BIOELECTRICAL ANALYSIS OF REGULATORY INTERACTION BETWEEN SYMPATHETIC AND PARASYMPATHETIC NERVOUS INFLUENCES ON THE CARDIAC RHYTHM

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During microelectrode recording of action potentials from cells of the pacemaker region of the isolated sinus node of the frog heart the sympathetic and intraneural parasympathetic reflex pathways of the heart were stimulated separately and together by currents of near-threshold strength. Separate stimulation of the intramural reflex system led to slowing or quickening of the heart rate depending on the time of year. In both cases the addition of activation of the sympathetic chain, which has a weak positive chronotropic effect on the rhythm, significantly increased both the parasympathetic slowing and the quickening of the rhythm. These effects were cholinergic in nature. Recording intracellular pacemaker activity revealed complex interactions between the sympathetic and parasympathetic spike-mediator action on slow diastolic depolarization as a prespike process, on the polarization of the membrane, and other parameters of the action potential. The possible mechanisms of this interaction are discussed.

KEY WORDS: cardiac rhythm; pacemaker; action potential; sympathetic-parasympathetic interaction.

In modern physiology of the autonomic nervous system it is being increasingly recognized that the parasympathetic innervation of the heart is the main regulatory system for cardiac activity [5-7]. This view is in harmony with the observed ability of the parasympathetic innervation to exert both positive and negative chronotropic influences on the cardiac pacemaker [1, 2]. It has been shown that both these influences consist essentially of cholinergic spike-mediator actions [2, 4].

The need accordingly arises for a reexamination of the regulatory role of the sympathetic innervation in relation to the cardiac pacemaker. In the light of modern data it has been suggested that during regulation of the cardiac rhythm the parasympathetic and sympathetic innervation systems function as a single regulatory mechanism [1, 2, 4].

This hypothesis served as the basis for the present investigation in which inhibitory and accelerating influences of the intramural parasympathetic apparatus of the heart were combined with activation of the sympathetic innervation of the heart.

EXPERIMENTAL METHOD

Experiments were carried out on male frogs (Rana temporaria) in the spring–summer and winter periods of the year. The preparation used in the experiment consisted of the isolated sinus region of the heart with dissection of the vagosympathetic trunks, sympathetic chains, and intramural nerves of the heart. The preparation was placed in a special chamber containing Ringer's solution. Separate and combined stimulation of the sympathetic chain and the central end of one of the intramural nerves of the heart was used. The intramural nerves were stimulated in order to activate intracardiac reflexes which, as was shown previously [3], are purely cholinergic. The parameters of stimulation were near-threshold (1.1-1.2 thresholds). Separate stimulation of the intramural nerve and sympathetic chain lasted 10-15 sec. During combined activation, stimulation of

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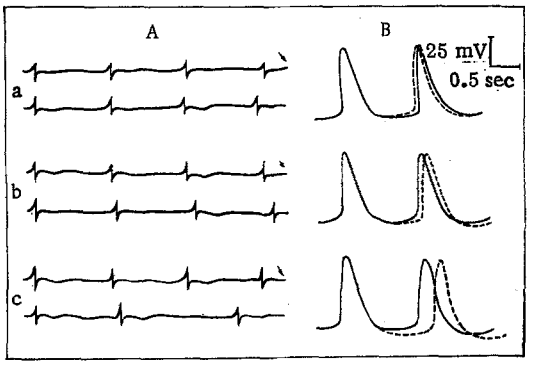

Fig. 1. Effect of activation of sympathetic chain on negative chronotropic effect during stimulation of intracardiac parasympathetic nerves and on AP of pacemaker cell. A) Activity recorded from sinus region, B) AP of pacemaker cell; results of superposition of original AP (continuous line) and AP recorded during maximal effect of stimulation (broken line) are shown. a) Stimulation of sympathetic chain (arrow above trace); b) stimulation of central end of intracardiac nerve (arrow above trace); c) combined stimulation of sympathetic chain and intracardiac nerve (time of addition of stimulation of intracardiac nerve to existing stimulation of sympathetic chain indicated by arrow above trace).

the sympathetic chain preceded stimulation of the intramural nerve by 3-4 sec. Electrical activity of the sinus region and bioelectrical activity of the pacemaker cells were recorded by glass microelectrodes with a tip under 0.5 μ in diameter, filled with 2M KCl solution. To test the mediator nature of the resulting chronotropic effects atropine sulfate (10^{-5} - 10^{-4} g/ml) and the β-adrenoblocker Obsidan (propranolol) (10^{-5} g/ml) were used.

