Effect of Thyrotropin-Releasing Hormone on Activity of Bulbar Cardiovascular Neurons

S. D. Mikhailova, G. I. Storozhakov, M. A. Popov, T. M. Semushkina, and N. A. Bebyakova

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Acute experiments on narcotized cats showed that intravenous injection of thyrotropin-releasing hormone (20 μg/kg) inhibited discharge activity of most afferent neurons and interneurons in the bulbar cardiovascular center.

Key Words: *bulbar cardiovascular neurons; impulse activity; thyrotropin-releasing hormone*

Abnormal function of bulbar cardiovascular center neurons plays an important role in the development of cardiac arrhythmias during myocardial ischemia [3]. We previously showed that intravenous injection of thyrotropin-releasing hormone (TRH) in a dose of 20 μg/kg during experimental myocardial ischemia produced a pronounced antiarrhythmic effect under conditions of stimulation of sensorimotor cortex [4].

Here we studied the effect of intravenous TRH on discharge activity of bulbar cardiovascular neurons.

MATERIALS AND METHODS

Experiments were carried out on 19 cats of both sexes weighing 2.5-4.0 kg. and narcotized with Nembutal (40 mg/kg intraperitoneally). After tracheostomy, the cats were artificially ventilated with a Vita-1 apparatus. TRH (20 μg/kg, Bokiron) was injected as a bolus into the femoral vein. The cat was fixed in a stereotaxic apparatus (Medicor).

Extracellular recording of bulbar neurons was performed with microelectrodes made of Pyrex glass (tip diameter 2-4 μ) filled with 2.5 M KCl. The occipital muscles were cut with a thermocauter and pulled apart with ligatures. A fragment of dura matter along the median line was removed to expose the rhomboid fossa. To prevent drying of exposed brain surface it was covered with warm mineral oil. The reference silver electrode was fixed subcutaneously in the occipital area. The search for active neurons was performed with a Medicor micromanipulator according to stereotactic coordinates 2 mm rostral and caudal to the obex (region of solitary tract). The signals were fed to a UBP 2-03 amplifier and then to a 4-channel M-42 myograph (Medicor) and SDR-41 tape-recorder (Nihon Koden). The data were processed with original software developed by A. V. Sokolov at Central Research Laboratory of Russian State Medical University.

Functional specificity of bulbar cardiovascular neurons was determined by their initial impulse activity according to criteria developed by G. I. Kositskii and co-workers [2]. Dynamics of discharge activity of cardiovascular neurons was assessed by changes in the discharge rate and by transformation of the train (the changes in the number of impulse trains per cardiac cycle, interval between trains, and their duration). These parameters were analyzed 0.5, 1, 3, 5, 10, and 15 min after injection of TRH. The response was recorded if at least one of the above parameters changed.

In parallel, ECG was recorded in standard lead II, and blood pressure (BP) was measured in the femoral artery with an EMT-35 electromanometer (Elema). The results were analyzed statistically using Student's t and χ^2 tests.

RESULTS

The responses of 27 bulbar cardiovascular neurons (5 afferent neurons and 22 interneurons) to intravenous administration of TRH were examined.

Russian State Medical University, Moscow

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Against the background of unchanged BP (baseline values were 142.54±6.80/118.67±8.40 mm Hg) TRH decreased the discharge rate of afferent neurons and interneurons by 60 and 73%, respectively, starting from 1-2 sec postinjection ($p<0.01$, Figs. 1 and 2). The changes in BP were observed only 3-5 sec postinjection.

Throughout recording, impulse activity decreased in 80% afferent neurons. Most interneurons (65%) also decreased impulse activity under the action of TRH. Moreover, $^1/_3$ reactive interneurons responded to TRH by transformation of group discharges, which manifested by changes in the duration of trains and the number of spikes in them.

Thus, TRH reduced impulse activity of most afferent neurons and interneurons of the bulbar cardiovascular center.

It was established that myocardial ischemia associated with fibrillation increased afferent traffic to neurons of the bulbar cardiovascular center [3,5-8]. Deep narcosis inhibiting CNS and centers responsible for the regulation of the cardiovascular system decreases the incidence of severe cardiac arrhythmias even during stimulation of the sensorimotor cortex [1].

The effect of sensorimotor cortex on bulbar cardiovascular center is mediated via the system of interneurons [3]. Under conditions of deep narcosis, the reaction of these neurons to myocardial ischemia during stimulation of the sensorimotor cortex is also suppressed, which can reduce the degree of disintegration of afferent neurons and interneurons leading to a decrease in the incidence of ischemic arrhythmias [1]. Similar drop in the incidence of cardiac arrhythmias (including ventricular fibrillation) was observed after administration of TRH, which can result from its ability to inhibit impulse activity of afferent neurons and interneurons of the bulbar cardiovascular center.

Thus, it can be assumed that TRH reducing impulse activity of cardiovascular neurons attenuates efferent traffic to the heart thereby decreasing the risk of severe cardiac arrhythmias and ventricular fibrillation.

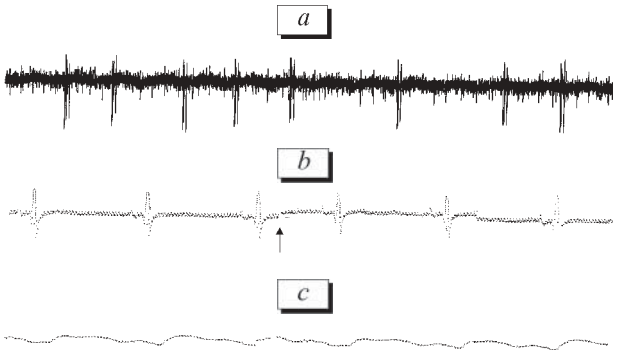

Fig. 1. Effect of TRH on afferent neurons. Here and in Fig. 2: *a*) neurogram; *b*) ECG (isoline elevation corresponds to injection of TRH: arrow marks the start of injection); c) blood pressure measured in the femoral artery.

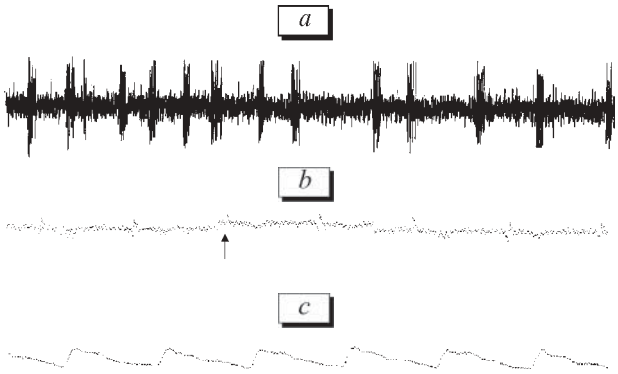

Fig. 2. Effect of TRH on interneurons.

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