The Influence of the Parasympathetic Nervous System on Atrioventricular Conduction

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IN THIS brief review I will attempt to amalgamate current findings with important historical concepts about the influence of the parasympathetic nervous system on atrioventricular (AV) conduction. I first will describe the innervation of the AV nodal region. Then I will discuss the influence of acetylcholine and associated cholinergic agents, the effects of vagal stimulation, and the role of the vagus in the genesis of arrhythmias. Finally, I will describe briefly certain cardiovascular reflexes that affect AV conduction. I have not attempted to provide an exhaustive list of references; rather, the most relevant works were arbitrarily selected to illustrate specific points. I regret that many worthy contributions had to be omitted.

Innervation of the AV Node

It has been known since the early part of this century that the autonomic nervous system can affect AV conduction profoundly. Anatomical studies during this era revealed that the AV node is richly innervated and that the density of nerve fibers in this region exceeds that in the myocardium. In subsequent years, it was found that ganglia, nerve fibers, and nerve nets lie in close proximity to the AV node in the human heart and that the terminations on nodal tissue vary from fine fibrils to complex reticular nets. It should be noted, however, that all of these early works were based upon light microscopy and variable staining techniques and, thus, not all of these results were accepted conclusively.

Most of the definitive work in this area has been done within the past 10-20 years. I first will review the neural pathways to the AV node, and then describe the terminal innervation of the node. Although the focus here is on the vagus, the adrenergic innervation will also be mentioned for completeness.

Geis et al. recently have delineated the various autonomic pathways to the AV node of the dog. They found that the left anterior limb of the ansa subclavia and the ventrolateral cardiac nerves innervated the AV node in each dog studied. The posterior ansa on the left side and both limbs of the ansa on the right side innervated the AV node in one-half to two-thirds of their dogs, whereas the innominate, the recurrent cardiac, the craniovagal, and the ventromedial cardiac nerves innervated the AV node in less than one-fourth of the animals. The right-sided sympathetic innervation of the AV node consisted of nerve fibers that accompanied the great vessels to the region where the inferior vena cava approximates the inferior border of the left atrium. The sympathetic innervation on the left side followed similar pathways, but additional fibers reached the node through the ventrolateral cardiac nerve. Both the left and right parasympathetic innervations traversed pathways along the superior left atrium and the region where the inferior vena cava lies close to the inferior margin of the left atrium.

Thus it has been demonstrated that nerve fibers from both sides of both autonomic divisions project onto the AV node. The differential effects of neural activity from the left and right sides is less clear, however. Historically it was thought that the nerves on the left side primarily control AV conduction, whereas those on the right side govern heart rate. This differential distribution was confirmed recently, both for the vagi and for the sympathetic nerves. Others have reported, however, that at submaximal stimulation levels, the right and left vagi produce an equal prolongation of AV conduction time. Also, with brief bursts of vagal stimulation, no consistent pattern of left vagal dominance of the AV node was found. However, equal efficacy of the right and left vagi was not firmly established here because constant stimulation parameters were not used. Thus, most evidence favors the dominance of the left- over the right-sided innervation of the AV node, at least with maximal stimulus intensities. The exceptions noted above make for some uncertainty, however, especially when the interactions of neural activity with other factors are taken into account. This will be discussed in more detail below.

Abundant terminals from both divisions of the autonomic nervous system innervate the AV node. The distribution of cholinergic terminals appears to be considerably more dense than that to the surrounding regions of the heart. The sympathetic innervation of the AV node...
also is extensive. However, the concentration of norepinephrine in the AV node is not significantly different from that in the neighboring cardiac tissues. Cholinesterase is abundant in the specialized conducting fibers in the right atrium that bypass the crest of the node to enter it along its convex surface. Vagal suppression of this bypass tract may be one mechanism that prevents it from short-circuited the AV node under ordinary conditions.

