# GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

# The Mechanism of Action of Laser Radiation on the Development of Ischemic Arrhythmias After Stimulation of the Sensorimotor Cortex

**S. D. Mikhailova, G. I. Storozhakov, A. V. Kudinova, and T. M. Semushkina**

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Acute experiments on Nembutal-anesthetized cats with occluded circumflex branch of the left coronary artery reveal an antiarrhythmic effect of laser radiation even against the background of the sensorimotor cortex stimulation. This effect may result from the correcting influence of intra-atrial laser irradiation on the activity of bulbar cardiovascular center through the afferent fibers of the vagus nerve and the opioid peptide system.

**Key Words:** *laser radiation; ischemic cardiac arrhythmias; stimulation of sensorimotor cortex; opioid peptides; vagus nerve*

Animals with experimental myocardial ischemia (MI) complicated by ventricular fibrillation show disintegrated neuronal activity in the bulbar cardiovascular center mainly because of increased flow of afferent information from the ischemic myocardium via the vagus nerves to the bulbar centers and cortical structures involved in the regulation of the cardiovascular system activity. Stimulation of these structures during MI considerably increases the occurrence of all ventricular arrhythmias [3]. The fact that cortical centers play an important role in the development of ischemic arrhythmias is confirmed by the high occurrence of severe arrhythmias in MI patients with emotional and other types of pathological stress [9,11].

Bearing in mind the effectiveness of laser therapy in the treatment of ischemic heart disease, we attempted to find out whether the antiarrhythmic effect of laser radiation is altered in animals with acute MI following stimulation of the sensorimotor cortex zone participating in the development of stress reactions.

Russian State Medical University, Moscow

## MATERIALS AND METHODS

The study was conducted on Nembutal-anesthetized (40 mg/kg intraperitoneally), artificially ventilated adult cats of both sexes weighing 2-4 kg. After thoracotomy, the pericardium was excised, the circumflex branch of the left coronary artery was dissected near its orifice, and a dederone thread was passed to that site. Myocardial ischemia was produced by clamping the left coronary artery for 15 min and followed by reperfusion. In all cats, electrostimulation of the sensorimotor cortex was started 10 sec prior to clamping the coronary artery and lasted 20 sec. Monopolar silver electrodes (tip diameter 0.8 mm) were inserted in the sigmoid sulcus after craniotomy and dissection of the dura mater. Stimulation was performed with rectangular pulses (1 msec, 30 Hz) from an ESL-1 apparatus. Pulse intensity ranged from 2.5 to 6.5 mA depending on the magnitude of the resistive voltage drop measured with an S1-48B oscillograph. The precise position of the stimulating electrode was ascertained after extensive craniotomy.

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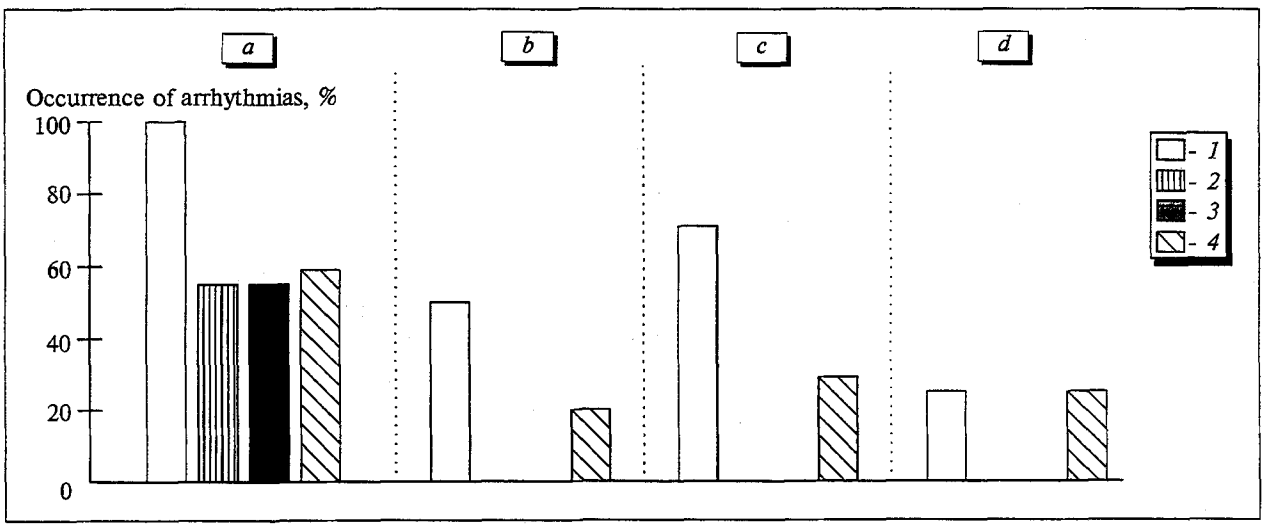


**Fig. 1.** Effect of stimulation of the sensorimotor cortex on the occurrence of ischemic arrhythmias in intact cats (*a*), intra-atrial laser radiation (*b*), intravenous infusion of dalargin (*c*), and bilateral vagotomy (*d*). *1*) pronounced idioventricular arrhythmias; *2*) polytopic extrasystoles; *3*) ventricular tachycardia; *4*) ventricular fibrillation.

