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Effect of Right Ventricular Pacing on Ventricular Rhythm During Atrial Fibrillation

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In 13 patients with atrial fibrillation, the effect of right ventricular pacing at various rates on spontaneous RR intervals was studied. Five hundred consecutive RR intervals were recorded and measured before and during varying right ventricular pacing rates. As anticipated, all RR intervals longer than the right ventricular pacing intervals were abolished. However, RR intervals shorter than the right ventricular pacing intervals were also eliminated.

It is difficult to explain the elimination of RR intervals shorter than the pacing intervals with the accepted concepts concerning the mechanisms governing the rate and rhythm of the ventricular response to atrial fibrillation. An alternative explanation may be that during atrial fibrillation the atrioventricular node behaves as a nonprotected pacemaker that is electrotonically modulated by the chaotic atrial electrical activity. The result is a random ventricular rhythm. With right ventricular pacing, the automatic focus is depolarized by the retrogradely concealed conducted ventricular impulses, the short RR intervals are not generated as a consequence and the rhythm becomes pacemaker dependent.

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Atrial fibrillation is defined as an irregular disorganized activity of the atria (1). In the absence of advanced or complete heart block, the ventricular response is random (2–4). This is generally thought to result from concealed conduction of the atrial impulses into the atrioventricular (AV) junction creating variable refractoriness (5–8). Accordingly, the strength, form, number, direction and sequence of the atrial impulses that reach the AV junction, and the electrophysiologic properties of the junction, determine the ventricular rhythm in atrial fibrillation (2,3,9–11). The long RR intervals during atrial fibrillation are attributed to repetitive concealed anterograde conduction (5–8,12), and the short(est) RR intervals are thought to reflect the functional refractory period of the AV junction (13–16).

Langendorf (17), Pritchett et al. (18) and several other investigators (19–23) demonstrated that ventricular extrasystoles or fixed rate right ventricular pacing in patients with atrial fibrillation lengthens the ventricular cycle after each artificially evoked or spontaneously occurring ventricular excitation. This phenomenon has been generally believed to result from the interception of anterograde conduction through lengthening of the AV refractory period by retrograde concealed conduction of the spontaneous or pacemaker-induced ventricular extrasystoles. The observations of Moore and Spear (24) and of Akhtar and coworkers (25,26) show, however, that facilitation rather than slowing of anterograde conduction results from retrograde concealed conduction.

We studied the ventricular response to atrial fibrillation in 13 patients with normal anterograde AV conduction and an implanted right ventricular pacemaker. As expected, in all patients right ventricular pacing abolished the long cycles; however, unexpectedly, the short RR intervals were also eliminated. Analysis of the data suggests that concealed retrograde conduction of the paced ventricular impulses into the AV conduction system and the consequent effects on junctional refractoriness or competition with anterogradely conducted impulses from the fibrillating atria cannot readily explain the observed phenomenon. The purpose of this paper is to report our observations and to propose a possible alternative explanation for the mechanisms involved.

Methods

Study patients (Table 1). At the time of the study all 13 patients had atrial fibrillation and had no evidence of an intrinsic AV conduction disorder. Nine women and four men

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Table 1. Relevant Clinical Data of the 13 Patients

Patient No.	Age (yr) & Sex	Symptoms	AF Since	Serum Digoxin (mg/liter)	Antiarrhythmic Agents	Associated Conditions
1	57M	Syncope	1981	1.3	Atenolol	MVP; hypertension
2	71F	DS	1982	1.1		Previous MI
3	77M	DS	1983	1.3	Disopyramide	SSS
4	57F	DS	1983	0.8		MVR
5	66M	Syncope	1976			MVR
6	74F	Syncope	1980	0.8	Verapamil	SSS;CHF
7	68F	DS	1981	1.3		MVR
8	59F	DS	1975	1.0		MVR
9	71F	DS	1961	0.4	Disopyramide	RBBB;ASD II corr
10	59M	DS	1977	1.8	Mexiletine	SSS;MVR
11	76F	DS; Syncope	1983	0.9		
12	58F	DS	1985	1.5	Flecainide	SSS;MVR;AVR
13	54F	DS	1981	0.7	Diltiazem	SSS;MVR; CHF;TR/AR

AF = atrial fibrillation; ASD II corr = atrial septal defect type II corrected; AVR and MVR = aortic and mitral valve replacement; CHF = congestive heart failure; DS = dizzy spells; F = female; M = male; MI = myocardial infarction; MVP = mitral valve prolapse; RBBB = right bundle branch block; SSS = sick sinus syndrome; TR/AR = tricuspid/aortic regurgitation.

with a mean age of 65 (54 to 77) years were included in the study. The indication for pacemaker implantation in all patients was either sick sinus syndrome or atrial fibrillation with dizzy spells or syncope, or both. Twelve patients had a multiprogrammable VVI pacemaker, type DPG 1 (Vitatron Medical BV, Dieren, The Netherlands), and one patient a DDD pacemaker, type Cosmos 283-1 (Intermedics Inc., Angleton, Texas).

