New Arguments for Positive Inotropic Vagal Influence on Cardiac Contractility in Cats

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Vagal influences on the heart were studied in narcotized cats, in which the cardiotropic effects of sympathetic nerves, heart rate, and pre- and afterload were excluded. Under these conditions vagus nerve exerted only a positive inotropic effect probably mediated by an unknown humoral factor.

Key Words: *cardiac contractility; vagus nerve*

Inhibition of atrial contractility in warm-blooded animals by the vagus nerve (VN) is axiomatic [6]. However, extrapolation of this phenomenon to the whole myocardium [9,12,13] can be erroneous, because heart ventricles are practically devoid of vagal terminals [10] and insensitive to acetylcholine [2]. The reason of this possibly erroneous although widespread view can be indirect decrease of ventricular contractility produced by vagal stimulation accompanied by vagal inhibition of sympathetic influences on the heart [7], cholinergic constriction of coronary vessels [8], moderation of the atrial pumping function [5,11], and bradycardia [14] associated with decreased afterload [5]. However, all these phenomena do not agree with escape rhythm under conditions of vagal stimulation [5,10] and postvagal potentiation of myocardial automaticity and contractility [5,10]. Consequently, our aim was to analyze the inotropic effects of VN, which are still the matter of vigorous discussion in cardiology.

MATERIALS AND METHODS

Experiments were carried out on 10 artificially ventilated temperature-controlled (37°C) cats (body weight 3.0-3.5 kg) anesthetized intraperitoneally with chloralose and nembutal (90+18 mg/kg). β-Adrenoceptors were blocked with propranolol (0.5-1.0 mg/kg intravenously). In all cats the right VN was cut on the neck and its peripheral end was stimulated with trains of 1-4 pulses (1 train per beat, 2 msec, 40 Hz, 6-fold threshold, 1 threshold=0.2-0.3 V) generated by an ESU-2 (Kursk) stimulator. The heart was paced with another ESU-2 stimulator (pulse parameters: 5 msec, 1.25-fold threshold, 1 threshold=0.6-0.8 V) via a bipolar platinum electrode inserted into the right ventricle. Intracardiac ECG was recorded with another electrode introduced into the right atrium. The left ventricular pressure was measured with an electromanometer [3]. The signals were recorded with an N3021-4 X-Y Plotter (Krasnodar) and monitored with an IM-789 8-channel oscilloscope (L'vov).

RESULTS

After injection of propranolol, heart rate, left ventricular systolic pressure (LVSP), and its maximum upstroke rate (V_{max}) were stabilized at 153±5 beats/min, 111±7 mm Hg, and 2734±236 mm Hg, respectively. When the right ventricle was paced at 175±5 beats/min, the atria switched to a retrograde mode of excitation and contracted after atrioventricular valves closing. This annihilated the pumping function of the atria, so LVSP and V_{max} decreased to 83±6 mm Hg and 1960± 51 mm Hg/sec, respectively, providing stable background conditions for studying of the isolated effects of VN on ventricles.

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Under these conditions, vagal stimulation never inhibited, but always enhanced myocardial contractility, so even minor hemodynamic shifts were highly significant. For example, when VN was stimulated with trains of 2 pulses, LVSP and V_{max} increased to 96±56 mm Hg ($p<0.001$) and 2164±64 mm Hg/sec ($p<0.001$), respectively. Similar effects were observed for other parameters of vagal stimulation (Fig. 1).

Enhancement of myocardial contractility was characterized by a pronounced (2-4 cardiac cycles) latency and long-term (up to 10 min) postvagal potentiation of the left ventricular contractility. Intravenous injection of atropine sulfate (0.2 mg/kg) prevented, but not eliminated the positive inotropic effect (Fig. 1).

Our data indicate that VN does not inhibit ventricular contractility directly, but reduced it indirectly via the rhythmoinotropic effect [14], reduction of pre- and afterload [5,11], and suppression of the trophic mechanisms [7,8]. The combination of these factors usually prevails over the opposite (positive) effect of VN manifested by cardiac escape from the effect of stimulated nerve and postvagal potentiation of heart automaticity and contractility. However, the absence of these phenomena under natural conditions due to prevailing of vagal influences led to a conclusion that they are artificial and result from simultaneous excitation of inhibitory and potentiating fibers in VN.

