PHYSIOLOGY

Chronotropic and Dromotropic Components of Cardiac Reflexes in Rabbits

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The relationships between dromotropic and chronotropic components of five reflexes were studied in rabbits: intravenous and intraarterial blood injections, occlusion of the carotid arteries, Aschner maneuver, and stimulation of depressors. All these stimuli reduced heart rate (except carotid artery occlusion, which induced approximately equal number of tachi- and bradycardic responses). The former three stimuli also reduced atrioventricular (AV) conduction velocity, the changes in these two parameters were proportional. Changes in heart rate induced by Aschner maneuver were more pronounced than changes in AV conduction. Stimulation of depressor induced co-directed shifts in these parameters during the first seconds, but then AV conduction increased, while heart rate remained decreased; bradycardia and AV acceleration persisted for long time after termination of stimulation. Our findings attest to independent regulation of heart rate and AV conduction velocity and to the absence of a strict relationship between these two parameters.

Key Words: *chronotropic influences*; *dromotropic influences*; *heart*; *nervous control*

Dromotropic (DT) effects, *i.e.* modulation of the rate and stability of atrioventricular (AV) conduction, were established more than 100 years ago. AV-node has abundant and complex innervation [13]. However, natural DT reflexes are little studied. First, most experiments on DT regulation used electrical stimulation of the cardiac nerves (an artificial event, which never occurs under normal conditions and only reflects potential cardiotropic effects of the nervous system). Second, in most studies these reactions were evaluated by changes in heart rate (HR), *i.e.* chronotropic component (CT) of cardiac reflexes. Less studies were focused at inotropic effects, and only few dealt with DT effects [7,10,12]. The aim of this work was to study the relationship between CT and DT components of various cardiac reflexes.

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MATERIALS AND METHODS

Experiments were carried out on 55 rabbits under pentobarbital narcosis (Nembutal 20-30 mg/kg, intravenously). If necessary, 10-20 mg/kg Nembutal was additionally injected in the course of the experiment. Blood pressure in the femoral artery was measured with an Elema-Schonander transducer. ECG in lead aVR was recorded with a P4Ch-02 polygraph coupled to an N3031-4 ink-pen written. The first derivative of the ECG was obtained using a differentiator unit of the polygraph and fed to a 8-bit Korvet PC via a parallel port. A threshold value for the first derivative of the ECG signal was determined in each experiment automatically. For aVR recordings, this threshold was reached at the end of *P* and *Q* waves (Fig. 1). AV-intervals were measured as the time between the two threshold points of the first derivative curve. Changes in AV-interval determined by the first derivative of ECG signal served as the measure of DT influences.

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This interval included atrial conduction time to AV-node, AV-delay, and initial conduction time in the ventricles, but only AV-delay is influenced by the autonomic nerves [14]. For more precise evaluation of DT influences, electrograms of the left ventricle and atrium were recorded via tantalum hook-shaped electrodes in 10 open-chest artificially ventilated rabbits. The threshold values for the first derivative of these cardiac electrograms were determined as described above. In these experiments DT effects were evaluated by changes in the intervals between atrial and ventricular excitation. These changes reflected only the shifts in AV-delay and, therefore, did not depend on the location of electrodes. The following stimuli were applied: intravenous bolus infusion of 10-20 ml blood (preliminary collected from the same animal) with dextran (group 1); intraarterial bolus infusion of 10-20 ml blood with dextran (group 2); uni- or bilateral carotid artery occlusion (group 3); eyeball pressing for 1 min (Aschner maneuver, group 4); electrical stimulation of the left or right depressor (group 5). The nerves were stimulated using a Medicor ST-21 electrical stimulator via bipolar steel electrodes (2 msec pulse duration, 10 Hz frequency). The amplitude of stimulating pulses was chosen depending on the characteristic blood pressure drop.

The percentage of responses (nonparametric data), which were characterized by significant shifts in *RR* and AV intervals and relative changes in these parameters (parametric data) in response to various stimuli were studied. The data were analyzed by Student's *t* test.

RESULTS

The stimuli used in groups 1-3 directly affected hemodynamics (bolus injections increased circulating volume, occlusion of the carotid arteries increased systemic vascular resistance). The other two stimuli produced cardiac responses via a reflex mechanism. Stimulation of depressors triggers reflex from vascular reflexogenig zones (pressure receptors of the aortic arch), while Aschner reflex is a complex reflex (*i.e.* is triggered from noncardiovascular zones).

