Physiologic Behavior of the *in Situ* Papillary Muscles[1] (37403)

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Introduction. The behavior of the *in situ* papillary muscles (1, 2) appears to be complex and does not correspond closely to their known *in vitro* behavior (3). Although papillary muscle contractility is augmented during periods of increased inotropism, during increased afterload the segmental force of papillary contraction may be diminished (1, 2). Investigations were therefore carried out to examine not only the *in situ* papillary muscle function during local length changes, but also what effects stretching a small myocardial segment may have upon other regions of the heart. The results of these experiments indicate continuous neural modulation of papillary muscle function with feedback limbs which influence behavior of the whole heart.

Materials and Methods. Forty-seven mongrel dogs of either sex, weighing from 16 to 25 kg, were anesthetized with phencyclidine hydrochloride (2 mg/kg, im) and alpha-chloralose (70 mg/kg, iv), and bilateral thoractomy was performed during positive pressure respiration. Four different groups of experiments were performed: In group I, 15 animals were employed to investigate the effects of extending the length of the left ventricular papillary muscles—eight anterior and seven posterior. While on total cardiopulmonary bypass, a Walton–Brodie force gauge was sutured under isometric tension to the longitudinal surface of papillary muscle with orientation parallel to the underlying fibers. Care was taken to fix the feet of the gauge approximately midway between the base and apex of the muscle. A Whitney mercury-in-salistic length gauge (o.d. 0.025 in., length ¾ in.) was sutured along the opposite side of the muscle, one end being fixed at the apex and the other at the base. A thread tied around the major chordae was led out through the atriotomy, passed through a Phipps and Bird Model ST-2 Linear motion transducer, and over a small pulley to a weight pan. Walton–Brodie force gauges were also sutured onto the epicardium of the anterior left ventricle. The apical portion of the ventricle was fixed in position by a small button at the inner left ventricular apex with a thread passing through the apex to a Grass F10 force transducer. Left intraventricular pressure was measured by catheter and a P23Db Statham pressure transducer. Ten-gram weights were added successively to the weight pan until a total of 300 g was achieved.

In group II, four animals during inflow occlusion had Walton–Brodie gauges applied to the longitudinal surface of the anterior papillary muscle of the right ventricle. A thread was attached to the chordae tendineae and after restoration of normal circulation, force gauges were applied to the conal and sinus epicardial surfaces of the right ventricle; intrasinal pressure was recorded with a P23Db Statham transducer (1). During normal contractions increasing weights up to 100 g were added to the chorda thread.

Since cavity pressures influence regional contractile force, twenty-four experiments were performed on the right ventricles during total cardiopulmonary bypass (group III). The anterior papillary muscle was approached via an atriotomy and the chordae were cut after being tied to a thread, in order to remove any influence of chorda–papillary muscle distention on the valve ring. A mercury length gauge and a Walton–Brodie force gauge were applied under tension to the longitudinal surface of the anterior papillary muscle. In twelve of the animals, the base of the papillary muscle was fixed by a

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metal ring to stabilize that region during chordae distention. Strain gauge arches were sutured to the epicardium of the conus of the right ventricle and to the middle anterior epicardium of the left ventricle, the gauges always being oriented parallel to the direction of the underlying muscle fibers. A Grass F10 force gauge was attached to the end of the anterior papillary chordae and the muscle extended in steps of 5 mm until a total distending length of 3.0 or 3.5 cm was achieved. In the remaining twelve experiments of group III, another thread was attached to the neighboring posterior papillary muscle chordae and free weights added. In eighteen of the group III animals the cervical vagi were cut and subsequently both stellate ganglia removed, extension of the muscle being performed between each procedure. In six other experiments, the stellate ganglia were removed first and the vagi were severed later. Frequently a thin white band of tissue crossed the right ventricular cavity from the free wall to a point near the base of the anterior papillary muscle; in order to free the muscle this was cut and each time ventricular fibrillation ensued. Procaine was infused into the ascending aorta or phenol injected into the base of the papillary muscle at the end of the experiments before a final papillary muscle distention. In the last group of four animals (group IV) the anterior papillary muscle was elongated during control states, after atropine, and finally after hexamethonium.

In ten additional experiments action potential traffic in the thoracic cardiac nerves was monitored. Left and right ventricular papillary muscles were extended via their chordae tendineae while afferent nerve activity was recorded utilizing bipolar stainless steel electrodes, and amplified by means of a Grass P9AC pre-amplifier and an amplifier.