Taking into consideration specific innervation of the ventricles, we assumed that the potentiating vagal fibers also terminate in the atria and stimulate the release of an inotropic factor, which is transported via the coronary arteries to all subdivisions of the myocardium. There is also evidence on the existence on non-mediator humoral stage in vagal potentiation of the cardiac contractility in frogs [4], which also supports this hypothesis. It cannot be excluded that under natural conditions, when inhibitory fibers in VN are not excited, its positive effect can be much more pronounced and even provoke the hyperkinetic hypertensive crises [1], when systolic pressure 2-fold surpasses the diastolic pressure, and which are resistant to β-adrenoblockers and vasodilating agents.

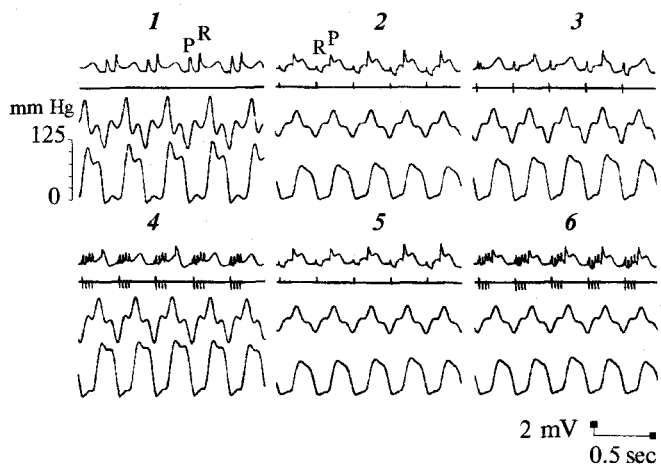

Fig. 1. Effect of train stimulation of the vagus nerve on contractility of the left ventricle under conditions of atrial retrograde excitation and propranolol blockade of sympathetic influences. From top to bottom: intracardiac ECG; the line with marks indicating stimulation of the right ventricle (upward ticks) and vagus nerve (downward ticks); the first derivative of left ventricular pressure; left ventricular pressure. Conditions of signal recording: *1*) initial state of the myocardium, blockade of β-adrenoceptors by propranolol (0.8 mg/kg), *2*) contractile activity of the left ventricle during retrograde atrial excitation, *3*) beat-to-beat stimulation of the vagus nerve by single pulse trains, *4*) stimulation of the vagus nerve by 4-pulse trains, *5*) 10 min after cessation of vagal stimulation and 1 min after injection of atropine (0.2 mg/kg), *6*) repetition of mode 4 of signal recording.

REFERENCES

1. B. Hoffmann and P. Kreunfield, *Electrophysiology of the Heart* [Russian translation], Moscow (1962).
2. V. M. Pokrovskii, G. S. Berlin, Yu. R. Sheikh-Zade, *et al.*, *Fiziol. Zh. SSSR*, **67**, No. 7, 1111-1113 (1981).
3. *Practical Cardiology*, Ed. V. V. Gorbachev [in Russian], Vol. 2, Minsk (1997).
4. T. M. Turpaev and T. G. Putintseva, *Usp. Fiziol. Nauk*, **5**, No. 1, 17-47 (1974).
5. Yu. R. Sheikh-Zade, *Analysis of Heart Function Paced with Vagal Stimulation Rhythm, Abstract of Doct. Med. Sci. Dissertation*, Kiev (1990).
6. W. M. Bayliss and E. H. Starling, *J. Physiol.*, **13**, 407-413 (1892).
7. A. Cevese, G. Verlato, and G. Cerutti, *J. Auton. Nerv. Syst.*, **28**, No. 2, 155-165 (1989).
8. J. Cinca, A. Carreno, L. Mont, *et al.*, *Circulation*, **94**, No. 5, 1101-1108 (1996).
9. R. J. Henning and I. Khalil, *J. Auton. Nerv. Syst.*, **28**, No. 1, 15-25 (1989).
10. C. B. Higgins, S. F. Vatner, and E. Braunwald, *Pharmacol. Rev.*, **25**, No. 1, 119-155 (1973).
11. Y. Inoue, Y. Furukawa, H. Nakano, *et al.*, *Am. J. Physiol.*, **266**, No. 3, Pt. 2, H861-H866 (1994).
12. S. A. Lang and M. N. Levy, *Ibid.*, **256**, No. 5, Pt. 2, H1295-H1302 (1989).
13. M. N. Levy, in: *Neural Regulation of the Heart*, Ed. W. C. Randall, New York (1977), pp. 97-129.
14. W. Matsumura, M. Sugimachi, T. Kawada, *et al.*, *Am. J. Physiol.*, **273**, No. 2, Pt. 2, H534-H539 (1997).