Interaction between Different Parts of the Autonomic Nervous System in the Regulation of Smooth Muscles in the Femoral Artery and Trachea

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We studied the interaction between the sympathetic and parasympathetic parts of the autonomic nervous system in the regulation of smooth muscles in the femoral artery and trachea. It was shown that this regulation involves ganglionic serotoninergic neurons transmitting excitation to 5-HT_2 receptors in the effector tissues.

Key Words: *artery; trachea; smooth muscles; serotonin*

Parasympathetic regulatory influences on the femoral artery and vein are mediated by acetylcholine and produce relaxation of smooth muscles in rat femoral vessels; in veins relaxation is more pronounced than in arteries [2]. A histochemical study of sympathetic fibers showed that femoral artery wall contains fluorescent adrenergic nerves. Rapid release of catecholamines from degenerating adrenergic nerves increases their contribution to early vasospasm of microvessels [3].

Various bioactive substances, including prostaglandins, nitric oxide, and serotonin, play a role in modulation of smooth muscle contraction in effector tissues [1]. Serotonin stimulates contraction of smooth muscles in the respiratory tract by increasing Ca^{2+} transport through the potential-dependent Ca^{2+} channel [4].

Apart from catecholamines, the contractile effect can also be produced by serotonin [5]. Polymerase chain reaction assay revealed the presence of mRNA for 5-HT_1D, 5-HT_2A, 5-HT_7, and 5HT_2B receptors that are involved in the regulation of vascular tone [6].

Here we studied the role of serotoninergic systems in the regulation of electromotor activity (EMA) in smooth muscles of the femoral artery and trachea.

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MATERIALS AND METHODS

Experiments were performed on Chinchilla rabbits weighing 3-4 kg. The animals were narcotized with 40 mg/kg nembutal. EMA of smooth muscles in the femoral artery and trachea was recorded with embedded bipolar silver electrodes (contact area 1.5-2.0 mm^2) using a Mingograf-82 device. Stimulation with rectangular pulses was applied to the peripheral segment of the right vagus nerve (amplitude 1-10 V, frequency 5-10 Hz, duration 2 msec) and peripheral segment of the left sympathetic trunk (amplitude 2.5-12.5 V, frequency 5-10 Hz, duration 2 msec).

We recorded baseline EMA of smooth muscles in the examined organs. Stimulation of the vagus nerve was accompanied by stimulation of the sympathetic trunk. Pharmacological study involved 5-HT_2 receptor antagonist spiperone (0.5-1.0 mg/kg) and 5-$HT_{3,4}$ receptor antagonist droperidol (0.5-1.0 mg/kg). Serotoninergic structures were activated with serotonin in doses of 1×10^{-5}-1×10^{-6} g/liter. The results were analyzed by Student's *t* test.

RESULTS

The baseline frequency and amplitude of EMA slow waves in smooth muscles of rabbit femoral artery

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were 3.0±0.3 per min and 0.45±0.06 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude to 3.4±0.3 per min (13%) and 0.70±0.07 mV (55.5%, $p<0.05$), respectively. Simultaneous stimulation of the sympathetic trunk and vagus nerve further increased EMA of arterial smooth muscles. The frequency and amplitude corresponded to 5.4±0.2 per min (58.8%, $p<0.05$) and 1.0±0.1 mV (42.9%, $p<0.05$), respectively. Sympathetic potentiation of parasympathetic influences on EMA of arterial smooth muscles was observed in 23% experiments with adult rabbits weighing more than 3 kg.

The stimulatory phenomenon was abolished after intraperitoneal injection of droperidol. After administration of the test preparation, the baseline frequency and amplitude of EMA in smooth muscles were 1.7±0.2 spikes per min and 0.47±0.04 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude to 4.3±0.6 per min (153%, $p<0.05$) and 0.73±0.03 mV (55.3%, $p<0.05$), respectively. After administration of droperidol, simultaneous stimulation of the sympathetic trunk and vagus nerve did not increase EMA of smooth muscles. The frequency and amplitude were 3.8±0.7 per min and 0.73±0.05 mV, respectively (Fig. 1, *a-c*). These data indicate that sympathetic potentiation of parasympathetic influences on smooth muscles of the femoral artery involves ganglionic serotoninergic neurons carrying 5-$HT_{3,4}$ receptors.