Results. Figure 1 demonstrates forces generated from the right ventricular anterior papillary muscle (ant pap), sinus epicardium (sinus), and conus epicardium (conus), as well as a standard ECG and right ventricular sinus pressure (RVP). The marker in the middle panel records the time of digital coarctation of the pulmonary artery; chamber pressure and sinus as well as conus epicardial forces were elevated, whereas the papillary muscle force was depressed. In the right panel, 50 g was added to the thread attached to the chordae tendineae and immediately a ventricular tachyarrhythmia was initiated; in-

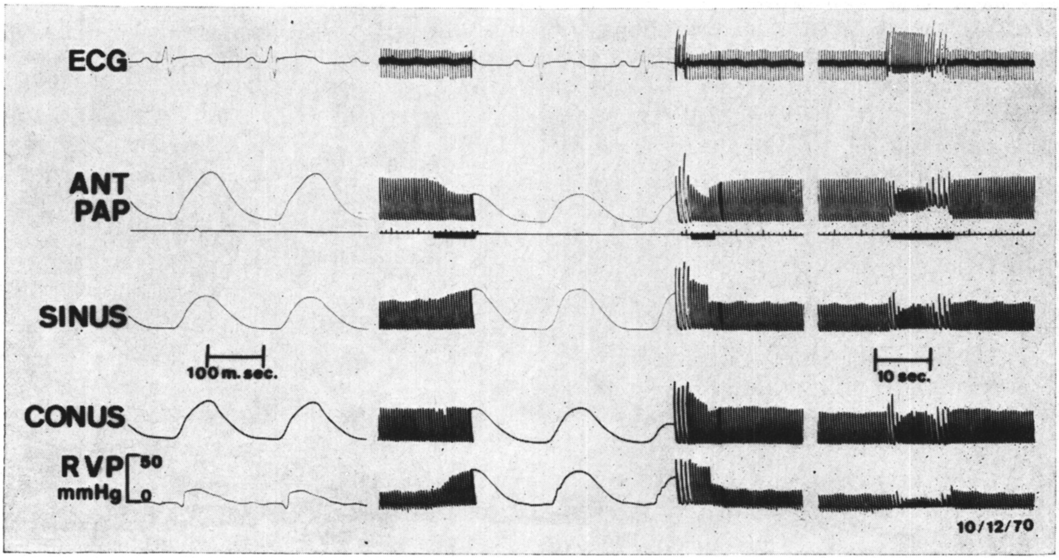

FIG. 1. An ECG, right ventricular anterior papillary muscle force (ant pap), sinal (sinus) and conal (conus) epicardial forces, and right ventricular pressures (RVP) are illustrated during control periods, while the pulmonary artery is partially occluded (middle panel), and after 50 g were added to the chorda of the papillary muscle (right panel).

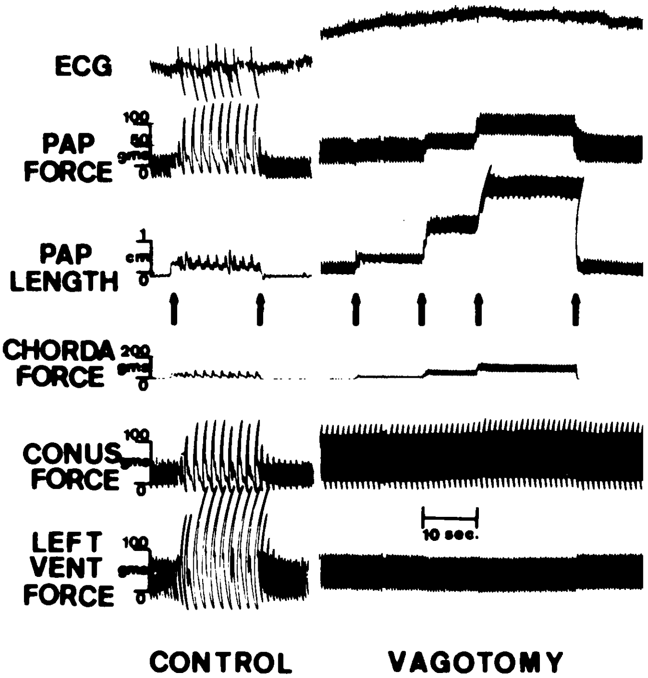

FIG. 2. A limb lead II EKG, regional right ventricular papillary muscle force (pap force) and length (pap length), chorda tendineae force (chorda force), as well as epicardial forces in the right ventricular conus (conus force) and anterior left ventricle (left vent force) are illustrated during distention of the right ventricular papillary muscle before (control) and after right vagotomy (vagotomy).

trasinal chamber pressure and contractile force were depressed. The papillary muscle systolic force was depressed and its diastolic force considerably elevated. Note the instantaneous cessation of arrhythmia when the load was removed.

