups were compared with each other with respect to the degree of regression of symptoms. The dynamics of the patients' state before, during, and after the treatment was assessed using clinical psychopathological classification of the state based on the Hamilton Depression Rating Scale–Seasonal Affective Disorder Version (HDRS-SAD) and Beck Depression Inventory (BDI).

While the first scale (HDRS) reflects the relatively objective opinion of attending physician (or expert physician) about the patient's state, BDI is based on subjective assessment by the patient of his/her state of health (the aspect of subjective experience of a distressing, morbid condition during the depression is one of the foci of clinical psychiatry), which reveals the nuances of therapeutic dynamics.

The clinical psychopathological method was used to distinguish two degrees of depression regression: elimination (more evident improvement of the state).

Elimination of the symptoms was demonstrated by a substantial regression of the morbid state and primarily included normalization of the affective background exhibited by the more or less rapid decrease in the intensity of the distressing affect, a steady improvement

Table 1. Characteristics of depressive episodes by the degree of manifestation in subjects from the studied sample group (by ICD-10)

Gender	Total		Degree of manifestation					
			light		medium		severe	
	abs	%	abs	%	abs	%	abs	%
Men	10	20.8	–	–	6	12.5	4	8.3
Women	38	79.2	14	29.2	18	37.5	6	12.5
Total	48	100	14	29.2	24	50.0	10	20.8

in mood, and the formation of a sustained sensation of normal vitality. Simultaneously with the complete elimination of the morbid affect, there appeared a sensation of vitality, vital force, and the wish for action and being occupied with domesticities. Appetite recovery and body weight normalization to the predisease level were somewhat slower; patients' sleep was normalized as well.

Reduction of the symptoms was a partial effect of the therapy manifesting itself in the partial elimination of pathological phenomena and the incomplete recovery of the predisease state. The therapeutic effect was exhibited primarily by the weakening of the morbid affect. The patients noted the reduction of internal tension associated with the morbid concentration of attention and a peculiar sensation of internal relaxation. Improvement of the state was also marked by the activation of the motivational–locomotor sphere. The clinical aspects of bright light therapy, in particular, the dynamics of the regression of morbid symptoms, are considered in more detail in [16].

The tolerance to phototherapy was assessed by recording and analyzing the data on undesirable events revealed during examination of the patients or based on the patients' spontaneous complaints. Insignificant side effects infrequently occurred in the first days of therapy: labile arterial blood pressure, orthostatic hypotension with vertigo, sleepiness after the morning session, tachycardia, and excessive sweating. These symptoms did not need additional correction and disappeared spontaneously on days 3–7 of treatment.

When estimating the results of our clinical physiological observations, we paid special attention to seasonal dependence as the leading criterion of pathology discrimination. PT efficiency was analyzed with due regard to the depth and intensity of depressive disorders according to the International Classification of Diseases (ICD-10) and to the clinical–syndromic estimation of depression structures accepted in domestic psychiatry. Depressive states in the context of the above-mentioned qualification rubric were presented in episodes with different degrees of manifestation, according to the ICD-10 criteria. The frequency of the occurrence of depressive episodes of different severities is given in Table 1.

A patient was sitting in an armchair at a distance of 1–3 m from four to eight light sources (elevation of the lamps, 0.5–1.5 m above the floor; duration of the session, 60 min). The duration of the PT course was 25 days. Two sessions of equal durations were made every day. A shorter time interval between the end of the morning session and the beginning of the evening session (no less than 8 h) fell during light hours or in the period corresponding to the light hours. Every day, the interval was increased by 10–20 min until reaching no less than 14 h (e.g., day 1 of therapy: 9:00 a.m., the beginning of the morning session; 4:20 p.m., the beginning of the evening session; day 2 of therapy: 8:50 a.m. and 4.30 p.m., respectively).

In group 1 (phototherapy in the optical range), the light was radiated by electroluminescent lamps (visible light, 400–800 nm). The lamps were as follows: LB-80, LD-80, and LBC 60. The number of light sources influencing the patient's eye media varied from four to ten.

In group 2 (UV-A phototherapy), the patient's eye media were exposed to the light imitating the structure of natural sunlight (visible and long-wave UV spectral regions). The electroluminescent lamps emitting visible light (390–780 nm) and the lamps emitting light in the range of 360–380 nm were LB-80, LD-80, LBC 60, LDCUV-80, and Phillips L/73. The number of light sources varied from five to ten, depending on specification. With the above arrangement, the UV radiation intensity at the level of the patient's outer eye media was 0.2 W/m^2 to 0.4 W/m^2. Visible light illumination was about 1500–4000 lx. Accordingly, the exposure dose of UV radiation per session was 3000 J/m^2, staying within the limits of the recommended safe level.