Before administration of spiperone, the baseline frequency and amplitude of EMA in smooth muscles were 2.8±0.5 per min and 0.37±0.04 mV, respectively. Vagus nerve stimulation increased the frequency and amplitude of smooth muscle EMA to 4.3±0.3 per min (53.5%, $p<0.05$) and 0.57±0.06 mV (54%, $p<0.05$), respectively. After administration of spiperone, simultaneous stimulation of the sympathetic trunk and vagus nerve had no effect on the frequency and amplitude of EMA (4.0±0.3 per min and 0.43±0.05 mV, respectively). Sympathetic potentiation of parasympathetic influences on smooth muscles of the femoral artery involves ganglionic serotoninergic neurons with 5-$HT_{3,4}$ receptors that transmit excitation to 5-HT_2 receptors in the effector tissues. The serotoninergic mechanism of this effect was confirmed in the next series with administration of exogenous serotonin and stimulation of the vagus nerve.

The baseline frequency and amplitude of EMA in smooth muscles were 1.5±0.3 per min and 0.35±0.04 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude of smooth muscle EMA to 3.8±0.2 per min (153%) and 0.70±0.07 mV (100%, $p<0.05$), respectively. Administration of serotonin during stimulation of the vagus nerve increased the fre-

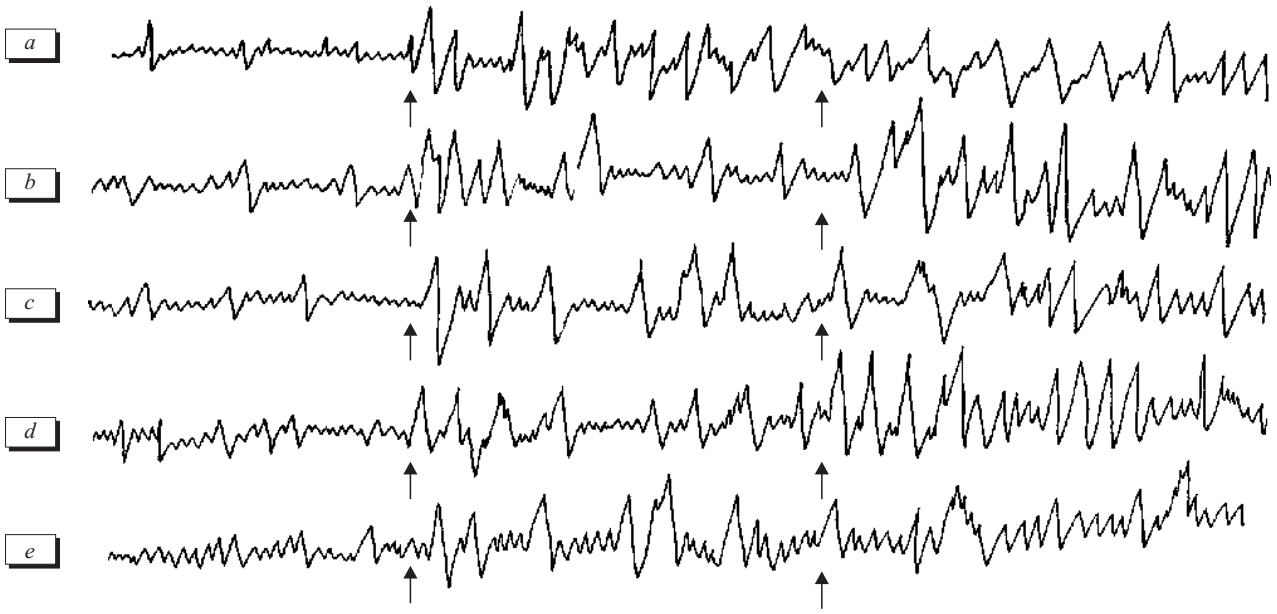

Fig. 1. Electromotor activity (EMA) of smooth muscles in the femoral artery under conditions of vagus nerve stimulation (*a*) and simultaneous stimulation of the sympathetic trunk and vagus nerve before (*b*) or after administration of droperidol (*c*); EMA of smooth muscles in the femoral artery under conditions of serotonin administration and vagus nerve stimulation before (*d*) or after treatment with spiperone (*e*). Left arrow: start of vagus nerve stimulation; right arrow, simultaneous stimulation of the sympathetic and parasympathetic nerves (*b*, *c*) or serotonin treatment during stimulation of the vagus nerve (*d*, *e*).

quency and amplitude to 4.3±0.2 per min (13.2%, $p<0.05$) and 0.50±0.05 mV, respectively (Fig. 1, *d*). These data indicate that treatment with serotonin during stimulation of the parasympathetic nerve is followed by an increase in the frequency of EMA slow waves.