Figure 2 demonstrates the effects of chorda tendinea distention (chorda force) upon a lead II EKG (upper trace), right ventricular anterior papillary muscle force (PAP force) and length (PAP length), as well as right ventricular (conus force) and left ventricular (left vent force) epicardial contractile forces. Distention of the chorda with 40-g force (control panel) initiated multiple ventricular ectopic rhythms. Following right cervical vagotomy (right panel) distention of the chorda by up to 150 g did not initiate cardiac dysrhythmias.

While recording action potentials from a single fiber preparation derived from the caudovagal nerve, alterations in afferent traffic became apparent upon distention of the right ventricular papillary muscle (Fig. 3). In panel A, a standard ECG, nerve action potentials, and right ventricular pressure (top to bottom) were recorded; the short dark lines (lower left) mark zero and 25 mm Hg pressure calibrations. Panel A is a control record demonstrating impulse traffic which occurred after the QRS wave of the ECG; a typical beat was characterized by afferent traffic of about eight spikes per cycle while alternate beats were accompanied by about three per cycle, a form of impulse alternans. Immediately prior to panel B twenty grams were added to the anterior papillary muscle–chorda complex and removed immediately before panel C. Note the abolition of the alternans as well as the increase in impulse traffic during the papillary muscle distention, followed by complete cessation of traffic after the weight was removed (panel C). In panel D the pulmonary artery was partially occluded

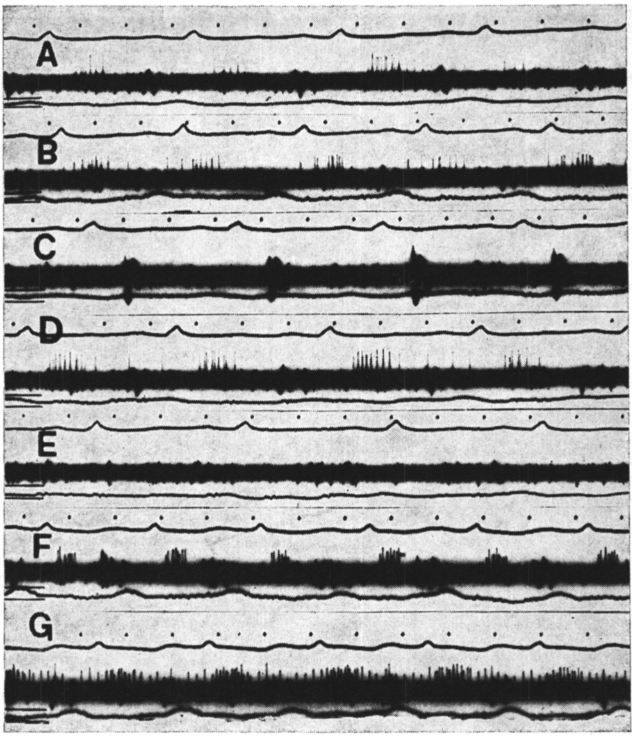

FIG. 3. In each panel, from above downward, is recorded an EKG, afferent nerve activity from a twig of the caudovagal nerve, and right ventricular pressure; the two lines on the left of each panel represent 0 and 25 mm Hg and the dots are 100 msec apart. Panel A is during control periods, B following 20 g, and C following the removal of the 20 g from the chorda. Panel D was taken during pulmonary artery occlusion, E inferior vena cava occlusion, and F following isoproterenol and G norepinephrine infusions.

causing an increase in impulse traffic to about fifteen per contraction, and panel E demonstrates the abolition of traffic while the inferior vena cava was occluded. Panel F demonstrates the results of isoproterenol infusion including an increase in heart rate and a clustering of the impulse traffic closer to the QRS wave, with about eight impulses per cycle. Norepinephrine infusion (panel G) augmented impulse traffic so that it was continuous throughout much of ventricular systole and diastole, being maximal between the QRS and 'T' waves, with an average of twenty-two impulses per systole. This mechanoreceptor was subsequently localized at the base of the right ventricular anterior papillary muscle.