It was believed initially that the nerve supply to the AV node is not distinct from that to the surrounding myocardium. It has been found, however, that small cardiac branches of the vagus can affect atrial contractility, AV conduction, and sinoatrial (SA) nodal rate independently. Furthermore, with focal excitation of intracardiac vagal fibers, axons stimulated near the SA node do not affect AV conduction, and those stimulated near the AV node do not affect heart rate. Normally, parasympathetic ganglia are not contained within the AV node itself, but such ganglia are located at its posterior margin, interposed between the node and the anterior wall of the coronary sinus.

It generally has been thought that nerve terminals do not come into direct contact with AV nodal cells. It has been reported more recently, however, that portions of the node are supplied richly with neuromuscular contacts. Both granular (presumably adrenergic) and agranular (presumably cholinergic) vesicular processes were described, although the latter predominated. The vesicular processes were found within sarcolemma-lined tunnels inside nodal cells, as well as along grooves in the cell surfaces. The functional significance of this pattern of terminal innervation remains to be defined. However, the incidence of such neuromuscular contacts varies tremendously from site to site within the node, and contact sites were found quite rarely in the nodes of some vertebrate species.

Cholinergic Effects

EFFECTS OF ACETYLCOLINE AND RELATED AGENTS

With the advent of microelectrode recording techniques, it became possible to elucidate the structural basis for the autonomic effects on AV conduction. In a pioneering study, Cranefield et al. added acetylcholine (ACh) to tissue baths containing preparations of isolated rabbit hearts. They found that, when complete AV block ensued, the transmission failure occurred at the atrial margin of the AV node. The characteristic action potential changes in these junctional fibers included slower depolarization, notching, and slurring of the upstroke, and decreased amplitude. It was concluded, however, that these effects were "secondary to the fragmentation of the action potential into several asynchronous components." Furthermore, the amplitude and upstroke velocity of a nodal action potential at the atrial margin depend, in part, on the width of the atrial potentials that drive it; thus, the decrease in the duration of the atrial action potential induced by ACh serves as a less effective driving stimulus and, per se, inhibits AV conduction. Retrograde stimuli passing first through lower nodal regions where action potential waveshape is relatively unaffected by ACh thereby elicit a more normal action potential amplitude in the upper AV nodal cells. An increase in heart rate exaggerates the depressant effect of ACh on conduction in the atrionodal marginal cells. There is little direct effect on the action potentials of the lower node or His' bundle. Using similar preparations, however, others have found that ACh exerts its principal effects on the action potentials in the middle area of the AV node rather than at the atrionodal junction. Furthermore, in these studies, the response appeared to be independent of the direction of propagation. That ACh can result in the reduction of nodal potential amplitudes has been a common finding by electrophysiologists, however. This effect is especially interesting since such graded action potential amplitudes seem to violate the "all or one" law of most other myocardial (and nerve) cell types, and thus indicates a fundamentally different membrane behavior.

It now is clear that an important mechanism of ACh action is to increase potassium conductance. This was shown indirectly by holding the cell membrane at a potential more negative than the Nernst potential for K⁺; the addition of ACh induced a partial depolarization rather than the hyperpolarization that ordinarily is obtained at the usual levels of resting potential. This shift toward the Nernst potential for K⁺ is the result expected, of course, if ACh increases K⁺ permeability. More direct evidence for the effect of ACh on K⁺ conductance has been provided by isotope experiments.

If the permeability to K⁺ is sufficiently high, attempts to elicit a propagated action potential in the AV node may fail. Even a large increase in Na⁺ permeability may not be able to shift the membrane sufficiently far from the resting level to evoke a regenerative depolarization. Surprisingly, potassium infusions at concentrations of 4.8-6.9 mM/liter alleviate the AV block induced by vagal activation, although, at higher K⁺ levels, parasympathomimetic actions are enhanced. Still higher concentrations of K⁺ cause AV block even in the absence of vagal activity. The antagonizing effects of the lower K⁺ concentrations are not mediated by catecholamine release. Instead, they may act by reducing the resting potential, thereby bringing it closer to the threshold level. Alternatively, the effect of ACh on the amplitude and rate of rise of the action potential may be inhibited, thereby allowing the cell to depolarize more rapidly.