RESULTS AND DISCUSSION

Both groups exhibited similar dynamics of the patients' state characterized by the rapid development of therapeutic effect. In 20.8% of the cases, the state of the patients was improved in the first week of phototherapy until the complete elimination of morbid manifestations. At the end of the fourth week, pathological symptoms without significant dynamics against the background of bright light therapy were observed only in four patients (8.3%). Most patients showed susceptibility to this procedure, demonstrating its therapeutic

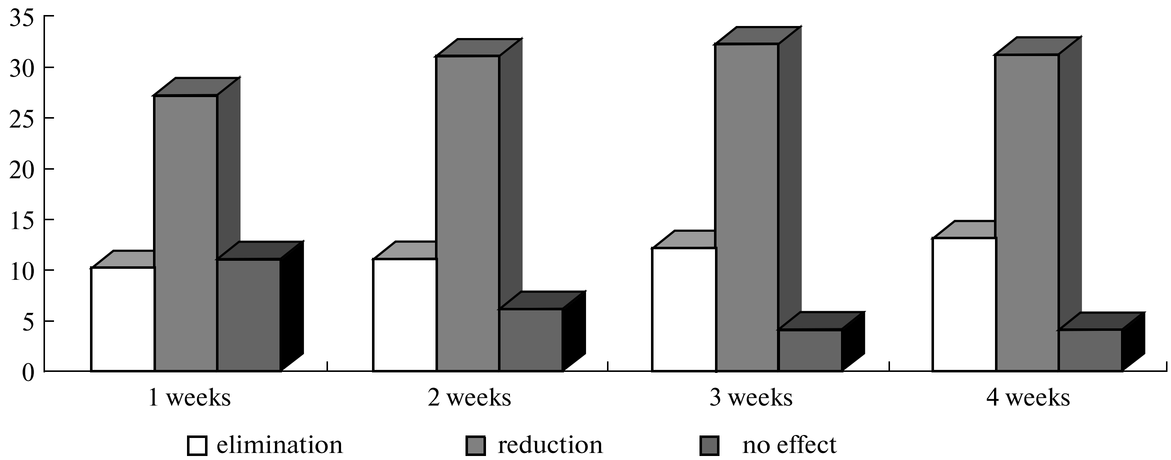

Fig. 1. The dynamics of the clinical state of patients with seasonal depressions during phototherapy (48 episodes) combined for the two phototherapy groups. The three columns show the extent of reduction of clinical symptoms relative to the initial level: elimination, the maximum effect; reduction, the medium effect; no effect, the minimum effect. The *Y*-axis shows the number of disease episodes when the treatment was done; the *X*-axis shows the duration of the therapy (weeks).

potential comparable with drug treatment and probably even exceeding it in terms of the rate of development of the curative effect. The dynamics of the patients' state is shown in Fig. 1.

The dynamics and degree of regression of the psychopathological symptoms were different in the groups under consideration, though not reaching the statistically significant difference level (Fig. 1). The data on the degree of regression of psychopathological symptoms during bright light therapy by the groups of patients are given in Table 2.

The differences in the dynamics of the regression of psychopathological symptoms by the results of patients' state estimation using the HDRS-SAD and BDI are more demonstrative. The data are presented in Fig. 2.

There is a distinct tendency to unidirectional changes in the results on the HDRS-SAD and BDI scales during bright light therapy; scale estimates decrease irrespective of the method of phototherapy. The above changes in scale estimates, coinciding with the clinical estimation data, reliably ($p < 0.05$) reflect the changes in the clinical state from the beginning to the end of therapy. The patients' state is most markedly improved in the first week of phototherapy irrespective of the method used. In the following weeks of therapy, the maximum efficiency was observed in the variant with combined optical and UV radiation.

The therapy with optical and UV radiation yields lower indices by both scales. Wilcoxon's test for pairwise comparison showed statistically significant differences in weeks 3 and 4 with respect to the HDRS-SAD scale ($p = 0.03$ and $p = 0.01$, respectively).

Before discussing the results, it should be noted that the two-phase PT regime modifies the natural photoperiod as a leading factor of SD etiopathogenesis. The photoperiod actually changes every day, and the amplitude of daily changes is determined by geographical latitude. Fundamental (in terms of adaptation) shifts in the photoperiod occur four times a year and are associated with three absolutely different regimes: light (L) > darkness (D), L = D, and L < D. It seems expedient to consider the climatic-geographical and helio-geophysical conditions of the environment, where an organism exists as a complex of ecological factors associated with the geographical latitude of residence and exposed to cyclic variations. The above symptoms are considered to be typical manifestations of the state of desynchronosis: systemic miscoordination of physiological reactions of the body [28] and compensatory inhibition of activity in response to the regular variations of ecological factors. It should be noted that in these terms the clinical vari-

Table 2. Estimation of the dynamics of patients' clinical state during phototherapy for each phototherapy variant separately (group 1: optical range; group 2: UV-A phototherapy)

Degree of regression of the symptoms	Weeks of therapy							
	1		2		3		4	
	Groups							
	1	2	1	2	1	2	1	2
Elimination	3	7	4	7	5	7	6	7
Reduction; No effect	16	11	16	15	15	17	14	17
No effect	5	6	4	2	4	–	4	–