Figure 4 demonstrates a lead II electrocardiogram, anterior papillary muscle segment contractile force (pap force) and total length (pap length), anterior papillary muscle–chorda distending force (chorda force), conal epicardial force (conus force), and left ventricular anterior epicardial force (left vent force) as the chorda–papillary muscle complex was distended by 0.5 cm increments. The arrows indicate the times at which the chorda–papillary muscle preparation was elongated, the last arrow denoting the return to control length. Papillary muscle regional force was first depressed and later progressively elevated; when the stretch was released the papillary force promptly returned to control values. Note the period of cardiac arrhythmia upon release. As the tension on the chorda increased (chorda force), papillary muscle systolic and diastolic lengths increased, but total length per contraction changed only minimally. The conus epicardium demonstrated a gradual augmentation of

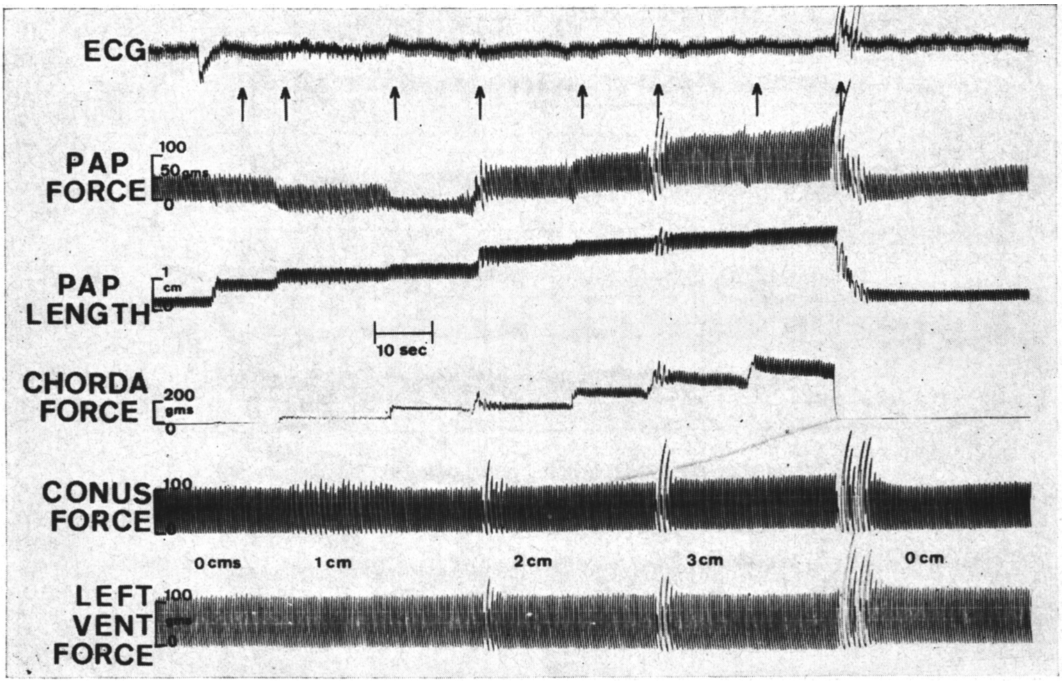

FIG. 4. An ECG, anterior papillary muscle force (pap force) and length (pap length), chorda force, and epicardial forces on the conus and anterior left ventricle are illustrated. As the chorda–papillary muscle complex was distended (distance in cm above left vent force trace) the papillary muscle segmental force first decreases and was then augmented. Little change in contracting length of the papillary muscle was noted and conal force was gradually augmented.

contractile force during increasing distention of the papillary muscle and this soon returned to control levels following release of papillary muscle distention. The left ventricular anterior epicardial force was only minimally effected.

Figure 5 illustrates the effects of bilateral vagotomy followed by bilateral stellatectomy in the same preparation as was illustrated in Fig. 4. Following bilateral vagotomy (heart rate 145/min as compared with a control rate of 125/min) there was a marked increase in papillary muscle contractile length and force. Elongation of the papillary muscle produced only minimal alteration in local force (pap force), again with minimal changes in length during each contraction. Upon release of papillary muscle distention there was an initial increase in papillary systolic force and length, these parameters returning slowly to control levels. Note that in this experimental series conal epicardial force was augmented during papillary muscle distention. After bilateral stellatectomy (right panel) the heart rate fell to 130/min, while papillary muscle augmentation was diminished and epicardial force augmentation was abolished.

