Ultradian Rhythms in Cells and Their Role in Stimulation of Regeneration

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Protein concentration in a cell increases during stimulation of ultradian rhythms by multifrequency irritation corresponding to the hierarchy of cell biorhythms. Physiotherapy synchronous with patient's pulse and respiratory rhythms accelerates regeneration of postoperative wounds and trophic ulcers. Rhythms of physiological regeneration stimulate the repair regeneration.

Key Words: *biorhythms; cell; regeneration; bioregulation; chronophysiotherapy*

Ultradian (circahoralian) rhythms of protein synthesis discovered by V. Ya. Brodskii [2,3] are important for practical medicine. Regulation of ultradian rhythms of protein synthesis [3], conditions of functional induction of excessive anabolism [1], and hierarchy of rhythms of the plastic processes (elongation, intracellular regeneration, and tissue proliferation) [8] are essential for modification of physiotherapy protocols aimed at stimulation of regeneration.

We investigated cellular and organism rhythms and their role in the stimulation of plastic processes.

MATERIALS AND METHODS

Single nervous cell of isolated crayfish mechanoreceptor was put into a special box with normal saline equiped with patch electrode for recording impulses activity and frequencies by means of a UBP-02 amplifier, frequency meter, and N-390 autorecorder. Adequate stimulation (muscle stretch) was carried out by one or three electric magnets simultaneously with modulation periods corresponding to natural mitochondrial aggregation rhythms measured by microdensitography [4]. Rhythms of plastic processes in the neuron were studied by microspectrophotometry on an Opton device (absorption at 265 and 280 nm) [7], differential difraction microscopy on a Jeneval Interfako microscope by measuring reticulum aggregation as an indicator of protein synthesis, and image splitting difraction microscopy under a MBIN-4 microscope by measuring wavelength shift as an indicator of protein content. Aggregation of the reticulum and mitochondria was evaluated by Fisher's information index and maximum values of the spectral function of cell photonegative densitograms. The levels and rhythms of blood microcirculation in patients with trophic ulcers and postoperative wounds were recorded by Doppler flowmetry on a Korall device. Biorhythmologically synchronized laser and electrotherapy were realized by Alto-bio and Garmonia devices, manufactured according to author's patents. The results of experiments and clinical trials were statistically processed using nonparametrical tests and factor dispersion analysis. The reliability of rhythmic periods was evaluated using a Keks software.

RESULTS

Cell experiments revealed hierarchy of the periods of rhythms of functional, energy, and plastic processes. The excitability and frequency of impulse activity of a crayfish neuron in response to controlled load, activities of energy metabolism enzymes, content and biosynthesis of proteins were higher in summer than in winter. A decrease in mitochondrial and reticular aggregation (indicator of energy and plastic metabolism) and a 12% increase in the threshold of impulse

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activity blockade after increasing the muscle stretch ($p<0.05$) at 21.00 in comparison with that observed on the same or next day at 9.00 indicated ultradian rhythms.

Ultradian rhythms of functional, energy, and plastic parameters (with 20-50-min periods) were recorded in a cell intravitally, in particular, significant oscilations were observed for reticular aggregation, ribonucleoprotein and protein concentrations, excitability (neuron impulse activity), and mitochondrial aggregation. Apart from ultradian rhythms, the same cells showed local oscilations of ribonucleoprotein and protein concentrations, frequency of impulse activity, mitochondrial aggregation, and oxygen consumption with periods of about 5 min, 28-35, 9-12, and 1-3 sec [4,5]. Intermediate values of periods were mainly observed during transitional processes in neurons.

The appearance of rhythms slower (10 and even 100 times) than the stimulation rhythm [6] suggested that factors with more rapid rhythms can accelerate slower rhythms of plastic processes. Experiments confirmed this hypothesis. The amplitude of ultradian rhythms of ribonucleoprotein and protein concentrations significantly increased in parallel with the increase in their concentrations in the cell (Figs. 1, 2).

Table 1 shows the effects of permanent, single, and multifrequency exposures. The content of protein

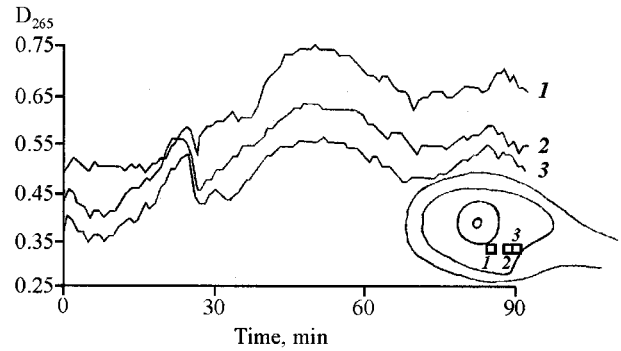

Fig. 1. Changes in 265 nm ultraviolet absorption at 3 sites of a neuron (S=15 μ²) immediately after 30-min multifrequency functional load. Measurment interval 1 min.

