PHYSIOLOGY

Effect of Serotonin on Impulse Activity of Bulbar Cardiovascular Neurons

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Translated from *Byulleten' Experimental'noi Biologii i Meditsiny*, Vol. 147, No. 2, pp. 124-126, February, 2009
Original article submitted 8 April, 2008

Alteration of impulse activity of afferent and intercalatory neurons of bulbar cardiovascular center upon serotonin microinjection was demonstrated in acute experiments in rabbit. Afferent neurons were more sensitive to serotonin than interneurons.

Key Words: *serotonin, impulse activity, cardiovascular neurons, bulbar cardiovascular center*

Serotonin is one of important mediators of mammalian and human central nervous system; it is involved in control over physiological systems of the body including the cardiovascular system. It was demonstrated that serotonin microinjection into different nuclei of medulla oblongata including the solitary tract area, leads to a shift in hemodynamic indices: heart rate, arterial blood pressure (ABP), cardiac output and total peripheral resistance [7-11]. The presence of serotonin receptors, involved in formation of neuron discharge rhythms, in the area of solitary tract was demonstrated in many studies [4-6]. We have previously shown that besides myocardium abnormalities, alteration of neuronal activity in medullar cardio-vascular center is also of great importance for the progression of severe ischemic arrhythmias. It was observed that myocardial ischemia, complicated by ventricle fibrillation, is accompanied by disagreement in activity of afferent and intercalatory neurons of bulbar cardiovascular center, while the changes of impulse activity of these neurons have a unidirectional character upon non-complicated course of myocardial ischemia [2].

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The aim of the study is to investigate the impulse activity of bulbar cardiovascular neurons upon serotonin microinjection into these cells.

MATERIALS AND METHODS

Experiments were conducted on 34 rabbits weighting 3-4 kg, anesthetized by thiopental (40 mg/kg of body weight, intraperitoneally). After tracheotomy animals were transferred to artificial ventilation, implemented by means of VITA-1 volume frequency respirator. Electrical activity of bulbar cardiovascular neurons was recorded in the area of solitary tract nucleus. Functional specificity of neurons was determined from characters of initial impulse activity according to previously developed criteria [3]. Synchronous recording of neuronal activity and serotonin microinjection were done using double-barreled glass electrodes. One electrode was filled with 2.5 M KCl, the other one was filled with serotonin solution (4×10^{-4} g/ml) or with Ringer solution. Dosed serotonin delivery was performed using a microsyringe with a micrometer head. ECG from standard leads I and II and ABP in the femoral artery were recorded simultaneously with neuronal impulse activity registration. All the recorded signals were amplified by 4-channel myo-

0007-4888/09/1472-0167

graph M-42 (Medicor) and were recorded on a magnetic film by a magnitograph SDR-41 (Nihon Kohden) and on the RF-3 film (70 mm) by a 4-channel recorder MR-4 (Medicor).

Obtained data was processed using conventional methods of statistical analysis.

RESULTS

To solve the assigned task first of all it was necessary to determine the volume which could be injected into the brain without derangement of haemodynamics. For this purpose we conducted 17 microinjection experiments where Ringer solution was administered in the volume from 10 to 0.5 ml during 40 sec. Initial ABP in animals from this group was 117±2/98±3 mm Hg, 241±12 HR min^{-1}. Injection of Ringer solution in the volume from 5 to 10 ml produced ABP decrease, which reached its maximum 30-40 sec later ($p<0.05$). No alteration of ABP or heart rate was observed upon injection of 0.5 to 3 ml of Ringer solution for 3 min ($p>0.5$).

After we had determined the volume of Ringer solution that had no effect haemodynamics, it was necessary to specify the volume which would not affect the impulse activity of bulbar cardiovascular neurons. For this purpose in a set of 7 experiments impulse activity of 25 afferent and intercalary neurons was recorded in the bulbar cardio-vascular center upon injection of 0.5 to 2 ml of Ringer solution. In none of the cases any alteration of ABP or heart rate was recorded (initially 116±3/96±3 mm Hg and 238±6 HR min^{-1}).

Analysis of neuronal impulse activity has demonstrated that it was altered by administration of Ringer solution in the volume beyond 0.5 ml. Administration of 0.5 ml Ringer solution did not alter impulse activity of any of the neurons. Thus, the volume of 0.5 ml could be used for serotonin delivery to a neuron by microinjection.

In the next set of experiments (10 experiments) we studied impulse activity of bulbar cardiovascular neurons upon serotonin solution (0.2 mg in 0.5 ml which is equal to 4×10^{-4} g/ml) delivery by microinjection during 40 sec. Initial ABP in animals from this group was 118±3/98±3 mm Hg, 240±16 HR min^{-1}. ABP was insignificantly altered upon serotonin injection (3.10±0.25 mm Hg). Heart rate alteration by 1 beat was noted in average 44.80±5.17 sec after the beginning of administration in 45% of cases. We analyzed impulse activity from 15 afferent neurons with constant regular activity and activity of 35 interneurons from bulbar cardiovascular center.