Figure 6 is a graphic representation of the anterior papillary muscle length changes (abscissa) occurring synchronously with papillary muscle force generation when the papillary muscle was extended during control states, following vagotomy, and after total denervation (vagotomy plus stellatectomy). Under control conditions (solid line) regional force first diminished as papillary muscle length increased and then increased with further extension (arrows direct sequence of force-length changes); upon cessation of papillary muscle distension the force rapidly decreased while the contractile length slowly returned to control levels. Thus, during elongation and relaxation of the contracting papillary muscle, the relationship between segmental force generation and total length of contraction was non linear. After bilateral va-

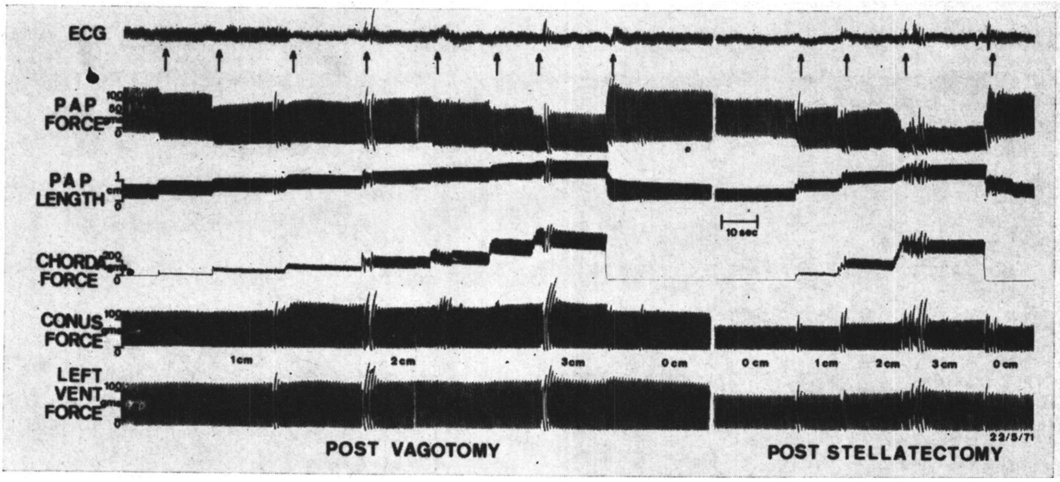

FIG. 5. In the same experiment as demonstrated in Fig. 4, the chorda papillary muscle complex is distended after bilateral cervical vagotomy (post vagotomy) and later after bilateral stellatectomy (right panel). In contrast to the control group, post vagotomy papillary force was barely changed during distention; chorda force was increased and the augmentation of conal force upon distention increased. Stellatectomy caused the papillary muscle force to be depressed and epicardial changes abolished.

gotomy, the same papillary muscles were elongated much more and generated considerably more force than during control states. When stellatectomy followed vagotomy, the papillary muscle systolic forces returned to control levels although the muscle still underwent greater length changes than during control states.

Table I summarizes data from the eighteen experiments in which the right ventricular anterior papillary muscle was extended while the animal was on cardiac bypass during control states, after bilateral vagotomy, and after combined vagotomy and bilateral stellatectomy. The mean heart rates for each group are listed in the left column. The lengths by which the chorda–muscle complex was extended (Δ chorda length) are shown in column 2; these lengths represent the control state in which there was no distention (0 cm) as well as average extending distances achieved when the chorda was pulled. The second line was the length achieved during maximal papillary muscle force suppression followed on the third line by the length when force was maximal. The next two lines represent the initial and later dynamic events following cessation of papillary muscle distention (fourth line represents the state achieved immediately following the distention and the fifth line 30 sec thereafter). Papillary muscle length changes (column 4) attained in sys-