(dry weight) and its distribution (by Fisher's information index of the reticular densitogram) were measured. Baseline value measured during 30-min passive state at 5-min intervals was taken for 100%. The mean concentrations of protein (% of initial content) were measured in each neuron (10 cells per series) during the first hour after stimulation; protein distribution was evaluated during the second hour after stimulation. Even a short multifrequency exposure corresponding to the neuron biorhythm hierarchy had a more potent activating effect on biosynthesis with a stable

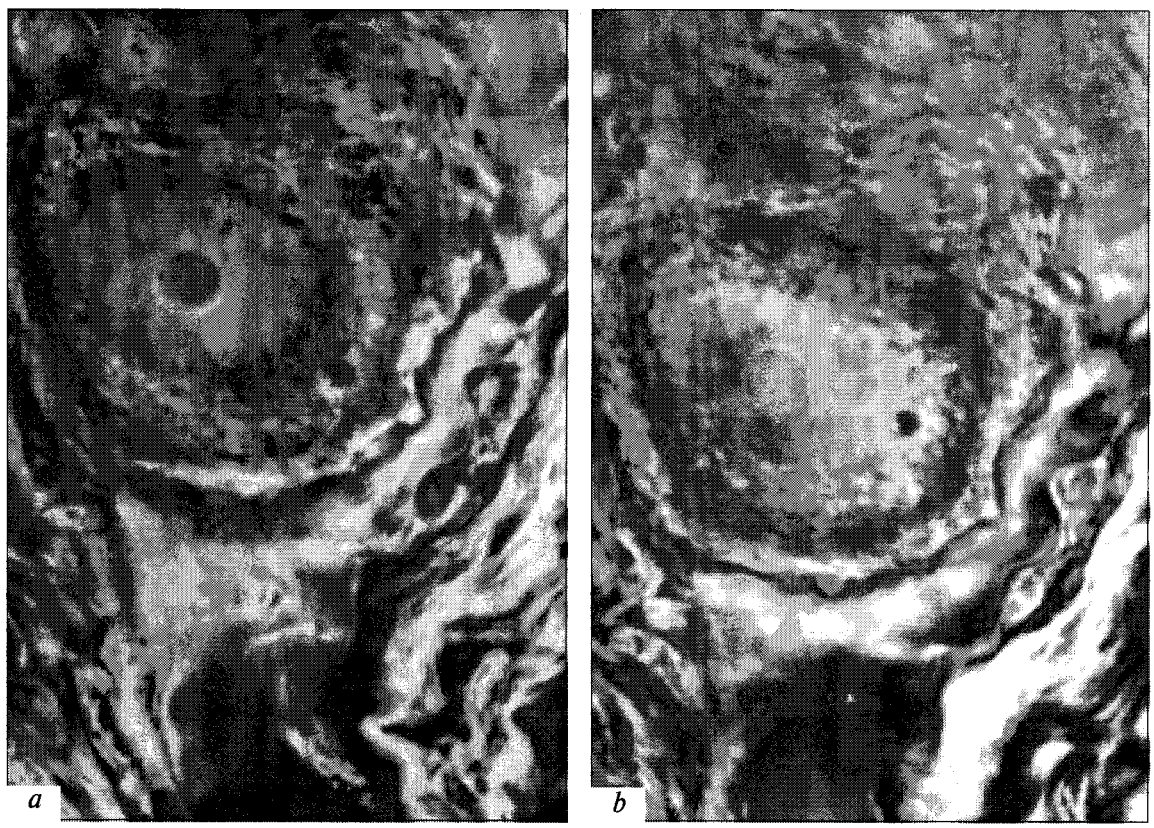

Fig. 2. Vital image-splitting difraction microscopy of a crayfish mechanoreceptor neuron, ×400. *a*) before exposure; *b*) 1 h after 30-min multifrequency functional load.

TABLE 1. Effects of Permanent and Rhythmic Single- and Multifrequency Exposures on Protein Content (Dry Weight, M) and Reticular Aggregation Evaluated by Fisher's Information Index (*I*) of the Crayfish Mechanoreceptor Live Neurons (*M±m*, *n*=10)

Type and duration of exposure	Mean values, % of mean initial values after exposure during			
	the first hour		the second hour	
	M	I	M	I
Constant stretch by 2 mm				
2 min	102±4	105±5	98±4	101±6
20 min	121±5*	147±10*	99±3	96±5
Single-frequency with 1-sec period by 2 mm				
2 min	94±6	100±4	107±6	103±5
5 min	97±9	112±5*	106±4	105±3
10 min	119±6*	117±5*	108±4	103±5
by 4 mm, 2 min	76±10*	95±13	92±5	102±8
Single-frequency with 11-sec period by 2 mm				
2 min	97±7	105±8	95±10	103±5
Single-frequency with 29-sec period by 2 mm				
2 min	105±4	106±7	97±6	98±6
10 min	89±3*	99±6	94±8	101±6
Multifrequency with periods of 1, 11, and 29 sec by 2 mm 2 min	134±5*	127±8*	140±7*	132±6*
10 min	127±5*	158±10*	125±6*	132±8*

Note. Measurements were performed at 5-min intervals. *$p<0.05$ *vs.* initial values.

high content of protein in comparison with continuous or single-frequency stimulation.

These findings suggested that exposure corresponding to physiological regeneration rhythms enhances the rhythms and level of reparative regeneration. We developed an analogous method of biorhythmological controlled physiotherapy consisting of laser or electric stimulation within the rhythm of tissue blood filling monitored by patient's pulse and respiration signals and amplified synchronously with the systole and inspiration.

The carrier frequency varied from 7 to 13 Hz and corresponded to the tremor and elongation rhythms. This stimulation normalized blood microcirculation rhythms and restored regular ultradian rhythms in exposed sites (trophic ulcers of the shin and postoperative wounds). Multifrequency bioregulated chronophysiotherapy was superior to common physiotherapy, as shown by the rate and quality of healing of postoperative wounds and rate and stability of healing of trophic ulcers [9].

Therefore, stimulation of ultradian rhythms of protein biosynthesis and intracellular regeneration effectively stimulates the repair processes at the tissue level. Ultradian rhythms are stimulated by adjusting them to energy processes rhythms by means of multifrequency biorhythmological exposures.

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