With respect to drugs that affect autonomic function, the cardiac vagus nerves are more susceptible to the blocking action of tetrodotoxin than are the sympathetic nerves. This drug also has a direct effect on cardiac cell membranes. The cardiac action potential appears to consist of relatively independent fast and slow components, involving separate channels in the cardiac cell membranes. The slow component predominates at the SA and AV nodes. The slow channels are relatively insensitive to tetrodotoxin, but the fast channels are very sensitive. The slow channels are effectively inhibited by verapamil via a noncholinergic mechanism.

Atropine slows SA nodal discharge rate in low doses, but accelerates it at higher doses in humans.
spontaneously beating heart, the curve of AV conduction time as a function of atropine concentration is U-shaped; i.e., it first decreases, as expected, but then surprisingly increases again. However, all values of conduction time are less than the control level. When the heart rate is held constant, on the hand, there is a consistent dose-related shortening of the AV conduction time. Thus, the lesser effect of higher doses of atropine on AV conduction in the un-paced heart could be explained entirely by an interaction with the depressant effect of the increased heart rate at these doses.

A comparison of the effects of ACh with those of local anesthetics and adenosine triphosphate has been made by selective perfusion of these agents into either the AV nodal artery or the anterior septal artery that supplies the bundle branches before the node. It was concluded that ACh blocks conduction proximal to the bundle branches, but procaine, lidocaine, and ATP impair conduction in the AV node as well as in the proximal bundle branches. It also was found that ACh infused into the anterior septal artery slows an AV nodal rhythm but has no effect on retrograde conduction, whereas ACh infused into the posterior septal artery has the opposite effect. It was concluded that AV nodal rhythms originate in the area supplied by the anterior septal artery. Conversely, the area supplied by the posterior septal artery has low automaticity but is highly susceptible to ACh and norepinephrine.

Finally, it was noted above that the SA and AV nodes contain a rich supply of cholinesterase. The ratio of cholinesterase distribution to nodal and non-nodal tissue may be of the order of 100:1. Furthermore, a protein-deficient diet results in an increase in cardiac acetylcholinesterase activity and a decrease in cardiac butyrocholinesterase activity. The latter may be the more important of the two for changes in the control of cardiac excitation. As expected, the cholinesterase inhibitors, neostigmine and phystostigmine, selectively perfused into the AV nodal artery produce dose-related AV block, and the effect is abolished by atropine.

**EFFECTS OF VAGUS NERVE STIMULATION**

In a discussion of the effects of vagal stimulation, it is desirable to distinguish between those studies involving protracted trains of stimuli and those with single or brief bursts of stimuli. Continuous supramaximal trains of vagal stimulation prolong AV conduction time with a latency of less than 1 second. In some dogs, left vagus stimulation, but not right, preferentially induces second degree heart block. Thus, the vagi may innervate two functional areas of the AV node; both vagi may be distributed to a site that controls the AV conduction time, but the left vagus alone may innervate an area with a considerably higher predilection to block. However, since heart rate was not kept constant in this study and since right vagal stimulation has a greater effect on SA nodal rate than does the left, the interaction of simultaneously changing heart rate and vagal activity on AV conduction (to be discussed in detail below) casts some doubt over this conclusion.

Supramaximal stimulus trains to the vagi induce bradydysrhythmias, with fixed or changing degrees of heart block. These responses are a monotonically increasing function of the stimulus amplitude. AV conduction may be prolonged by about 50–70% of control before block appears. Vagal stimulation will slow an AV junctional rhythm, just as it does an SA nodal rhythm. The degree of prolongation of AV conduction depends strongly on the concomitant degree of SA nodal slowing. This interaction of the direct vagal effect on the AV node and the concomitant indirect effect of a lengthened cardiac cycle increase the difficulty of deriving quantitative conclusions about AV conduction in those studies in which the heart is not paced. This interaction will be discussed in detail below.