EXPERIMENTAL RESULTS

Activation of the intramural parasympathetic pathways of the heart in the fall and winter caused bradycardia in most cases (series I), whereas in the spring and summer as a rule tachycardia was recorded (series II). The results of one experiment of series I are illustrated in Fig. 1. Separate stimulation of the sympathetic chain caused a small increase in heart rate (Fig. 1A, a). Recording action potentials (AP) of the pacemaker cell revealed an increase in the steepness of rise of slow diastolic depolarization (SDD), but the remaining parameters of AP remained unchanged (Fig. 1B, a). Stimulation of the intramural nerve led to bradycardia accompanied by slight hyperpolarization of the membrane (Fig. 1A, B, b). Combined activation of the sympathetic and parasympathetic pathways caused distinct bradycardia, the effect being much stronger than that of separate stimulation of the intracardiac nerve (Fig. 1A, c). Slowing of the rate of rise of SDD and of hyperpolarization of the membrane and also a decrease in the duration of the AP were recorded under these circumstances (Fig. 1B, c). In the experiments of series II activation of the intracardiac reflex apparatus at near-threshold strength caused slight tachycardia (Fig. 2A, b). This increase in heart rate was due to an increase in the steepness of rise of SDD of AP of the pacemaker cell (Fig. 2B, b). Combination of this stimulation with activation of the sympathetic chain, whose separate stimulation slightly increased the cardiac rhythm (Fig. 2A, a), led to an even further increase in the heart rate (Fig. 2A, c). This increase in the effect was greater than the result of algebraic summation of the increases in frequency observed during separate stimulation of the two nerve pathways. Recording AP revealed a still greater increase in the steepness of SDD; sometimes slight hyperpolarization of the membrane developed at the same time (Fig. 2B, c). In some experiments (experiment 7 in series I and experiment 5 in series II), at the end of combined stimulation of the nerve pathways, atropine (10^{-4}-10^{-5} g/ml) was injected into the perfusion fluid and combined stimulation was repeated. Atropinization blocked both the negative and the positive chronotropic effects observed during simultaneous stimulations of the sympathetic and parasympathetic systems. Usually a small increase in cardiac frequency remained: This was sympathetic in nature for it was abolished by the β-adrenoblocker Obsidan (Table 1).

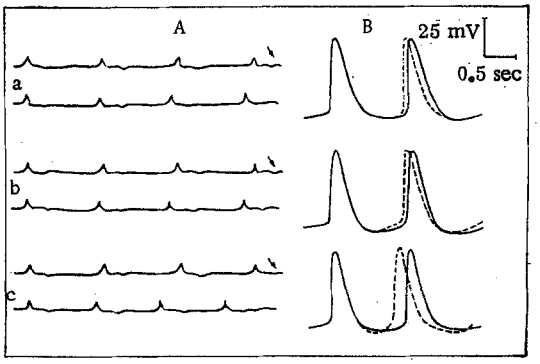

Fig. 2. Effect of activation of sympathetic chain on positive chronotropic effect to stimulation of intracardiac parasympathetic nerves and on AP of pacemaker cell. Notation as in Fig. 1.

TABLE 1. Changes in Chronotropic Effect during Separate and Combined Stimulation of Intracardiac Parasympathetic Nerves and Sympathetic Chain. Effect of Cholinergic and Adrenergic Blocking Agents on Chronotropic Effects of Combined Stimulation of Nerves

Series and number of experiments	Chronotropic effect (in beats/min) during activation of				
	sympathetic chain	intracardiac nerve	sympathetic chain and intracardiac nerve together		
			initially	after atropine, 10^{-4}-10^{-5} g/ml	after Obsidan, 10^{-5} g/ml
I (16)	+1,57±0,49c	—3,75±0,97a	—6,36±1,01b	+1,32±0,37d	0
II (14)	+1,2±0,51c	+2,2±0,92a	+5,3±0,89b	+1,03±0,42d	0

Legend. Effect marked by index "b" differs statistically significantly from effect marked by index "a". Effect marked by index "d" does not differ statistically significantly from effect marked by index "c".

