Sympathetic Modulation of Vagal Chronotropic and Arrhythmogenic Influences on the Heart

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In acute experiments on cats, stimulation of the caudal cardiac nerve inhibited tonic and synchronizing components of the vagal chronotropic effects and suppressed arrhythmogenic effect of vagal stimulation. By contrast, stimulation of ansa subclavia potentiated the effects of vagal stimulation. A novel model of vagosympathetic interactions in the heart of mammals is proposed.

Key Words: *vagus nerve*; *stellate ganglion*; *caudal cardiac nerve*; *ansa subclavia*; *neurogenic atrial fibrillation*

Nervous regulation of cardiac activity is intensively studied. However, vagosympathetic interactions in the heart are still poorly understood, probably because oversimplified model of extracardiac nervous control usually subdivided into chrono-, bathmo-, dromo-, and inotropic influences. At the same time, burst activity in vagal efferents [8,9] and synchronization of cardiac rhythm with vagal stimulation [1,2,10-12] were demonstrated. Now it is established that in addition to the well-known tonic component, vagal chronotropic effect on the heart includes also a cycle-related (or synchronizing) component, which can not be detected during standard stimulation of the vagus nerve. This component ensures synchronization of cardiac cycles with highly variable rhythmic activity formed in the brain and passed to the heart via the vagus nerve [3]. Simultaneous stimulation of the sympathetic nerves showed that stimulation of the ansa subclavia (Vieussens loop) potentiates, while stimulation of the caudal cardiac nerve (*n. cardiacus cervicalis iferior*) inhibits the above-mentioned vagally induced effects [6,7]. It was firmly established that vagal stimulation does not only fails inhibit, but even enhances myocardiac excitability [4], which can lead to the development of atrial fibrillation [5]. It is accepted that ventricular myocardium in most mammals has no parasympathetic innervation.

Our aim was to study the development of neurogenic atrial fibrillation (NAF) during stimulation of various sympathetic nerves. Changes in chronotropic effects of the vagus nerve served as a marker of sympathovagal interaction.

MATERIALS AND METHODS

Acute experiments were carried out on 17 cats weighing 2.5-3.5 kg. The animals were anesthetized with chloralose (75 mg/kg intraperitoneally) and nembutal (15 mg/kg) and artificially ventilated. Body temperature was maintained at 37°C. Two bipolar platinum probes were introduced into the right atrium via the jugular and femoral arteries. One probe was used for myocardiac stimulation and the other for recording of intracardiac ECG. The cervical part of the right vagus nerve was exposed and cut. The peripheral end of the vagus nerve was placed on bipolar wire electrodes (made from the insulin injection needles) and covered with wax-mineral oil mixture. The distance between the stimulating electrodes was 2 mm. The right stellate ganglion was approached extrapleurally [6,7]. The

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caudal cardiac nerve (or the ansa subclavia) was placed on the miniature bipolar wire electrodes (distance of 1.5 mm) and also covered with wax-vaseline grease. Other branches of the ganglion were cut.

The baseline *PP* interval was determined by the ECG before stimulation. The vagus nerve was stimulated with triple pulses of 6-threshold amplitude and duration 2 msec, delivered at 40 Hz, which were applied synchronously to the *P*-waves on the ECG. The synchronizing component of the vagus nerve was evaluated by a stepwise increase in the test *PP* interval relative to the duration of the last pre-stimulus cardiac cycle. The tonic component was evaluated by the maximum elongation of the cardiac cycle, which was observed a few cycles after the cycle where the synchronizing effect was detected [3].

NAF was induced with 2 electrical pulses (5 msec, 4 thresholds, 40-msec interval) applied to the right atrium during cardiac arrest induced by vagal stimulation (2 msec, 40 Hz, 6 thresholds). This stimulation always induced paroxysms of tachyarrhythmia [5]. The duration of NAF was measured before and during sympathetic stimulation (2 msec, 20 Hz, 1.25-2.00-fold threshold).

Two dual-channel ESU-2 stimulators were used for simultaneous stimulation of the myocardium and extracardiac nerves. ECG signals were monitored visually on a IM-789 oscilloscope and recorded with an N338-4 ink-pen recorder using a specially designed intervalograph [2-7].

The results were expressed as means and standard errors ($M \pm m$) and statistically analyzed by Student's t test.

RESULTS

Suprathreshold stimulation of the caudal cardiac nerve (the chronotropic threshold was 760±40 mV) 3-fold reduced the synchronizing component of vagal chronotropic effect and by more than 1.5-fold decreased its tonic component (Table 1). Similar results were obtained, when the changes in cardiac intervals induced by vagal stimulation were expressed as percentage of their baseline duration. This complies with the accepted conception on the direct antagonism existing between the sympathetic and parasympathetic influences on the heart. Accordingly, sharp decrease in NAF duration during stimulation of the caudal cardiac nerve is a regular consequence of that cholinergic mechanism plays a key role in NAF genesis. At the same time, a moderate increase in the strength of electrical stimulation (up to 2 thresholds) changed the components of vagal chronotropic effect insignificantly, while NAF length became considerably shorter. The latter can be due to peculiarities of the bathmotropic effect of the vagus nerve, which consists of only tonic component [4] and manifests an exclusive tendency to summation, much more pronounced than that observed for the tonic component of vagal chronotropic effect [3].