The dynamics of the processes that occur at the vagal nerve endings in the AV node are best studied with single vagal stimuli or with brief bursts of stimuli. In our laboratory, the effects on AV conduction were extremely variable when we used un-paced dog-heart preparations. Either an increase or a decrease in the AV conduction time was obtained, depending upon the timing of the stimulus within the cardiac cycle. This variability in the direction of the response was ascribed mainly to the indirect effects of the concomitant changes in cardiac cycle length on AV conduction. In a subsequent study, single vagal stimuli produced a consistent prolongation of AV conduction when the heart was paced. In this study, "vagal effect curves" were used to represent the total dynamic response to a single stimulus. The responses from a series of separate stimuli, given at increasing increments of delay in the cardiac cycle, were combined in a single curve, as originally devised by Brown and Eccles for the heart rate responses. Such curves clearly show that the magnitude of the AV conduction response is critically dependent on the time in the cardiac cycle at which the stimulus is given.

Figure 1 shows two such curves from the same animal, in which the heart was driven at two different atrial pacing intervals (AA). The large circle, square, and triangle in Figure 1 represent the effects of one vagal stimulus over three consecutive cardiac cycles. The stimulus that caused this set of responses was given in the cardiac cycle that just preceded the cycle represented by the circle (precisely, at t = 0 on the time axis). The figure shows that the vagal

![Figure 1: Vagal effect curves from the same dog at two different atrial pacing intervals. The abscissa axis indicates the time elapsed from a single vagal stimulus burst given at t = 0. The ordinates are the percent change in AV conduction time over a sequence of consecutive cardiac cycles with the circles, squares, and triangles being measured in the first, second, and subsequent beats after the beat in which the stimulus is given. (Adapted, with permission, from Martin.)](image-url)
effects at the AV node are rapid and transitory. Most of the response disappears in less than two seconds, just as in the SA node. Efferent vagal activity in the intact animal can occur as discrete bursts in the cardiac cycle. Thus, a given burst can affect AV conduction in the very next cardiac cycle, and it is therefore possible for AV conduction to be controlled on a beat-to-beat basis. This makes it possible for the vagus to play a role in the genesis of certain arrhythmias, a concept that is developed below.

Double peaks are found in curves derived from 62% of the dogs studied. The points at the first and second peaks are derived from the same stimulus. The peak of the curve signifies that the AV interval is lengthened maximally. Concomitantly, the effective refractory period is prolonged maximally. Hence, the AV node has less time to recover before its next activation. Consequently, the next atrial impulse arrives earlier in the relative refractory period of the AV junction. A given quantity of ACh released at the nerve terminals is likely to have a greater effect on AV conduction time if the node is in a more refractory state. Therefore, the atrial impulse that arrives at the AV junction when its ability to conduct is maximally depressed (e.g., at the first peak) is likely also to be conducted very slowly. Hence, it will be at or near the second peak. A similar explanation has been advanced by Spear and Moore, who also used a form of the vagal effect curve. Rarely is a third peak evident, as in Figure 1, but when it occurs, the mechanism is similar. This figure also illustrates that the amplitude of the curve increases with the pacing frequency when the vagal stimulation parameters are constant. At more rapid heart rates, the AV node is more refractory and, therefore, a given vagal stimulus will have a greater effect.

Brown and Eccles concluded that the shape of a vagal effect curve for the SA node is related directly to the time course of ACh concentration near the affected cells. The vagal influence on AV conduction was simulated recently with a mathematical model of the release, diffusion, and inactivation of ACh, combined with a relaxation oscillator model of AV nodal cells. It was concluded from this analysis that, for the AV conduction system, the time course of the tissue concentration of ACh need not correspond to the configuration of a vagal effect curve. Particularly, it was concluded that the second peaks are a property of the nodal cells per se, since the simulated ACh concentration declines monotonically.