Ten of 15 afferent neurons responded to serotonin administration, with impulse activity alteration of 7 neurons preceding shift in haemodynamics (Fig. 1). Latent period for afferent neurons response was 3.33±0.81 sec from the beginning of serotonin administration. The response of 3 neurons, which showed alteration of impulse activity, was preceded by ABP alteration. Impulse activity of 5 afferent cardiovascular neurons was not altering upon serotonin administration. Thus, 46.7% of afferent neurons responded to serotonin microinjection.

Out of 35 recorded bulbar cardiovascular interneurons 34 neurons responded to serotonin. Impulse activity of 21 neurons altered previous to the shift in haemodynamics (Fig. 2). The latent period of response for these neurons was 5.77±0.79 sec. In 13 neurons alteration of impulse activity was preceded by ABP decrease. One neuron had unaltered impulse activity during the whole observation period. Thus, 67.7% of interneurons responded to serotonin administration.

Neurons with single constant activity (5 neurons) did not respond to serotonin microinjection prior to alteration of haemodynamics.

Thus, it can be concluded that there are afferent and intercalary serotonin-sensitive neurons in the

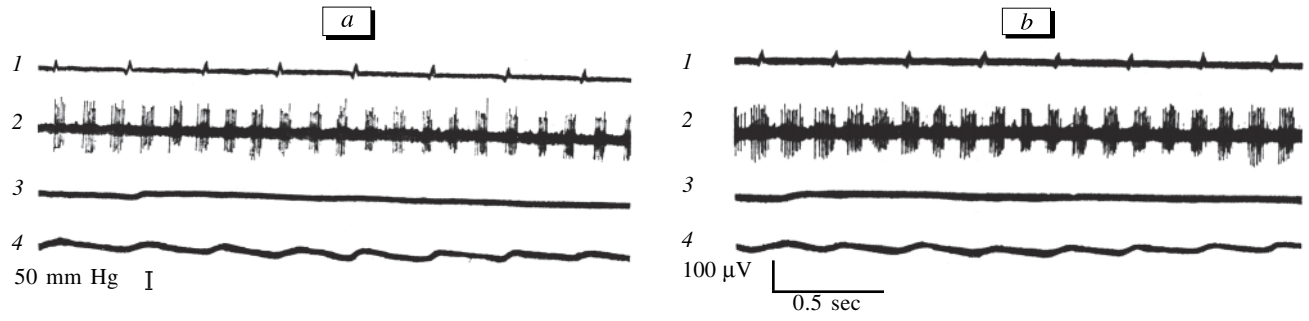

Fig. 1. Impulse activity of afferent cardiovascular neuron upon serotonin administration. *1* — ECG, *2* — impulse neuronal activity, *3* — pneumogram, *4* — ABP. Here and on Fig. 2: *a* — background neuronal activity; *b* — neuronal activity against the background of exposure to serotonin.

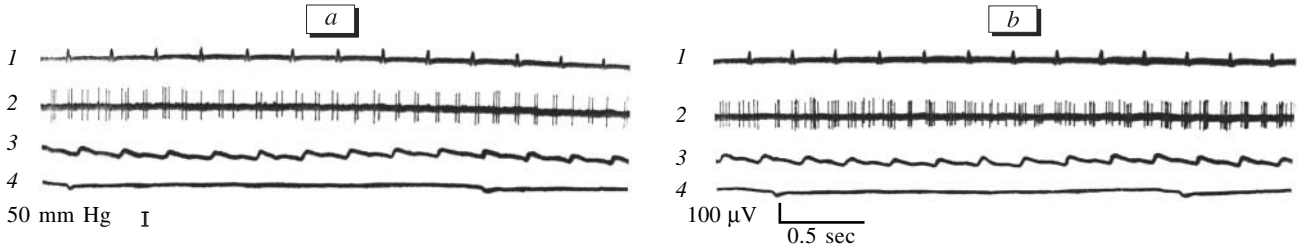

Fig. 2. Impulse activity of intercalary cardiovascular neuron upon serotonin administration. *1* — ECG, *2* — impulse neuronal activity, *3* — ABP, *4* — pneumogram.

bulbar cardio-vascular center, *i.e.* nerve cells that change their impulse activity prior to alteration of haemodynamics upon serotonin microinjection. These neurons have unlike sensitivity thresholds. Different duration of latent periods for alteration of impulse activity in serotonin-sensitive cardiovascular neurons in response to serotonin administration indicates that afferent neurons of the bulbar cardiovascular center are the most sensitive to serotonin. This is confirmed by shorter latent periods of alteration of impulse activity in afferent neurons than in intercalary cardiovascular neurons.

The previously revealed disintegration of afferent and intercalary bulbar cardiovascular neurons activity, which precedes severe heart rate abnormalities upon myocardial ischemia, can be linked to serotonin-sensitive afferent and intercalary neurons activity alteration which emerges when the afferent information from ischemic myocardium is changed [1].

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