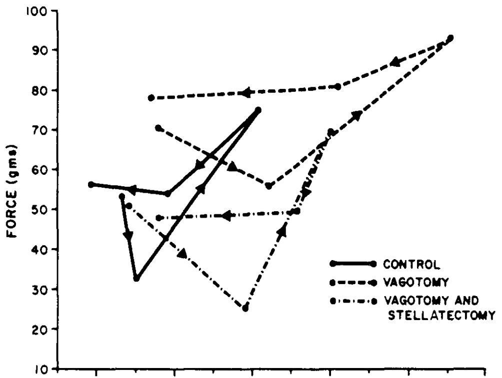

FIG. 6. The regional papillary muscle force development (force) in response to increasing and then decreasing (arrows denote sequence) the papillary muscle length (length) are graphed for control, post vagotomy, and finally stellatectomy following vagotomy groups. Note the initial depression in force during minimal papillary muscle lengthening; after vagotomy the papillary muscle generates more force and is more distensible. In the vagotomy and stellatectomy group forces return towards control, however the preparation is more distensible than the control state.

TABLE I.[a]

Heart rate	Δ Chorda distention (cm)	Papillary force (g)	Papillary length (mm) (systole/diastole)	Δ Pap length (mm)	Work index (g/cm)	Chorda force (g) (systole/diastole)	Δ Chorda force (g)	Conal force (g)	Left vent. force (g)
					Control (n = 18).				
129 ± 11	0	54.0 ± 5.5	3.8 ± 0.8/ 0	3.8	20.5	0	0	110.5 ± 9.0	118.0 ± 11.0
	1.6 ± 0.2	33.5 ± 4.6	10.7 ± 2.1/ 6.7 ± 1.3	4.0	13.5	142 ± 30/ 86 ± 22	56	115.5 ± 10.5	125.5 ± 11.8
	2.8 ± 0.2	70.5 ± 5.5	20.2 ± 1.8/14.6 ± 1.3	5.6	39.2	318 ± 52/208 ± 46	110	113.5 ± 6.0	118.5 ± 14.4
	0	54.5 ± 6.5	5.2 ± 0.9/ 0.8 ± 0.1	4.4	23.8	0	0	105.5 ± 8.5	116.5 ± 11.0
	0	56.0 ± 5.0	3.4 ± 0.5/ 0	3.4	18.9	0	0	107.0 ± 9.0	113.0 ± 10.5
					Vagotomy				
137 ± 9	0	70.5 ± 7.5	4.3 ± 0.8/ 0	4.3	30.3	0	0	103.5 ± 5.5	106.5 ± 7.5
	1.5 ± 0.3	55.5 ± 15.0	14.9 ± 2.5/ 9.2 ± 2.7	5.7	31.6	188 ± 58/110 ± 40	78	111.0 ± 7.0	107.0 ± 12.0
	2.4 ± 0.2	93.5 ± 13.5	21.4 ± 2.5/13.4 ± 2.1	8.0	74.8	298 ± 72/194 ± 58	104	145.5 ± 7.0	119.5 ± 9.0
	0	81.0 ± 10.0	8.0 ± 0.9/ 1.4 ± 0.4	6.6	53.5	0	0	108.0 ± 6.5	117.0 ± 9.0
	0	78.0 ± 11.0	4.4 ± 0.6/ 0.3 ± 0.06	4.1	31.9	0	0	103.0 ± 6.0	107.0 ± 8.0
					Vagotomy and stellatectomy				
103 ± 7	0	50.5 ± 6.5	3.9 ± 0.8/ 0	3.9	19.7	0	0	87.0 ± 6.5	85.5 ± 6.0
	1.6 ± 0.3	25.5 ± 5.0	15.2 ± 2.5/ 9.8 ± 1.9	5.4	13.8	144 ± 32/ 80 ± 26	64	88.5 ± 8.0	84.5 ± 7.5
	2.9 ± 0.2	69.5 ± 10.5	22.2 ± 2.5/15.7 ± 2.1	6.5	45.2	246 ± 54/150 ± 46	96	81.5 ± 6.0	87.0 ± 6.5
	0	49.5 ± 8.5	6.8 ± 1.0/ 0.7 ± 0.1	6.1	32.2	0	0	88.0 ± 6.0	87.0 ± 6.5
	0	48.0 ± 7.5	4.3 ± 0.6/ 0	4.3	20.6	0	0	87.0 ± 7.0	84.5 ± 6.0

[a] The data obtained by distention of the papillary muscles (column 2) in 18 dogs is tabulated in control states as well as following bilateral vagotomies and subsequent bilateral stellatectomies. Following control conditions (line one) the chordae were distended until minimal papillary muscle force was achieved (line two); further distention was accompanied by augmentation of papillary muscle force (line three). The last two lines of each group represent the state of the papillary muscles immediately (line four) and thirty seconds (line five) following cessation of distention. Note that following vagotomy the papillary muscles were much more distensible.