All stimuli induced cardiac responses associated with HR changes (≥92% events, Fig. 2, *a*). In the first three groups, significant changes in AV intervals were also noted (co-directed to changes in *RR* interval).

In groups 1 and 2, HR and AV conduction velocity decreased, while in group 3 these parameters increased and decreased in approximately equal number of cases, but their shifts remained codirected. Differences in cardiac responses to carotid artery occlusion can be explained by the involvement of two components: 1) cardioexcitatory response to blood pressure drop near the carotid pressure receptors; and 2) cardioinhibitory response due to activation of aortic pressure receptors in response to blood pressure rise (Fig. 3, a) produced by changes in systemic vascular resistance associated with occlusion of great vessels (carotid arteries).

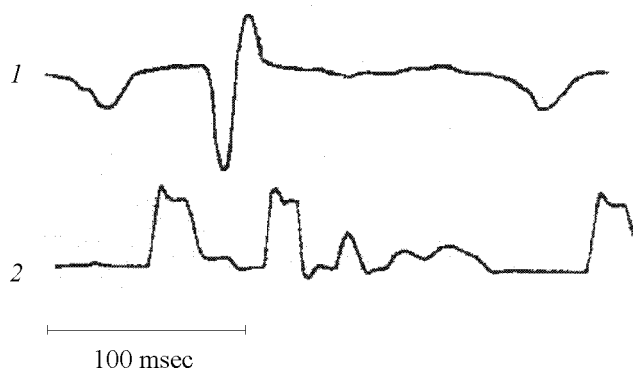

Fig. 1. ECG in the lead aVR (*1*) and its first derivative (*2*). Peaks on the first derivative curve correspond to the ends of waves *P* and *Q*.

In groups 1-3, the relationship between CT and DT components of cardiac reflexes was similar: DT responses appeared in most cases (CT responses in all cases) and the observed shifts in HR and AV conduction were co-directed. This is clearly seen from parametric data: CT/DT ratios (the ratio of changes in *RR* interval to changes in *PQ* interval) were similar in groups 1-3 (Fig. 2, *c*).

Cardiac responses induced by stimulation of depressors or by Aschner maneuver were different. Analysis of nonparametric data (Fig. 2, *a*) revealed lower incidence of significant DT responses in group 4 (34%) compared to other groups, *i.e.* during Aschner maneuver CT component prevailed over DT component. In group 5 changes in AV conduction velocity were often seen, but only 48% changes were co-directed to HR changes. Thus, the latter two types of stimulation decreased HR in practically all cases, but had no effect on AV conduction (Aschner reflex) or accelerated it (in 52% cases during stimulation of depressor).

When analyzing parametric data the difference between the responses observed in groups 1-3 and in groups 4 and 5 becomes more evident (Fig. 2, *c*). The ratio CT/DT was considerably higher in groups 4 and 5 compared to groups 1-3.

Considerable number of opposite CT and DT changes in response to stimulation of depressors prompted us to analyze these responses more thoroughly (Fig. 3, *b*). During the first seconds of depressor stimulation both HR and AV conduction velocity decreased, but then AV conduction increased, while HR remained decreased; after termination of stimulation, trace bradycardia and AV acceleration persisted for a long time. Thus, in the beginning of stimulation chan-

ges in these parameters were co-directed (Fig. 2, *b, d*), while then became opposite.

Thus, the relation between CT and DT components of cardiac reflex responses is complex. The same changes in HR can be accompanied by different (sometimes opposite) changes in AV conduction time, depending on the nature of applied stimuli. The optimal value of AV delay for a given HR can vary depending on the mode of cardiac function. This implies the existence of complex nervous regulation these parameters. Such regulatory influences cannot be classified simply as positive or negative, but should be attested as a coordinated regulation of cardiac function.

