LITERATURE CITED

1. K. V. Anokhin, in: Systemic Mechanisms of Motivation [in Russian], Moscow (1982), pp. 219-221.
2. I. Yu. Orbachevskaya, "The role of gastrin in the central mechanisms of food behavior," Author's Abstract of Candidate's Dissertation, Moscow (1982).
3. S. K. Sudakov, Zh. Vyssh. Nervn. Deyat., No. 2, 378 (1983).
4. J. D. Falasco, G. P. Smith, and J. Gibbs, Physiol. Behav., 23, 887 (1979).
5. J. Gibbs and G. P. Smith, Peptides, 3, 553 (1982).

POSSIBLE SEROTONINERGIC MECHANISM OF INTRACARDIAC INTERACTION BETWEEN VAGUS AND SYMPATHETIC NERVES

G. I. Kositskii,* A. É. Lychkova, V. M. Smirnov, and A. A. Lychkov

UDC 612.178.1:612.178.2

KEY WORDS: heart; regulation; sympatho-parasympathetic interaction; serotoninergic mechanism.

The intensity of function of several internal organs is largely determined by interaction between the sympathetic and parasympathetic nervous system. Stimulation of the sympathetic ganglion reduces the inhibitory effect of the vagus on the heart [1, 8]. However, during weak stimulation of the stellate ganglion accompanied by stimulation of the vagus nerve, potentiation of vagus inhibition of the cardiac rhythm is observed [1, 7, 9]. Similar data also were obtained during an investigation of the effect of different concentrations of catecholamines and acetylcholine when applied simultaneously to the isolated frog's heart [2, 6]. The aim of this investigation was to study the mediator nature of structures involved in the realization of this effect.

EXPERIMENTAL METHOD

Experiments were carried out on chinchilla rabbits weighing 2.5-3 kg anesthetized with hexobarbital (100 mg/kg, intraperitoneally) using artificial ventilation of the lungs by the AID-3 apparatus. Altogether 40 experiments were carried out, in which separate and combined stimulation of the right stellate ganglion and the peripheral end of the divided left vagus nerve were applied (in all series of experiments). During combined stimulation of the nerves, stimulation of the sympathetic ganglion began 7-15 sec after vagus nerve stimulation began, when a stable decrease in the heart rate was established. The parameters of vagus nerve stimulation were near-threshold strength, causing slowing of the heart rate by 20-30% of the spontaneous rhythm. The duration of vagus nerve stimulation was 40-60 sec. The stellate ganglion was stimulated from 10-20 sec by means of an ÉSU-1 stimulator. The absolute arterial pressure (in mm Hg) and the pulse pressure were recorded, so that changes in heart rate and systemic arterial pressure could be judged. Arterial pressure was recorded in the right carotid artery by means of an EMT-35 pressure transducer and UBP2-03 biopotentials amplifier. To evaluate the contractile properties of the heart muscle, the impedance of the myocardium also was recorded by means of electrodes connected to an RG 4-01 rheograph. The recording was made on an N3020-5 automatic ink-writing recorder. To test the mediator nature of the chronotropic effect, trimeperidine (1-2 mg/kg), promethazine (1-2 mg/kg), and chlorpromazine (0.1-1 mg/kg) were used. All drugs were injected intravenously. The investigation comprised 10 acute experiments and 30 chronic experiments. In the latter, the right vagus nerve was divided in the neck under sterile conditions 2-3 weeks before the main part of the experiment, in order to cause its degeneration and to prevent the action of loops of current on parasympathetic fibers during stimulation of the right stellate ganglion.

*Corresponding Member, Academy of Medical Sciences of the USSR.

Department of Normal Physiology, N. I. Pirogov Second Moscow Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 98, No. 7, pp. 7-9, July, 1984. Original article submitted July 15, 1983.

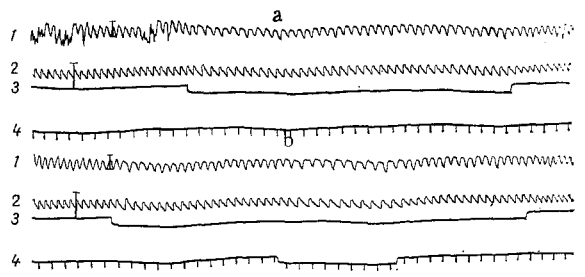

Fig. 1

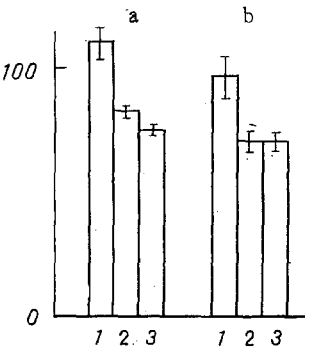

Fig. 2

Fig. 1. Negative chronotropic effect during stimulation of vagus nerve (a) and its potentiation on stimulation of right stellate ganglion (b): 1) impedance of anterior wall of left ventricle (calibration 10 Ω); 2) blood pressure (scale 1-100 mm Hg); 3) zero line with marker of vagus nerve stimulation; 4) time marker (1 sec) with marker of stimulation of stellate ganglion.

Fig. 2. Heart rate before beginning of nerve stimulation (1), during stimulation of vagus nerve (2), and on switching on stimulation of stellate ganglion (3) before (a) and after (b) injection of trimeperidine (1 mg/kg, intravenously), ordinate, heart rate, beats/min.