After administration of spiperone, the baseline frequency and amplitude of EMA in smooth muscles were 2.7±0.4 per min and 0.43±0.04 mV, respectively. Vagus nerve stimulation increased the frequency and amplitude to 4.5±0.5 per min (66.6%, $p<0.05$) and 0.50±0.01 mV (16.3%, $p<0.05$), respectively. Administration of serotonin after pretreatment with spiperone and stimulation of the vagus nerve had no effect on EMA of smooth muscles. The frequency and amplitude were 3.8±0.2 per min and 0.40±0.03 mV, respectively (Fig. 1, *e*).

These data indicate that serotoninergic potentiation of vagal stimulation of EMA in smooth muscles of the femoral artery involves excitation of 5-HT_2 receptors in effector tissues.

The baseline frequency and amplitude of slow waves in EMA of tracheal smooth muscles were 2.6±0.7 per min and 0.38±0.10 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude of EMA slow waves to 4.4±0.8 per min (69.2%, $p<0.05$) and 0.64±0.11 mV (68%, $p<0.05$), respectively. Simultaneous stimulation of the sympathetic trunk and vagus nerve potentiated vagal stimulation of tracheal smooth muscles. The frequency and amplitude of EMA slow waves increased to 5.2±0.6 per min and 1.1±0.1 mV, respectively. Sympathetic potentiation of vagal stimulation of EMA in tracheal smooth muscles is observed during simultaneous stimulation of the sympathetic and parasympathetic nerves.

The baseline frequency and amplitude of slow waves in EMA of tracheal smooth muscles were 3.1±0.6 per min and 0.37±0.07 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude of EMA slow waves to 5.2±0.7 per min (67.7%, $p<0.05$) and 0.61±0.07 mV (64.8%, $p<0.05$), respectively. Simultaneous stimulation of the sympathetic trunk and vagus nerve under conditions of 5-$HT_{3,4}$ receptor blockade did not increase the frequency and amplitude of EMA slow waves (4.4±0.5 per min and 0.60±0.15 mV, respectively). These data indicate that sympathetic potentiation of vagal stimulation in tracheal smooth muscles involves ganglionic neurons carrying 5-$HT_{3,4}$ receptors.

Before administration of spiperone, the frequency and amplitude of EMA slow waves in tracheal smooth muscles were 2.0±0.2 per min and 0.33±0.04 mV, respectively. Vagus nerve stimulation was followed by an increase in the frequency and amplitude of EMA slow waves to 3.9±0.3 per min (95%, $p<0.05$) and 0.37±0.04 mV respectively.

After administration of spiperone, the baseline frequency and amplitude of EMA slow waves in tracheal smooth muscles were 3.2±0.5 per min and 0.50±0.03 mV, respectively. Vagus nerve stimulation increased the frequency and amplitude of EMA slow waves to 5.0±0.4 per min (56.3%, $p<0.05$) and 0.52±0.05 mV, respectively. Simultaneous stimulation of the sympathetic trunk and vagus nerve had no stimulatory effect. The frequency and amplitude of slow waves were 4.3±0.6 per min and 0.42±0.03 mV, respectively. These data indicate that sympathetic potentiation of vagal stimulation of EMA in tracheal smooth muscles involves activation of ganglionic serotoninergic neurons transmitting excitation to 5-HT_2 receptors in tracheal smooth muscles.

The last series with administration of serotonin during stimulation of the vagus nerve confirmed these data.

The baseline frequency and amplitude of EMA slow waves in tracheal smooth muscles were 3.5±0.6 per min and 0.27±0.04 mV, respectively. Vagus nerve stimulation increased the frequency and amplitude of EMA slow waves to 4.7±0.6 per min (34.3%, $p<0.05$) and 0.47±0.09 mV (74.1%, $p<0.05$), respectively. Administration of serotonin during stimulation of the vagus nerve potentiated vagal stimulation of EMA in tracheal smooth muscles. The amplitude and frequency were 0.75±0.01 mV (59%, $p<0.05$) and 5.3±0.5 per min, respectively. Therefore, exogenous serotonin potentiates vagal stimulation of tracheal smooth muscles.

Administration of a 5-HT_2 receptor antagonist spiperone abolished the modulatory effect of exogenous serotonin. The peripheral effect of this bioactive amine is realized via preferential binding to 5-HT_2 receptors.

We conclude that the regulation of tracheal smooth muscles by various parts of the autonomic nervous system involves ganglionic serotoninergic neurons transmitting excitation to 5-HT_2 receptors. Activation of these receptors contributes to serotoninergic potentiation of vagal stimulation of EMA in tracheal smooth muscles.

The serotoninergic mechanism of regulation of tracheal smooth muscles should be taken into account in the therapy for chronic obstructive diseases of the lungs.

Serotoninergic potentiation of vagal stimulation of EMA in smooth muscles of the femoral artery and trachea involves excitation of 5-HT_2 receptors in effector tissues.

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