What is a physiological role of this CT/DT coordination and DT influences? A possible answer can be obtained from studies with electrical cardiac pacing (in humans). In these studies, AV interval can be set experimentally and the effects of different pacing modes on various hemodynamic parameters can be evaluated. It was established that non-optimal AV-interval can lead to blood regurgitation from ventricles during systole, impairment of ventricular filling, and other abnormalities in cardiac [1,5,11] and general hemodynamics [11]. So, an optimal AV interval is set in the modern pacemakers (usually 100 to 150 msec) [2]. However, the existence of DT influences means that the optimal AV interval is not a constant parameter, but varies depending on the mode of cardiac function. In light of this, various models of adaptive pacemakers were proposed. In some modifications, a

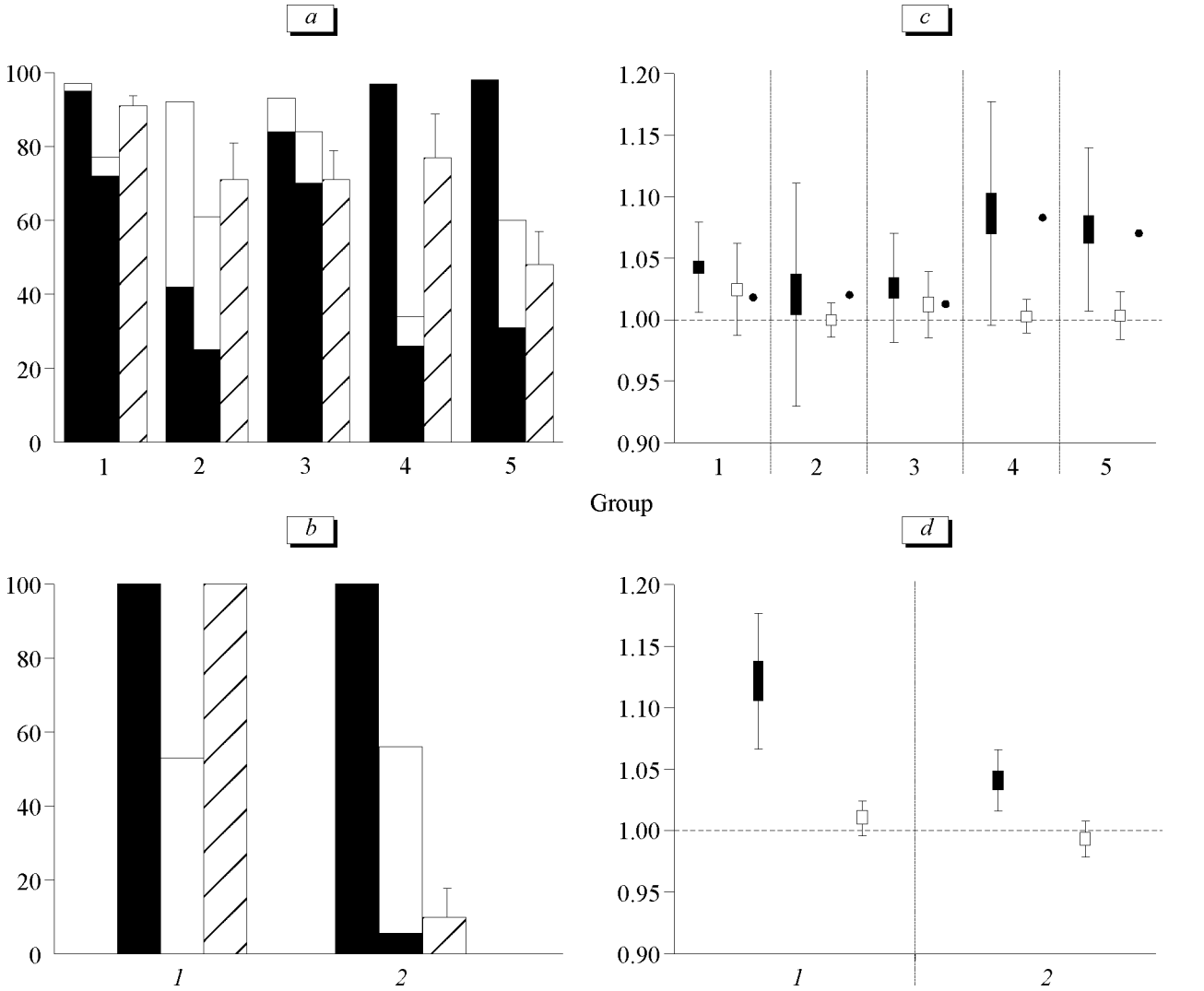

Fig. 2. Changes in heart rate (*RR*-intervals) and atrioventricular conduction time (AV-intervals) in response to various stimuli. *a, b*) nonparametric data. Ordinate: percentage of significant responses. In each groups of bars: the first and second bars show changes in *RR* intervals and in AV-intervals, respectively (light and dark areas correspond to increase and decrease, respectively), and the third bar shows the percentage of co-directed changes in *RR* and AV intervals (from the total number of responses). *c, d*) parametric data. Ordinate: changes in *RR*-intervals (dark bars) and AV-intervals (light bars, expressed as ratios of their mean values before and during stimulation), and chronodromotropic index (dark circles, shifts in *RR*-intervals divided by the corresponding shifts in AV-intervals). *1*) start of stimulation of depressors, *2*) termination of stimulation.