tole and diastole, as well as the systolic lengths achieved (Δ pap length) are listed in columns 4 and 5; the product of the papillary muscle systolic force and length (ΔL) is tabulated as a relative work index. The forces developed by the chorda in systole and diastole are tabulated (column 7) along with the change in chorda force generation (Δ chorda force); finally, distant epicardial forces generated by myocardial segments of the conus and anterior left ventricle are tabulated. In the control group, as the chorda was stretched (column 2) the maximum force developed by the papillary muscles first diminished then increased; the change in length of the papillary muscle during contraction (Δ length) simultaneously increased so that the work index almost doubled. Upon release of the chorda the regional papillary force returned gradually to normal. Simultaneous changes in epicardial muscle contractile force (RV conal force and left vent force) were not signifiant. After vagotomy, with its concomitant increase in heart rate, papillary muscle force was augmented ($p > 0.001$) as compared with control measurements. Upon chorda stretching a higher peak regional papillary muscle force was generated for similar chorda forces as in the control group. The papillary muscle shortening (Δ length) was greatly augmented so that the work index achieved considerably higher values over the controls. In contrast to the control situation epicardial muscle contractile force increased concurrently with extension of the papillary muscle, the RV conus more strikingly ($p > 0.001$) than the left ventricular segment ($p > 0.05$). Note that upon release from stretch, the papillary muscle force and length remained augmented and only after a time returned to control values. When stellatectomy was combined with vagotomy the average heart rate fell to 103 ± 7 beats/min. Papillary muscle extension was accompanied by local force and length changes which had returned to nearly control levels, so that the work index was similar to the control values. Epicardial forces were now unaltered.

Discussion. Since Frank (4) described the relationship between ventricular filling and pressure, concepts of cardiac function have been dominated by this thesis. However, segmental myocardial force measurements (1, 2), particularly of the *in situ* papillary muscles, have demonstrated that such a concept may not adequately describe regional cardiac dynamics. Contrary to *in vitro* observations (3) increasing tension on the *in vivo* chordae tendineae decreased local force generation capabilities of the papillary muscle, particularly in the right ventricle (1, 2). During ventricular outflow obstruction, with a concomitant increase in chamber size, the papillary muscle is distended and cannot generate as much local force (Fig. 1). This same phenomenon can be reproduced by distention of the papillary muscle with application of increasing weights to the papillary muscle via the chordae (Fig. 1); local distention not only reduces the systolic force, but greatly alters also the diastolic tone. These complex local interactions occur when the ventricular cavity is empty (Fig. 3) or generating pressure.

Initially during papillary muscle distention segmental force generation is decreased concomitantly with increasing length. As local distention increases, rather than a further decrease in force, local force of contraction is augmented until it is well above control levels (Fig. 3, Table I). These alterations are influenced by the autonomic nerves as bilateral vagotomy or stellatectomy caused significant changes in the papillary muscle work (Fig. 4, Table I). For instance, following bilateral vagotomy the initial depression of papillary muscle force during distention is minimized and followed by a considerable augmentation of force upon further distention, so that the work index did not diminish but rather became augmented. The increased length changes demonstrate that the papillary muscle became much more distensible (Fig. 5), altering its systolic and diastolic tone. Thus it is evident that withdrawal of parasympathetic regulation changes the papillary muscle segment so that it can generate much greater work.

In contrast to the right ventricle the left ventricular papillary muscles are minimally effected by increasing chordae force. Receptors have been reported in the ventricles (5–

7) but their physiological behavior is still in doubt. Ventricular receptors were located only within the right ventricular papillary muscles, not those of the left, which may account for the almost total lack of dynamic changes noted when left ventricular papillary muscles were distended.

