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Interaction of myogenic and neurogenic mechanisms that control heart rate

(myogenic reactions/pacemaker action/cardiac control)

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ABSTRACT **Interaction of neurogenic and myogenic factors that control heart rate was studied. Sympathetic nerve actions and stretch of the sinoatrial node both have an accelerator effect which appears to be competitive, and additive rather than facilitatory. In contrast with this, the accelerator effects of sinoatrial node stretch were proportionately greater when stretch was applied during a slowing produced by vagus nerve stimulation. The hyperpolarizing effect of vagus nerve stimulation or acetylcholine apparently potentiates the accelerator effects consequent to the depolarizing actions of stretch. The myogenic reaction can be considered as playing a role in maintaining cardiac output and preventing excessive slowing or diastolic distension and a deficient circulation.**

It has been known since the time of Bainbridge (1) that excess filling and distension of the right atrium affects heart rate. Although it is now recognized that such distension and/or directly applied stretch of the sinoatrial node causes an acceleration that is in part myogenic in origin (2–5), this is usually ignored or considered to be of small consequence. Heart action is generally thought to be regulated solely by autonomic nerves and humorally transmitted agents such as the catecholamines (6–8). Stretch of the right atrium does initiate a reflex action that increases cardiac sympathetic tonic activity (9, 10), but the resulting cardiac acceleration is only slightly greater (10–20%) than that which can be contributed by the myogenic response (4, 9). This matter of the relationships between myogenic and neurogenic control requires more investigation. The present report describes results obtained in a study of what happens when sympathetic nerve stimulation and stretch are applied together and when the seemingly contradictory actions of vagus stimulation and right atrial stretch are superimposed.

MATERIALS AND METHODS

The hearts of Nembutal (30–50 mg/kg)-anesthetized dogs and other animals used were exposed by thoracotomy after instituting artificial respiration. The vagi and sympathetic cardiac nerves were cut and attached to electrodes in preparation for their electrical stimulation. Preparations were also made for graded stretching of the sinoatrial node by stitching a ligature to the midportion of the node; the ligature was led over a pulley for subsequent attachment of weights, as described (3, 9). In order to prevent distortion of the heart during the stretching, ends of the node were fixed to rigid bars. Stretch was applied for 30-sec periods before, during, and after vagus or sympathetic nerve excitations that produced and maintained various degrees of cardiac slowing or acceleration. The vagal slowing was maintained for 90 sec in order to obtain a constant rate before the stretch and to permit observation of consequences after stretch. Stretch was also superimposed on similar durations of sympathetic stimulation. Stretch was applied 30 sec after the beginning and ended 30 sec before termination of the nerve stimulations. Ultimately atropine and guanethidine were used to block vagus and sympathetic nerve actions, thus eliminating mixed transmitter release due to possible peripheral nerve interactions which conceivably could have contributed to the effects of stretch. Results to be reported were obtained from six dogs, but similar reactions were observed in six cats and four rabbits.

RESULTS AND DISCUSSION

Stimulation of the sympathetic trunks caused a cardiac acceleration which minimized the effects of stretch, but the two together produced a greater acceleration than either alone. Sympathetic blockade (guanethidine, 15 mg/kg) abolished sympathetic nerve effects on the heart but left the myogenic induced acceleration unaffected.

It was more surprising to find that vagus stimulation augmented the proportionate change produced by stretch (Table 1). The stretch-induced acceleration sufficed to abolish vagal

Table 1. Effect of vagus nerve action on response to stretch of the sinoatrial node (dog heart Exp. 5)

Test	Rate before stretch	Stretch, g	Peak response	Change	
				Rate	%
		Before guanethidine			
		Control			
1	126	20	142	+16	13
14	132	20	150	+18	13
4	138	30	156	+18	13
13	132	30	144	+12	9
22	144	30	160	+16	11
		During vagus stimulation			
10	114	20	138	+24	21
16	114	20	138	+24	21
8	84	30	110	+26	30
17	108	30	140	+32	29
25	102	30	140	+38	37
		After guanethidine			
		Control			
27	198	30	216	+18	9
29	180	30	198	+18	10
30	180	30	192	+12	7
		During vagus stimulation			
28	150	30	200	+50	33
31	138	30	180	+42	30
35	130	30	190	+60	46
		After atropine			
39	174	30	192	+18	10
		During acetylcholine perfusion			
41	150	30	198	+48	32