Another relevant property of the AV conducting system is that the response to a single vagal stimulus depends on the time passed after the preceding vagal activity. In a recent study in the paced heart, two identical, brief stimulus bursts were separated by an increasing time interval, and each burst was given at the same point in its respective cardiac cycle. To normalize the data, change in AV conduction time (ΔAV) was expressed as the ratio of the response to the second stimulus burst (ΔAV₂) to that of the first (ΔAV₁). The results are shown in Figure 2, in which the abscissae are the time intervals between bursts. The mean minimum ratio was 0.67 and it occurred at a stimulus separation of about 5 seconds; i.e., when the two stimuli were separated by about 5 seconds, the magnitude of the second response was only 67% of the magnitude of the first response. The ratio did not return to unity until about 1 minute had intervened between stimulus bursts. When the left and right cervical vagi were stimulated alternately over an equivalent range of delays, essentially the same results were obtained (Fig. 2, open circles). This indicates that the mechanism of the depression of the second response probably is not associated with processes governing the synthesis, release, or depletion of acetylcholine. These processes are independent for the two nerves; stimulation of one side should not affect the synthesis, release, or depletion of ACh from the terminals on the other side. This would require, of course, that there be no convergence of the left and right efferent fibers on common parasympathetic ganglia; such a lack of convergence has been reported.

One mechanism for the attenuation of the response to the second vagal stimulus (Fig. 2) might involve a transient enhancement of cholinesterase activity by the first stimulus. I could find no work to support this possibility. Alternatively, the burst of ACh released during the first stimulus might desensitize the receptor transiently to pulses of ACh released during subsequent vagal bursts. This latter concept has been used to explain vagal escape for the SA node possibly associated with local changes in sodium concentration. The results of Figure 2 similarly provide an explanation of vagal escape at the AV node.

I also have studied the interaction of the direct effects of single vagal stimuli on the AV node with the indirect effects of concomitant changes in atrial cycle length (heart period). To accomplish this, I subtracted the vagal effect curve derived from the paced heart preparation from that obtained in the unpaced heart preparation in the same dog. The changes in cycle length produced by vagal stimulation in the unpaced heart were stored in the memory of a digital computer. The SA node of the dog then was crushed, and these sequences of changing cycle lengths were "played back" in real time from the computer into pacing electrodes attached to the right atrium near to the SA node. Thus, the AV conduction response to the applied sequence of cycle lengths could be assessed in the absence of the interacting effects of vagal stimulation. It was found that, over some portions of the vagal effect curves, AV conduction time decreased more when...
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both vagal activity and changing cycle length were simulta-
neously imposed than when the cycle length changes alone were imposed; that is, the AV conduction time was ac-
tually less in the presence of vagal activity than in its absence, a paradoxical response.

The top panel of Figure 3 shows the effects of vagal stimulation in the presence and absence of pacing in one dog. It is evident that the curve for the unpaced heart (U) has substantial troughs of decreased conduction times, whereas the curve for the paced heart (P) displays purely inhibitory responses. The dashed curve (D) in the bottom panel was obtained by subtracting these two curves. When the identical sequences of cycle lengths recorded from the unpaced heart were used to trigger the pacing stimulator, the dynamic effect on AV conduction appears as the “playback curve” (PB) in Figure 3. If there were a linear summation of the direct vagal effects and the indirect cycle length effects, the difference curve and playback curve would have coincided. That is, the difference represents the linear subtraction of the direct vagal component from the vagal effect curves. It represents the effect of the changing cycle lengths and of the interaction of cycle length and vagal activity on AV conduction. The disparity between curves D and PB reflects the magnitude of the interaction between the direct and indirect effects of vagal activity. Changing atrial activation patterns and cardiac pacemaking sites with vagal stimulation were found to be important contributors to the paradoxical effect. Mechanisms residing in AV nodal (or lower) structures also contributed importantly, being possibly related in part to the facilitatory effect of ACh on some His' bundle fibers.35, 36