EXPERIMENTAL RESULTS

Activation of the β-adrenoreceptors of the heart with propranolol led to the development of the phenomenon chosen for study. In each experiment on 10 rabbits, the vagus nerve and stellate ganglion were first stimulated separately, in order to test their functional state. Slowing or quickening of the heart developed respectively. Propranolol was then injected and the above nerves again stimulated in turn. The vagus nerve under these circumstances as a rule inhibited the work of the heart, whereas the sympathetic ganglion had no effect. Combined stimulation was then applied to both nerves. Initially weak stimulation was applied to the left vagus nerve, causing a small decrease in heart rate from 166 ± 8 to 130 ± 4 (22%, $P < 0.05$), after which stimulation was applied to the right stellate ganglion, and this caused further slowing of the heart to 117 ± 3 (10%, $P < 0.05$). Fragments of one experiment are illustrated in Fig. 1.

It can be tentatively suggested that the probable mechanisms of this inhibitory phenomenon are excitation of α-adrenoreceptors, which have an inhibitory influence on the heart [10], or activation of hypothetical cholinergic neurons, connected synaptically with the preganglionic sympathetic fibers of the stellate ganglion [11], or excitation of other structures, serotoninergic for example.

However, the results of this series of experiments also showed that sympathetic nerve fibers do not relay to intracardiac cholinergic neurons in rabbits. This is shown by the absence of inhibition of the work of the heart during isolated stimulation of the stellate ganglion against the background of blocking of the β-adrenoreceptors of the heart (the development of an inhibitory effect through the spreading of loops of stimulating current to the vagus nerve was ruled out under these conditions).

The view of possible participation of cardiac α-adrenoreceptors in the mechanism of this inhibitory effect likewise was not confirmed. In experiments on 10 rabbits using dihydroergotoxin (0.1 mg/kg, intravenously) as a rule vagus inhibition of the cardiac rhythm was potentiated initially by the sympathetic nerve against the background of the action of propranolol. The animal was then given dihydroergotoxin, which blocks α-adrenoreceptors and, against this background, the left vagus nerve was again stimulated, evoking slowing of the heart rate (in this series from 98 ± 2 to 65 ± 1; 33%; $P < 0.05$), and the right stellate ganglion also was stimulated. As a rule this led to additional slowing of the heart to 59 ± 1 (9%; $P < 0.05$). During blockage of β- and α-adrenoreceptors potentiation of the inhibitory effect of the vagus by the sympathetic nerve was thus also observed.

The possibility that serotoninergic structures may participate in the mechanism of the inhibitory phenomenon was studied in the experiments of series III, on 10 rabbits, using trimeperidine, which blocks M-serotonin receptors of ganglionic structures [4, 5]. Potentiation of vagus inhibition of the work of the heart by the sympathetic nerve under these conditions was not observed. These facts are evidence of the participation of M-serotoninergic receptors of intracardiac ganglia in the mechanism of the inhibitory phenomenon (Fig. 2).

The serotoninergic nature of potentiation of vagus inhibition of the work of the heart by the sympathetic nerve was confirmed, in our opinion, by the results of the last series (IV) of experiments, undertaken on 20 rabbits with the use of chlorpromazine (10 experiments) and promethazine (pipolfen) (10 experiments), which are known to block D-serotoninergic tissue receptors [3-5]. In the present series of experiments, addition of stimulation of the stellate ganglion to vagus nerve stimulation, against the background of injection of propranolol, as a rule caused additional slowing of the heart from 91 ± 1 to 81 ± 2 (11%; $P < 0.01$), which was blocked by administration of chlorpromazine or promethazine to the experimental animal.

It can be postulated on the basis of the results of these experiments that serotoninergic intramural neurons with specific M-serotonin receptors and D-serotoninergic receptors on myocardiocyte membranes participate in the mechanism of potentiation of vagus inhibition of the cardiac rhythm by the sympathetic nerve. The presence of this serotoninergic link, which the writers postulate, in the chain of interactions between sympathetic and parasympathetic nerves expands the functional possibilities for realization of their effects on the animal heart.

LITERATURE CITED

1. O. L. Kamardina, in: State and Regulation of Autonomic Functions during Health in Man and Animals [in Russian], Part 1, Vladimir (1975), pp. 112-113.
2. L. R. Krivosin'skii and A. N. Kudrin, in: Problems of Pharmacologic Regulation of Cardiac Activity [in Russian], Moscow (1969), pp. 29-33.
3. I. N. Pidevich, in: Pharmacology of Monoaminergic Processes [in Russian], ed. V. V. Zakusov and N. V. Kaverina, Moscow (1971), pp. 276-313.
4. I. N. Pidevich, Pharmacology of Serotoninergic Structures [in Russian], Moscow (1977).
5. I. N. Pidevich, in: Biochemical Pharmacology [in Russian], Moscow (1982), pp. 169-192.
6. B. A. Smirnov, Fiziol. Zh. SSSR, No. 9, 1078 (1962).
7. N. A. Sokolova, M. A. Kaverin, and M. G. Udel'nov, Byull. Éksp. Biol. Med., No. 3, 195 (1979).
8. A. V. Solov'ev, Fiziol. Zh. SSSR, No. 6, 906 (1938).
9. M. G. Udel'nov, Nervous Regulation of the Heart [in Russian], Moscow (1961).
10. P. Posner, E. L. Ferrar, and C. R. Rambert, Am. J. Physiol., 231, No. 5, Pt. I, 1415 (1976).
11. M. Szentivanyi and E. Kiss, Acta Physiol. Acad. Sci. Hung., 10, 337 (1956).