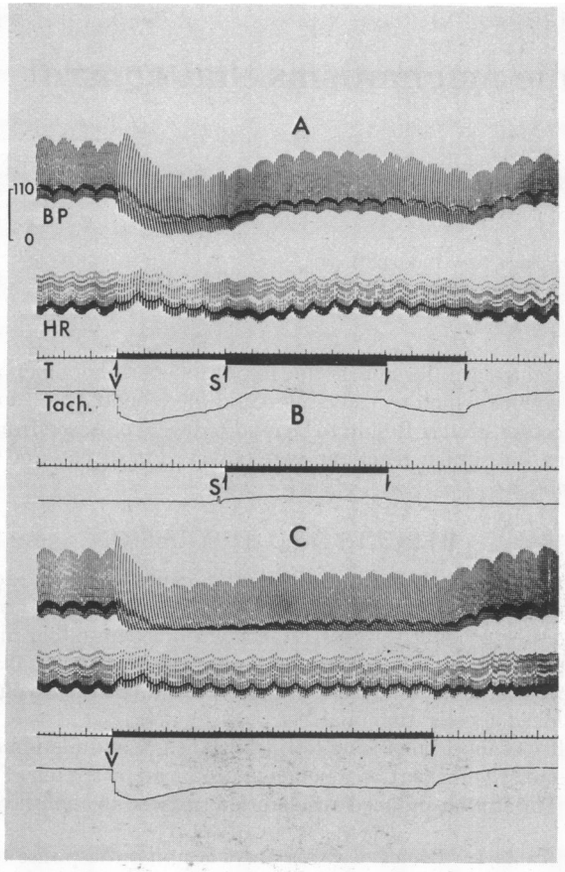

FIG. 1. The changes in heart rate induced by stretch (30 g) of the sinoatrial node of the dog heart (external nerves cut) before and during stimulation of the vagus nerve. Records shown were obtained after guanethidine administration. *A*, Stretch during vagus stimulation; *B*, stretch alone; *C*, vagus effects alone. BP, blood pressure; HR, heart rate; T, time (1 and 5 sec); Tach, tachogram; V↓, vagus stimulation on and off, respectively; S↓, stretch on and off, respectively.

effects during vagus nerve stimulations, and heart rates frequently rose above the control levels (Fig. 1). Use of sympathetic blocking agents did not diminish this vagus-facilitated stretch response, but atropine did. The same augmentations occurred during acetylcholine administration. Most definitely neither left nor right vagus nerve stimulations abolished or depressed the myogenic response to distension of the right atrium. This intrinsic reaction can thus serve to diminish or terminate vagus effects should too great a degree of slowing lead to excessive diastolic distension of the atrium.

Both sympathetic nerve stimulation and stretch are thought to act by increasing the presynaptic vesicle (catecholamine) discharge. Stretch has been shown to accelerate vesicle release from junctional membranes (11). To what degree action of stretch depends on this remains to be demonstrated. However, if vesicle liberation is responsible, it may be rate-limited and the two types of stimuli would thus be diminishing of each other but additive until maximum rate of release is attained.

The vagus nerve and acetylcholine are known to have hyperpolarizing actions on pacemaker cells (12, 13). Stretch apparently exerts its effect by producing a degree of depolarization (4). Hyperpolarization and an initially lower rate render the stretch-induced depolarization more effective as an accelerating mechanism. Not only does this myogenic reaction cooperate with reflexes arising from the right atrium when distension occurs, indicating need for a greater cardiac output, but it serves as a homeostatic device that can counteract excessive cardiac slowing.

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