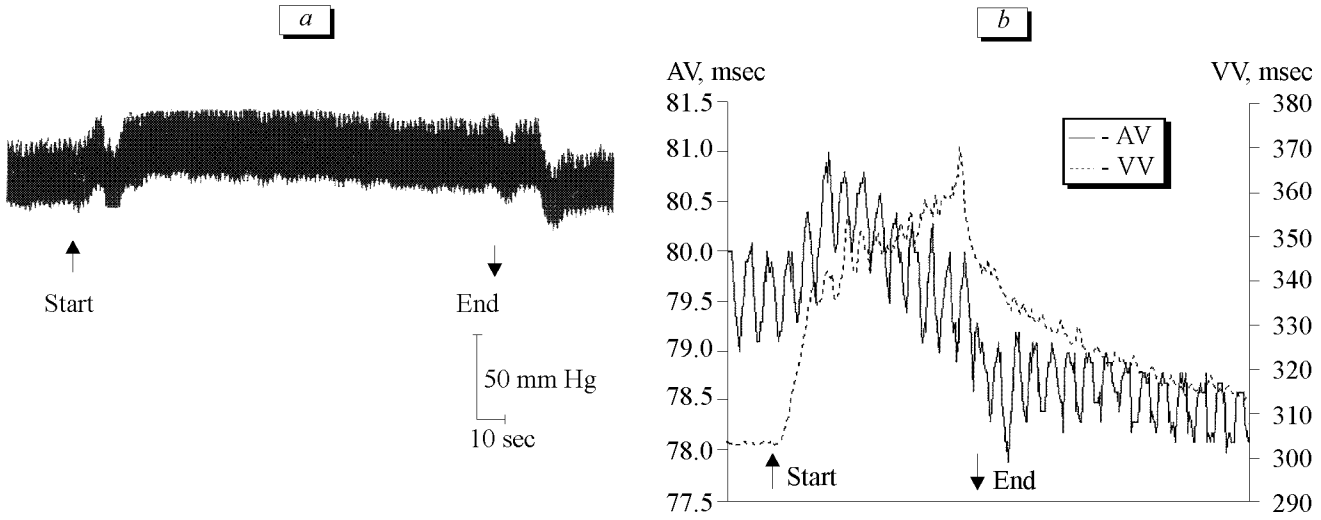

Fig. 3. Blood pressure response to occlusion of the carotid arteries (*a*) and changes in *RR*- and AV-intervals in response to stimulation of depressor (*b*). *a)* blood pressure sharply increased at the beginning and decreased at the end of occlusion. A transient decrease in blood pressure observed few seconds after the start of occlusion is probably a baroreflex response. *b*) data from the left atrial and left ventricular electrograms recorded after thoracotomy. AV: interval between the atrial and ventricular excitation; VV: interval between successive systoles.

rate-adaptive approach is used, which is based on linear inverse relationship between AV interval and HR observed during exercise [4] and, probably, during orthostasis [9]. However, this relation is not valid for some other conditions [8]. Our results suggest that HR and AV conduction time are not closely related. The relation between these parameters depends on the nature of stimulation. As a more reasonable alternative to the rate-adaptive approach, the optimal AV intervals can be selected according to cardiac hemodynamics measurements [3] or phasic parameters of the cardiac cycle [6].

Thus, analysis of CT/DT coordination can not only disavowal unknown mechanisms of cardiac regulation, but can also be of importance in clinical applications.

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