The Vagus and the Ventricles

THE ROLE of the vagus nerve in modulating the electrical activity of the mammalian ventricles and the specialized fibers distal to the atroventricular node remains a puzzle. For many years, interest in the effects of the vagus on cardiac electrical activity focused on changes in transmembrane potentials of fibers in the sinusatrial and atrioventricular nodes and of the specialized and working fibers of the atria. These sites are innervated densely by what appear to be postganglionic vagal fibers, and vagal stimulation and administration of acetylcholine exert clear and consistent effects.

Study of the ventricles has not presented as clear a picture. Early investigations on the effects of acetylcholine on transmembrane potentials of ventricular muscle fibers and Purkinje fibers from canine hearts showed minimal effects even at quite high concentrations. In spite of clear demonstrations that vagal activity exerted a negative inotropic effect on the ventricles, it was generally assumed that, for fibers distal to the a-v node, vagal stimulation was unlikely to cause significant changes in rate or rhythm or the propagation of the impulse. This view was held in spite of some reports that vagal stimulation could modify ventricular pacemaker function in dogs. The conclusions reached, on the basis of studies on experimental animals, led to certain assumptions about arrhythmias in humans—for example, that tachyarrhythmias terminated by reflex vagal activation almost certainly originated at a supraventricular site.

Recently, data have become available that strongly implicate the vagus in the modulation of ventricular electrical activity in human and canine hearts, and histological techniques have shown that, in contrast to the sparseness of cholinergic innervation of ventricular myocardium, the ventricular specialized conducting system of human as well as canine hearts receives a rich cholinergic innervation, particularly in the region of the left bundle branch.

Studies on isolated canine cardiac Purkinje fibers have shown that, for the proximal His-Purkinje system as well as for more distal Purkinje fibers, acetylcholine decreases the slope of phase 4 depolarization and slows impulse initiation. Many investigations have demonstrated effects of vagal stimulation on ventricular electrophysiological function in the dog. Vagal stimulation increases the ventricular fibrillation threshold of both the ischemic and non-ischemic dog heart and also increases the threshold for repetitive extrasystoles.

It must be emphasized that not all recent studies have shown a protective effect of vagal stimulation. R. G. G. James and his co-authors have reported that, at constant heart rate, vagal stimulation does not alter the ventricular fibrillation threshold. In reviewing studies concerned with vulnerability to ventricular fibrillation, one is impressed by differences in techniques which may have modified the results. Also, the mechanism by which vagal activation modifies electrical activity in ventricular or Purkinje fibers is not certain. Even though evidence is beginning to accumulate to show that acetylcholine has direct effects on the transmembrane potential of these fibers in vitro, evidence also has been presented that the effects of the vagus on fibrillation thresholds may result from an inhibition of sympathetic effects on the heart.

In spite of these uncertainties, evidence from studies on patients supports the concept that vagal activity can modify ventricular rhythm and conduction. Recently, M. B. Waxman and R. W. Wald reported on 12 patients in whom injection of phenylephrine terminated episodes of ventricular tachycardia. To elucidate the mechanism by which phenylephrine exerted this action, they studied the effects of edrophonium, atropine, and carotid sinus massage. Their results are consistent with a vagally mediated mechanism of action in that edrophonium enhanced and atropine diminished the efficacy of phenylephrine and, after administration of edrophonium, carotid sinus massage was effective in suppressing the ventricular tachycardia. It is clear that in order to demonstrate consistently these effects of acetylcholine there probably is a need for it to be present in high concentrations. If this is the case, then one must consider the possibility that, at least in part, acetylcholine is acting on a muscarinic receptor at the sympathetic terminals. It also may be that acetylcholine has less marked effects on normal fibers than on fibers that have a reduced membrane potential and either are firing automatically because of an abnormal mechanism or are generating an abnormal action potential that permits reentrant excitation.

We are left with many uncertainties but the evidence from studies on patients both supports the concept that vagal activity can modify ventricular rhythm and conduction and emphasizes the need for additional and more definitive studies in experimental animals. It would be most satisfying if the question of what the vagus does—and how it does it—could be settled with certainty.

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