The paradoxical effect described above illustrates the problem of the interpretation of AV conduction responses to vagal stimulation when the heart is permitted to beat spontaneously. The mechanisms of such responses clearly are complex and not ascribable to direct vagal effects on AV nodal cells alone. Similarly, studies in the unpaced heart that purport to assess the functional dominance of the left over the right vagus on AV conduction also must be interpreted carefully. The right-sided vagal dominance over the SA node seems indisputable.34-36, 61-64 Hence, a given stimulus to the right vagus produces a greater lengthening of the heart period than does that same stimulus applied to the left vagus. Thus, there will be a greater interaction between the direct and indirect effects at the AV node during right than during left vagal stimulation. Therefore, in order to compare the responses to left and right vagal stimulations, these interactions must be assessed properly.

ARRHYTHMIAS AND THE VAGUS

The important contribution of the autonomic nervous system to the genesis of arrhythmias has been reviewed recently.57 It was noted that nearly every clinically observed arrhythmia can be reproduced by stimulation of sites in the diencephalon and mesencephalon.58 The arrhythmias resulting from hypothalamic stimulation can be abolished by autonomic blockade.59 Disruption of the normal balance between sympathetic and parasympathetic influences may result in the shifting of cardiac pacemakers.60 Stimulation of the ventrolateral cardiac nerve, which is predominantly a sympathetic link from the central nervous system to the heart, but which also includes vagal fibers in the dog, leads to various degrees of heart block, total AV dissociation, and AV junctional rhythms.61 These nodal effects are probably secondary to the sympathetically induced increase in cardiac rate, but vagal fibers may also be involved.

An emerging concept is that vagal activity may help to allay certain arrhythmias, (e.g., extrasystoles and paroxysmal tachycardias), especially under such pathological conditions as ischemia and drug intoxication.62 Atropine, in fact, contributes to AV nodal reentry in man, supposedly by providing the prerequisite balance between nodal conduction velocity and refractoriness within reentrant pathways.62 Atropine also shortens the functional and effective refractory periods of the AV node. Consequently, His-Purkinje block and aberrant ventricular conduction may emerge during premature atrial stimulation.63 However, atropine also shortens AV conduction time and increases the atrial pacing rate at which AV nodal Wenckebach rhythms occur.64

![Figure 3](http://circres.ahajournals.org/)

**Figure 3** Top panel: vagal effect curves from the same preparation in which the vagus was stimulated and the heart was paced (P) and unpaced (U). Bottom panel: the effect of vagal stimulation on atrial rate (ΔAA) measured simultaneously with the unpaced heart curve (U) above. When these same sequences of changing atrial rates are used to pace the atrium without vagal stimulation, the effect on AV conduction is measured as the curve labeled PB. The curve labeled D is the arithmetic difference between the unpaced and paced heart curves at each point in time. See text for discussion. (Reprinted from Martin64 by permission of the American Heart Association, Inc.)
Three distinct periodicities in vagal activity have been observed in cats. One of the periods corresponds to the respiratory rate, and it may play a role in the oscillatory changes in AV conduction time. As noted above, some vagal traffic occurs as discrete bursts within each cardiac cycle. These phasic changes in activity may play a role in "supernormal" AV conduction, i.e., in better conduction than would be expected in a depressed node, but which is still more depressed than in a normal node. It is likely that periodic bursts of vagal activity produce overlapping vagal effect curves (Fig. 1). If the cardiac cycle lengths are not constant, or if these periodic bursts do not occur at the same point in each cardiac cycle, the peak of each overlapping vagal effect curve will appear at different times in subsequent cardiac cycles. For some cardiac cycles, the peak will occur at or just prior to the time at which the AV node is excited, thus causing a prolongation or even a block of AV conduction. For other cardiac cycles, the vagal effect curve will begin its steep ascent just after the AV node has been excited. AV conduction will then be relatively unaffected, and the AV conduction time will be less than for other beats. Hence AV conduction for that beat would appear to be "supernormal." Similar mechanisms may be involved in other arrhythmias, as has already been suggested for the AV nodal Wenckebach phenomenon.