Right ventricular papillary muscle dynamics were clearly influenced by the autonomic nerves (Fig. 5)—both the tone and contractile force of these muscles operate under constant neural modulation. Ventricular tone has been considered an important determinant of cardiodynamics in the past (8). In this preparation, it is evident that regional ventricular length and therefore tone, as measured by length gauges, not only is sensitive to neural influences but also is greatly altered by the load subtended by a particular myocardial segment; the diastolic tone—as well as force of contraction of a segment of myocardium—is constantly fluctuating under neural and humoral influences. Local distention of the anterior right ventricular papillary muscle has a profound influence on the electrophysiological status of the heart. As opposed to left ventricular papillary muscle distension, their lengthening consistently initiates severe tachyarrhythmias—generally of ventricular origin. Neuronally induced cardiac tachyarrhythmias have been reported (9) and transection of the white band of tissue connecting the right ventricular anterior papillary muscle to the free wall regularly initiated ventricular fibrillation. These chronotropic effects were strongly modified and sometimes completely abolished by cardiac neurectomies (Fig. 2). Thus it appears that local papillary muscle distention, which effects local receptor afferent traffic (Fig. 3) modifies the efferent neuronal influence upon regional as well as distant myocardial dynamics (Table I). Atropine and hexamethonium also abolished or greatly attenuated the tachyarrhythmias, as well as contractile alterations, initiated by right ventricular anterior papillary muscle distention.

The autonomic nervous system exerts a highly discrete efferent control on the heart (10). Afferent nerves from the heart also come from highly discrete regions, the anterior papillary muscle of the right ventricle having a particular concentration of mechanoreceptors. Thus the neural mechanisms are present for reflex control of the heart similar to that reported in the urinary bladder (11). A neuronal cardio-cardiac controlling mechanism which involves both parasympathetic and sympathetic limbs, and modulated through local as well as central nervous system reflex arcs (Fig. 7) is proposed. Cardiac receptors have afferents in both the parasympathetic (5–7) and sympathetic (11, 12) components of the autonomic nervous system; presumably these afferents terminate in the vagal nuclei (X) and tend to modulate efferent sympathetic (SNS) and parasympathetic (PSNS) traffic. This efferent nerve traffic in turn modifies the chronotropic, dromotropic, inotropic, and tonotropic status of that region of cardiac tissue adjacent to the effected receptor (proximate cardiac effector) as well as other regions of the heart (distant cardiac effector). Afferent nerves may also terminate as local neural cells to activate local efferent nerves (local reflex).

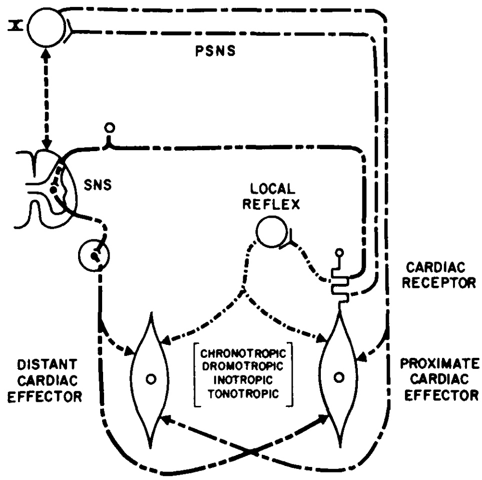

FIG. 7. The diagrammatic representation of the hypothesized neural reflexes involving the myocardium demonstrates both local and central reflex arcs. The receptor tissue effects local contraction (proximate cardiac effector) and distant cardiac sites (distant cardiac effectors). These mechanisms appear to regulate heart rate (chronotropic) cardiac conductivity (dromotropic), cardiac contraction (inotropic), and resting tone of cardiac muscle (tonotropic).

There may also be considerable amount of interaction between central vagal nuclei and the spinal cord to modulate both sympathetic and parasympathetic neural efferent activity. These cardio-cardiac neural reflexes may be of paramount importance when considering electrical and mechanical behavior of the heart. Numerous physiologically active receptors are located in the ventricles, as well as the atria and great vessels (13); alteration of the milieu of such receptors presumably alters cardiovascular dynamics from instant to instant throughout each cardiac cycle.

Summary. Distention of the intact right ventricular papillary muscles induced both mechanical and electrophysiologic changes in the whole heart. Severe dysrhythmia accompanied tension exerted upon the right, but not upon the left ventricular chordae tendineae. The right ventricular papillary muscles contain numerous receptors, stimulation of which induces marked changes in afferent impulse traffic in the cardiac nerves. Local papillary muscle contractile force was initially depressed and then elevated while that of distant myocardial segments was augmented during local papillary muscle distention. These responses were shown to be influenced by both sympathetic and parasympathetic cardiac nerves. A physiologic cardio-cardiac neural control mechanism is proposed to account for these dynamic cardiac events.

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