Editorial Comment

Sinus Node During Atrial Fibrillation
To Beat or Not to Beat?

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Postmortem reports from human subjects who suffered from chronic atrial fibrillation indicate significant damage to the sinus node, to the surrounding tissues, and to the sinus node artery. The association of paroxysmal atrial fibrillation with the sick sinus syndrome is well known. Atrial fibrillation is also one of the most common complications of cardiac surgery, occurring in a substantial number of patients undergoing coronary artery bypass operations. Although autopsy studies in such patients have demonstrated some damage to the sinus node artery, the only clinical variables identified as predictors of postoperative atrial fibrillation, in a number of reviews, are advanced age and β-blocker withdrawal; sinus node dysfunction has never been demonstrated to be associated with postoperative atrial fibrillation. The experimental suppression of sinus node activity by surgical ablation or injection of toxic chemicals into the sinus node artery reduced both the incidence and duration of electrically induced atrial fibrillation. Thus, conflicting notions exist regarding the role of the sinus node in the genesis and perpetuation of atrial fibrillation.

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This issue of Circulation presents an important contribution by Kirchhof and Allessie investigating impulse formation in the sinus node during atrial fibrillation. With intracellular action potential recordings in rabbit atrial preparations, they have shown that a high degree (5:1) of sinoatrial entrance block occurs and protects the sinus node pacemaker fibers from activation by the atrial fibrillatory impulses. There was a difference, however, albeit a slight one, between the rates of pacemaker discharge measured during atrial fibrillation and sinus rhythm. These authors put forth strong evidence that this difference in rate as well as the irregularity of pacemaker cell firing during atrial fibrillation might have been caused by the variable electrotonic influence of blocked fibrillatory impulses on sinus node automaticity. To the authors’ credit, this extraordinary degree of insight was achieved by overcoming the very demanding technical problems posed by investigation of cellular activity within the sinoatrial node, especially during atrial fibrillation.

Sinoatrial Entrance Block

It has long been suspected that the sinus node might be protected from atrial impulses during tachyarrhythmias. Massing et al reported that overdrive suppression of the sinus node did not occur upon cessation of supraventricular tachycardia; this suggested that atrial impulses did not retrogradely depolarize the sinus node, perhaps because of perinodal conduction block. In isolated rabbit atrial preparations, Kerr and Strauss demonstrated that the shortening of sinus node recovery time with rapid atrial pacing might be explained by the presence of atriosinus block and by a reduction in the number of impulses that could reach the pacemaker site in the sinus node, thereby preventing overdrive suppression. Thus, it was logical to postulate that, during atrial fibrillation, the sinus node might be protected from invasion by the multiple wavelets of atrial fibrillation. In fact, Gomes et al reported evidence of sinoatrial entrance block during atrial fibrillation in humans using extracellular catheter recordings.

Mechanism of Atrial Fibrillation

Through detailed atrial mapping, Allessie and his group raised the point that the two classic explanations for atrial fibrillation, i.e., rapidly firing ectopic foci and multiple reentry, are not necessarily mutually exclusive. The chance of termination of atrial fibrillation by simultaneous cancellation of wavelets is low. When incidental termination of atrial fibrillation does occur, the generation of an impulse shortly thereafter, either from some abnormal pacemaker or the sinus node itself, will almost certainly reinitiate the arrhythmia. Although it supported this possibility, the present study did not demonstrate such a “restart” of atrial fibrillation by a sinus impulse. Can sinus rhythm resume early enough to take advantage of inhomogeneous recovery of excitability to reinitiate atrial fibrillation? The authors have previously shown both in animal preparations and in the human heart that the wandering wavelets could propagate around electrically silent areas. The demonstration that these areas can be invaded by a wavelet originating near the sinus node and associated with a spontaneously generated action potential would prove the point. In postoperative atrial fibrillation where overt sinus node dysfunction is not apparent but where acute, reversible damage to the sinus node or its arterial supply can occur, the subsid-
iary pacemakers of the atrium could play an important role in the induction of atrial fibrillation.