Cardiovascular Reflexes and AV Conduction

The arrhythmogenic effects of discrete bursts of vagal activity discussed above suggest that such arrhythmias might appear in the course of certain cardiac reflexes. Repetitive bursts of vagal activity are induced reflexly by the pulsatile pressure sensed by the arterial baroreceptors. Carotid sinus massage may induce a decrease in atrial rate and a Mobitz type II AV block, as recently documented in patients with myocardial infarction. In dogs with chronic, complete AV block, the changes in heart rate and arterial blood pressure evoked by the carotid sinus reflex are twice those in normal dogs. Such differences are abolished after vagotomy. Heart block often is associated with an increase in stroke volume and pulse pressure and a decrease in ventricular rate. These changes may alter the baroreceptor input in such a manner as to enhance the gain of the baroreceptor reflexes. The increased reflex gain, if also present in humans with heart block, may serve a protective function by allowing a more complete and rapid cardiovascular response to the fluctuations in blood pressure that occur in complete heart block.

It has been shown recently that the dye employed during angiocardiography exerts both a direct and a reflexly mediated depression of cardiac excitation and conduction. It was thought that the reflex effects are mediated by left ventricular chemoreceptors via vagal afferent and efferent pathways, possibly the counterpart of the Bezold-Jarisch reflex. The effects on AV conduction are not precisely defined, due to the interaction of the direct vagal effect with the indirect effect of the concomitant increase in heart period. The existence of a vagovagal reflex influence on AV conduction time and heart rate has been confirmed by the detailed study of the responses to stimulation of various small cardiac nerves. It now is appreciated that cardiac reflexes are extremely complex, since the simultaneous effects on contractile force, heart rate, AV conduction, and peripheral resistance may be highly specific. For example, with both vagi intact, heart rate may be only slightly affected by stimulation of the left cervical sympathetic trunk, while the AV node may be blocked and right atrial force markedly diminished.

Conclusions

The parasympathetic nervous system plays a significant role in the normal process of AV excitation. The AV node is innervated richly by vagal fibers. Even relatively low levels of brief or sustained vagal stimulation may alter AV conduction profoundly. However, the effect of autonomic activity on the overall AV conduction process is not dependent solely on the direct response of the AV node to neural activity. Neural activity also has appreciable effects on cardiac rate, pacemaker location, and atrial activation patterns. Furthermore, neurally induced changes in the action potential from higher AV nodal regions can markedly alter the conduction time through the lower elements of the conducting system. Each of these indirect responses also has an effect on AV conduction time, some in a direction just opposite to those of the direct neural influences. The overall effect of vagal activity on AV conduction, then, is the summated resultant of the direct and the many indirect effects.

There will undoubtedly be a much better definition in the future of the neural effects on discrete elements of the AV conduction system and of the interactions among the various elements. Perhaps such work will lead to an enhanced understanding of the functional significance of discrete bursts of vagal activity in a cardiac cycle and of the role of the autonomic nervous system in the genesis of arrhythmias. These areas have not received sufficient attention.

Acknowledgments

The extensive assistance in the editorial preparation of this work by Dr. Matthew N. Levy is gratefully acknowledged.

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The influence of the parasympathetic nervous system on atrioventricular conduction.

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Circ Res. 1977;41:593-599
doi: 10.1161/01.RES.41.5.593

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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