The experiments thus showed that during moderate stimulation of the innervation systems sympathetic spike-mediator action widens the range of regulatory capacity of the intramural parasympathetic system of the heart, potentiating both the negative and positive chronotropic effects of parasympathetic origin.

Changes in bioelectrical activity of the pacemaker cells suggest the existence of complex interaction between sympathetic and parasympathetic spike-mediator effects on SDD, as a prespike process, and on the initial membrane polarization and other parameters of AP. This interaction is evidently not antagonistic. By acting jointly with the parasympathetic innervation, sympathetic influences lose their regulatory specificity, which is manifested during separate stimulation as acceleration. Strengthening of chronotropic effects of parasympathetic origin, arising during simultaneous stimulation of sympathetic and parasympathetic nerve pathways, may perhaps be explained by the fact that in its function and in relation to pacemaker activity the sympathetic innervation has an adaptive-trophic role, similar to its regulatory action on skeletal muscle, as representatives of Orbeli's school have shown. Profound disturbances of intracellular metabolism and of the reactive properties of the membranes of pacemaker cells, developing as a result of sympathetic spike-mediator action can probably create new conditions for the response of pacemaker formations to regulatory parasympathetic influences.

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ACTIVITY IN MYELINATED FIBERS OF A CAT CUTANEOUS NERVE IN RESPONSE TO HEATING

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It was shown by the colliding impulses method combined with methods of distinguishing weak signals in a nerve from apparatus noise that heating the hairy skin causes a change in the character of activity recorded in fibers of the A_γ, A_{δ_1}, and A_{δ_2} groups and in the group of "mixed" fibers. A relatively large number of fibers of these groups is excited, and only a few of them inhibit their activity in response to heating the skin receptors. An increase in the spontaneous discharge and relaxation of the skin were shown to take place during heating.

KEY WORDS: myelinated nerve fibers; afferent impulsation; heating the skin.

Among investigators who have studied temperature reception in the hairy skin of the cat the view is held that heating the skin causes excitation only of those receptors which are innervated by unmyelinated fibers [9, 11]. However, myelinated fibers which participate in the conduction of afferent impulses arising during heating have been found in the skin of the nose and in the tongue of the cat [7]. Activity has been recorded in afferent myelinated fibers of the hairy skin of the cat in response to its rapid heating [13]. Similar fibers have been found in the cutaneous nerves of primates [8].

In the course of investigations of changes in combined activity of a whole nerve during heating of the skin receptors contradictory results have been obtained: Some workers consider that spontaneous activity is reduced [12], others found no change in activity in the cutaneous nerves during heating [5], and the third group observed an increase in activity of the whole nerve during heating [14].

The object of the present investigation was to determine the degree of participation of thin myelinated fibers in the transmission of information about heating the hairy skin in cats.

EXPERIMENTAL METHOD

Experiments were carried out on cats under intramuscular hexobarbital anesthesia. Nerve structures responsible for the perception of cold stimuli are considered to be located in the superficial layers of the skin and those responsible for the perception of heat stimuli in its deeper layers [10]. A dissected skin flap was therefore placed in a thermode, so that the temperature of its superficial and deep layers could be changed simultaneously. The skin temperature was changed by changing the temperature of the water flowing through the thermode. The rate of heating of the skin, measured on its hairy surface by means of a type TPM-1 thermometer, was 1 °C/sec. To ensure that because of inertia of the thermometer the skin was not heated to an injurious temperature (45° C), in control experiments a calibrated semiconductor thermistor was inserted beneath the epidermis. Temperature changes recorded by the thermistor exceeded the values of temperature obtained by means of the TPM-1 thermometer by a maximum of 1.5-2.0°C.

The skin temperature varied from +32 to +42° C. After application of the temperature stimulus and restoration of the skin temperature to the adaptation temperature, an interval of 15 min was allowed before stimulation was repeated.

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