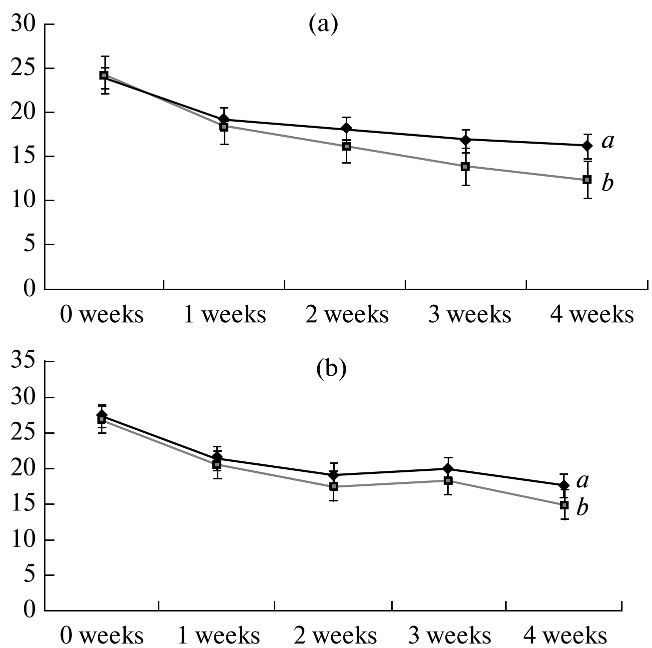

Fig. 2. The dynamics of the state of patients with seasonal depressions during different variants of phototherapy: the values of the Hamilton Depression Rating Scale–Seasonal Affective Disorder Version (*HDRS-SAD*), (a) the values of the Beck Depression Inventory (*BDI*), (b) Group 1, *a*; group 2, *b*. The *X*-axis shows the weeks of phototherapy.

ants of SAD are partial manifestations of disturbances in the system of regulating biological rhythms [29].

The findings show the significance of the spectral composition of light used in the phototherapy of SD patients, which is probably correlated to the etiopathogenetical aspects of the disorders under consideration. The stronger effect of UV-A therapy demonstrates the role of natural sunlight as a factor that influences the processes of autonomic and psychoemotional regulation. The dependence of seasonal affective disorders on the duration of daylight (depending, in turn, on the time of year and the geographical latitude of the patient's residence), which has been noted by many authors [15, 30], is mediated by the genetically determined mechanism of photoperiod sensitivity [31] in the system of circadian photoreceptors [3]. This adaptive ability of living organisms appeared in the course of evolution as a tool of adaptation to the cyclic environmental processes [32]. Synchronization of the physiological rhythms as a fundamental biological process is mediated by an external pacemaker [33], namely, the natural photoperiod. The assumption that the therapeutic effect of phototherapy becomes stronger the more similar the artificial light used in phototherapeutic systems is to the natural sunlight is confirmed by the data obtained (see Table 2).

Our data show that the patients' state is most markedly improved in the first week of therapy, irrespective of the method used. In the following weeks of therapy, the increase in the curative effect slightly slows but the higher efficiency is observed for the treatment by combined optical and UV radiation (UV-A phototherapy). The group of patients receiving UV-A phototherapy exhibited not only a quicker (during the second week) but also a more complete therapeutic effect: positive changes in the psychoemotional state were observed in almost all patients. The results of estimating the patients' state by HDRS and BDI generally reflect the similar dynamics of changes in their state. The slight increase in BDI values by the third week of therapy in both groups was probably due to the revival of hypochondriac ideas against the improvement of the state of the patients.

Thus, the stronger effect of UV-A therapy demonstrates the leading role of natural sunlight as a factor influencing the processes of autonomic and psychoemotional regulation. The neurobiological mechanisms of clinical efficiency of UV-A phototherapy, according to modern concepts, are connected with the functioning of specialized light-sensitive retinal cells containing the photopigment melanopsin: they trigger the complex cascades of intracellular molecular reactions at different levels of the CNS, which leads to the inhibition of the onset of sleep regulating neuropeptide (melatonin) and prolonged suppression of activity of the clock genes. Some observations demonstrate that the peak of melatonin suppression corresponds to the blue region of visible light (460 nm) [21]. Our data show that the shortwave spectral region (UV-A) used in the presented phototherapy technique is more efficient for synchronizing biological rhythms and, accordingly, has a higher potential for correcting pathological states (a quicker and more complete reduction of scale points in the second group of patients).

CONCLUSIONS

(1) Phototherapy can be successfully used for correcting the state of patients with seasonal depressive disorders, both in the variant of bright light therapy and in the variant of combined optical and long-wave UV radiation. The main therapeutic results of phototherapy are achieved in the first four weeks of treatment.

(2) UV-A phototherapy by the original method developed by the authors, with a light flux enriched in a long-wave ultraviolet light (360–780 nm, UV-A) to model the structure of natural sunlight, has proven to be more efficient than bright light therapy.

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