In the first series of experiments, the right atrium was irradiated using a ULF-01 helium-neon laser: N=3-5 mW, $\lambda$=632.8 nm, two 20-min sessions before MI, during ischemia and the first 5 min of reperfusion. In the second series, dalargin (Cardiology Research Center, Russian Academy of Medical Sciences, Moscow) was infused intravenously for 15 min during MI in a dose of 10 μg/kg body weight. In the third series, bilateral vagotomy was performed 5 min before ischemia. In all experiments, electrocardiogram was recorded in standard leads II and III, and blood pressure was measured in the femoral artery with a Biocomb-8 polyphysiograph.

Grouped and polytopical ventricular extrasystoles, allorhythmias, ventricular tachycardia, and ventricular fibrillation developing during 15 min of ischemia or the first 15 min of reperfusion were recorded and analyzed. The significance of differences was evaluated by the $\chi^2$ test.

## RESULTS

In the first series of experiments, we studied the effect of intra-atrial laser radiation on the development of the ischemia-induced arrhythmias under conditions of cortical stimulation. Myocardial ischemia was produced in 10 cats on the 20th min of the second 20-min period of laser radiation when the sensorimotor cortex was stimulated. In all cats, MI was complicated by ventricular fibrillation in 20% of the animals, by grouped extrasystoles in 40%, and by allorhythmias in 20%; in five cats no severe idioventricular disturbances of cardiac rhythm were observed, nor were polytopic extrasystoles or ventricular tachycardia noted in any animal. A comparison of these results (Fig. 1, *b*) with those obtained on ischemic cats with stimulated sensorimotor cortex (Fig. 1, *a*) showed that laser radiation elicited an antiarrhythmic effect: the percent of cats with arrhythmias was significantly lower ($p<0.001$), with a threefold reduction in the occurrence of ventricular fibrillation (Fig. 1, *b*). This indicates that the antiarrhythmic effect of intra-atrial laser irradiation was preserved even against the background of the sensorimotor cortex stimulation.

The sensorimotor cortex, like the bulbar centers, contains large amounts of opioid peptides, including leu-enkephalins [1,10]. The blood content of leu-enkephalins depends on the severity of ischemia. Dalargin (DG), a synthetic analog of leu-enkephalins, diminishes idioventricular arrhythmias [2,5,6]. Since the blockade of opiate receptors with naloxone reduces the antiarrhythmic effect of laser radiation, the second series of experiments was designed to evaluate the antiarrhythmic effect of DG in animals with stimulated sensorimotor cortex. The peptide was infused intravenously in a dose of 10 μg/kg body weight in 7 cats with MI. Myocardial ischemia was complicated by grouped extrasystoles in 14.28% of the animals, by allorhythmias in 28.57%, by ventricular tachycardia in 14.28%, and by ventricular fibrillation in 28.58% (Fig. 1, *c*), i.e., the occurrences of ventricular tachycardia and ventricular fibrillation were approximately 3.9 and 2 times lower, respectively, than in cats with MI and stimulated sensorimotor cortex. Being administered intravenously in a dose known not to cross the blood-brain barrier, DG prevents (similarly to intra-atrial laser radiation) the development of severe cardiac arrhythmias associated with stimulation of the sensorimotor cortex.

This indicates that the mechanism of the antiarrhythmic effect produced by laser radiation even upon stimulation of the sensorimotor cortex may involve opioid peptides, which normalize the activity of the bulbar cardiovascular center and directly inhibit the activity of the sympathetic nervous system [8].

The fact that laser radiation and DG have common antiarrhythmic mechanisms is confirmed by disappearance of their effects after blockade of the vagus nerves [6,7]. Therefore, in the third series of experiments we evaluated the role of the vagus nerves in the development of ischemic arrhythmias in cats with stimulated sensorimotor cortex. To this end, bilateral vagotomy was performed in 8 cats 5 min before ischemia. After occlusion of the circumflex branch of the left coronary artery, idioventricular arrhythmias were observed in 25% of the animals, including ventricular fibrillation in 25% and allorhythms in 12.5%. Other cats (75%) did not develop idioventricular arrhythmias. None of the animals developed polytopic ventricular extrasystoles or ventricular tachycardia (Fig. 1, *d*). These results indicate that interruption of the afferent information flows via the vagus significantly ($p<0.001$) reduces the occurrence of cardiac arrhythmias in animals with stimulated sensorimotor cortex. The occurrence of ventricular fibrillation was 2.4 times lower than that in cats with intact vagus under the same conditions.

Thus, transection of the vagus in cats with stimulated sensorimotor cortex lowers the occurrence of ischemic idioventricular arrhythmias (including tachycardia and fibrillation) to the same degree as does intra-atrial laser irradiation of the blood. Disappearance of the antiarrhythmic effect of laser radiation after blockade of afferent fibers of the vagus implies a considerable correcting effect of laser radiation on the afferent information flow conveyed from the ischemic myocardium to the bulbar cardiovascular center [7].

Our results indicate that laser radiation produces an antiarrhythmic effect (even during stimulation of the sensorimotor cortex) by correcting the activity of the bulbar cardiovascular center via the opioid peptide system and afferent fibers of the vagus, thus diminishing the activating influence on the sympathetic nervous system. Intra-atrial laser irradiation may be used to correct cardiac arrhythmias in stressed patients with ischemic heart disease.

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