Behavior of Subsidiary Pacemakers

Several studies have demonstrated that multiple subsidiary pacemakers exist in the right atrium in addition to the sinus node.17-19 The characteristics of the sinus node shown in the present study—concealed automaticity, concealed conduction, and entrance block—remain to be demonstrated for these pacemakers in order to determine their role in atrial fibrillation. The complex sinoatrial border protecting the sinus node does not exist in the subsidiary atrial pacemaker complex. If they kept some degree of autonomy, however, a link between spontaneous action potentials in these pacemakers and the site of origin of a restarting wavelet would suggest a role for atrial pacemakers in the maintenance of atrial fibrillation. A recent study by Schuessler et al20 shed some light on this subject. During spontaneous resumption of activity after acetylcholine-induced suppression of sinus node in the isolated canine right atrium, they demonstrated, with detailed mapping, that closely coupled beats originated from several distinct foci along the crista terminalis and that critically coupled beats could initiate a reentrant tachyarrhythmia. The demonstration by Kirchhof and Allessie8 that spontaneous depolarization of the sinus node indeed occurs during atrial fibrillation, in conjunction with the findings of Schuessler et al,20 suggests that two or more subsidiary pacemakers depolarizing asynchronously and protected from resetting by entrance block could generate a reentrant arrhythmia in the adjacent atrial myocardium. Because the subsidiary pacemakers are known to be more susceptible to changes in sympathetic tone, they might contribute to the generation of atrial fibrillation in acute (e.g., postoperative) situations.

Analogy Between Atrioventricular Node and Sinus Node

The irregularity of atrioventricular conduction during atrial fibrillation is also a poorly understood phenomenon. Does the atrioventricular node operate during atrial fibrillation as an irregularly conducting pathway (the gatekeeper theory), or does it irregularly discharge newly generated impulses? Meijler and Wittkampf21 recently postulated that the atrioventricular node might behave as an electrotonically modulated pacemaker. In this context, the demonstration of sinus node autonomy during atrial fibrillation in Kirchhof and Allessie’s study suggests that the atrioventricular node may provide grounds for a similar phenomenon, with the difference of having its outlet through the His bundle. There is no such specialized conduction system after the sinus node to manifest its irregular discharges, because the surrounding atrial myocardium, which is virtually always refractory, does not offer any possibility for outward conduction. Meijler and Wittkampf’s hypothesis implies that, during atrial fibrillation, atrial impulses of sufficient strength and proper timing might trigger atrioventricular pacemaker discharge in a random fashion. An atrio–atrioventricular node entrance block similar to the one demonstrated in Kirchhof and Allessie’s article at the level of the sinus node might occur during atrial fibrillation. The irregular ventricular response would then result from inhomogeneous penetration of electrotonic potentials inside the atrioventricular node modifying the interval between spontaneous diastolic depolarizations of atrioventricular nodal cells.

Mapping of Experimental Atrial Flutter–Fibrillation in the Canine Pericarditis Model

We reported that the activation sequence during unstable atrial flutter and atrial fibrillation in the canine pericarditis model may share some similarities with that of normal sinus rhythm.22 Ortiz et al23 confirmed this observation in the same model but emphasized that unipolar electrograms recorded in the sinus node region had different morphologies during atrial fibrillation and sinus rhythm, suggesting that activation of the right atrium did not originate from the sinus node during atrial fibrillation. These studies do not contradict the work discussed here, considering that extracellular recordings alone and limited mapping resolution were used by Ortiz et al23 and ourselves.22

Neuropharmacological Manipulations

Another approach to investigate the role of persisting sinus node activity during atrial fibrillation would be to modulate this activity with adrenergic and cholinergic agonists. Conversely, modulation of atrial refractoriness might modify the electrotonic influence of fibrillatory impulses on sinus node activity.

Clinical Implications

Because overdrive suppression of the sinus node does not necessarily occur during atrial fibrillation, Kirchhof and Allessie suggest that a prolonged sinus pause occurring after spontaneous termination of atrial fibrillation in the clinical setting may be indicative of sinus node dysfunction. In patients with paroxysmal atrial fibrillation who do not have evidence of sick sinus syndrome or posttachycardia sinus arrest, Coumel et al24 have reported the beneficial effect of atrial pacing. The present study suggests also that overdrive suppression is not the likely mechanism of action of this therapy, but rather that atrial pacing would maintain a high degree of exit block from all atrial pacemakers susceptible to reiniteate atrial fibrillation. The concept of concealed automaticity may also have some bearing on recently developed surgical therapies of atrial fibrillation.25,26 If the sinus node proves to be the main focus responsible for the reinitiation of atrial fibrillation, then a surgical procedure consisting of a simple isolation of the sinus node could be effective. However, the high degree of atrial isolation that is required to achieve clinical success suggests that such a concept is oversimplified and tends to support the theory that the whole atrial pacemaker complex is involved in the process.

Conclusions

In contrast to the experimental observations in which a healthy sinus node was shown to be essential for atrial fibrillation, the clinical studies suggest that atrial fibrillation is associated with a diseased sinus node. However, with further work using Kirchhof and Allessie’s powerful techniques, this paradox may prove to be as illusory as Hamlet’s dilemma.
References


KEY WORDS • sinoatrial node • fibrillation, atrial • Editorial Comments
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doi: 10.1161/01.CIR.86.1.334

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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