In the second series, we studied the development of NAF during stimulation of the ansa subclavia. Of interest are longer duration of the cardiocycle and NAF before sympathetic stimulation and more pronounced changes (absolute or relative) in the tonic and synchronizing components of the vagal effect during suprathreshold stimulation of the ansa subclavia (800± 40 mV chronotropic threshold, Table 2). Duration of NAF during suprathreshold and 2-fold threshold stimulation of the ansa subclavia 5.5- and 42.8-fold surpassed that during similar stimulation of the caudal cardiac nerve (Table 2).

No further potentiation of the vagal chronotropic effects was observed when the strength of electrical stimuli applied to the ansa subclavia increased up to 2 thresholds (Table 2). This can be due to electrical stimulation of the peripheral end of the caudal cardiac nerve lying only few millimeters apart from the stimulatory electrodes.

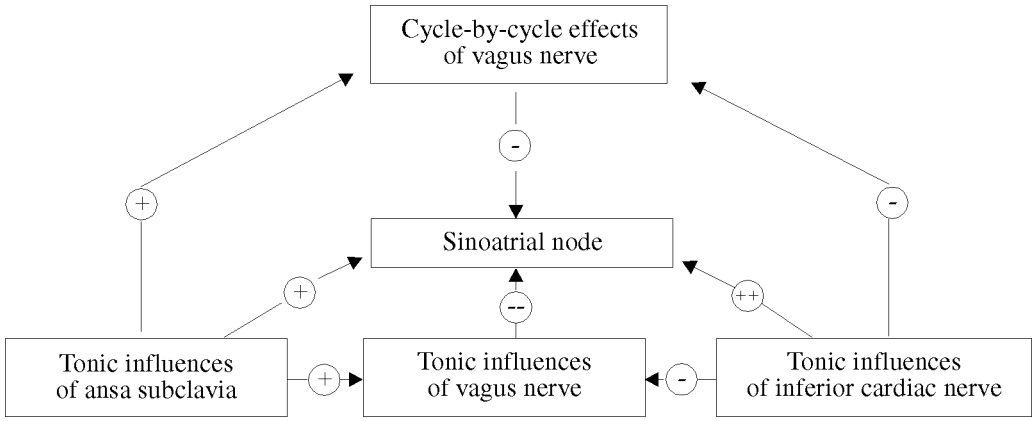

Fig. 1. Scheme of intracardiac chronotropic sympathovagal interactions in cats. Potentiation and inhibition are denoted as «+» and «-».

TABLE 1. Effects of Stimulation of Inferior Cardiac Nerve on Chronotropic and Arrhythmogenic Effects of Vagus Nerve in Cats ($M \pm m$, n=12)

Parameters	Baseline value (before stimulation)	Stimulation			
		1.25 thresholds		2.0 thresholds	
		abs.	% of baseline	abs.	% of baseline
Background *PP* interval, msec	352±6	321±8*	91	312±7*	89
Excitation threshold of vagus nerve, msec	410±30	420±40	102	420±40	102
Chronotropic effect of vagus nerve					
synchronizing component, msec	309±32	116±20*	38	106±26*	34
%	88±9	36±6*	41	34±8*	39
tonic component, msec	98±7	58±13*	59	52±15*	53
%	28±2	18±4*	64	17±5*	61
Duration of NAF (neurogenic atrial fibrillation), sec	198±19	74±16*	37	21±8*	11

Note. Here and in Table 2, *p<0.05 compared to the initial value.

TABLE 2. Effects of Stimulation of Ansa Subclavia on Chronotropic and Arrhythmogenic Effects of the Vagus Nerve in Cats ($M \pm m$, n=5)

Parameters	Baseline value (before stimulation)	Stimulation			
		1.25 thresholds		2.0 thresholds	
		abs.	% of baseline	abs.	% of baseline
Background *PP* interval, msec	386±15	340±10*	88	328±6*	85
Excitation threshold of vagus nerve, msec	380±10	390±10	103	390±10	103
Chronotropic effect of vagus nerve					
synchronizing component, msec	410±57	348±52	85	282±38*	69
%	106±14	103±16	97	86±11*	81
tonic component, msec	142±24	166±25*	117	150±18	106
%	36±6	49±7*	136	45±5*	125
Duration of NAF (neurogenic atrial fibrillation), sec	321±52	409±74*	127	916±318*	285

Different changes in vagal chronotropic and arrhythmogenic effects produced by stimulation of different branches of the stellate ganglion confirm the existence of vagotropic sympatho-sympathetic balance [6,7] playing a role in the mechanism of the intracardiac sympathovagal interaction (Fig. 1). The functional state of this peripheral interaction can be evaluated not only by the baseline duration of cardiac cycle but also by its variability (which depends on the synchronizing component of vagal chronotropic effect) and arrhythmogenic effects of extracardiac nerves.

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