Seven of the 13 patients had previous mitral valve replacement. The five patients with the sick sinus syndrome developed permanent atrial fibrillation after pacemaker implantation. The electrocardiograms (ECG) were recorded on F.M. magnetic tape (TEAC R-71). A limb lead with tall R waves was chosen to facilitate subsequent measurement of the RR intervals. All medications were withheld in five patients, for 1 week, after which the recording protocols and subsequent analyses were repeated.

Data collection. In each patient recordings were made with and without pacemaker interference. "Off" settings were obtained in the VVI mode by interval durations of 2,000 ms and subthreshold stimulation. A variety of right ventricular pacing rates were programmed using the following protocols:

1. Thirty minute rest.
2. Ten minute recordings with the pacemaker "off" until ≥500 consecutive spontaneous RR intervals were obtained.
3. Ten minute recordings with the pacemaker in VVI mode. Right ventricular pacing intervals were chosen so that approximately 30% of all QRS complexes were paced complexes.
4. Ten minute recordings with the pacemaker programmed to a shorter right ventricular pacing interval (shorter than in item 3).
5. Repetition of item 4 until at least 95% ventricular-paced QRS complexes (<5% anterogradely conducted) were obtained. This was done to establish the relation between RR intervals before pacing and the applied pacing intervals.

Data analysis. For each step of the protocol ≥500 consecutive RR intervals were measured using a specially made R wave detector circuit. Particular care was taken with the paced complexes to ensure that the detector circuit was

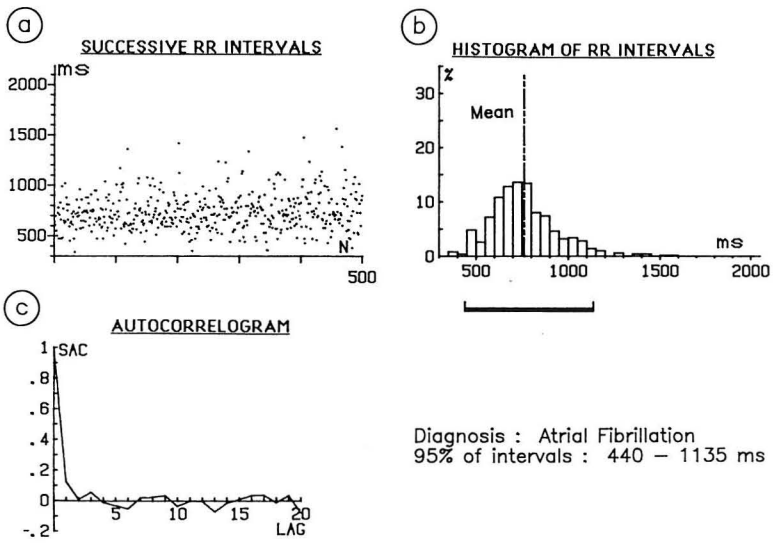

Figure 1. Patient 2. **a**, RR interval duration versus sequential interval number of 500 successive RR intervals, **b**, histogram and **c**, autocorrelogram of the same RR intervals of a representative patient with atrial fibrillation before right ventricular pacing. The ventricular rhythm is random. SAC = serial autocorrelation coefficient.

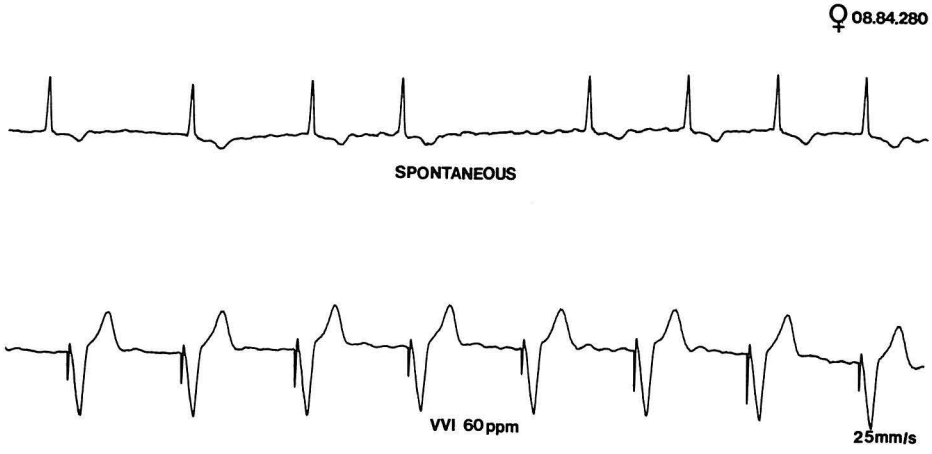

Figure 2. ECG of a patient with atrial fibrillation before (spontaneous) and during right ventricular pacing (VVI). For further explanation see text. This patient is not included in the study.

triggered by the R wave. In only three patients was it necessary to correct some of the values manually because of maltriggering due to high T waves. All RR intervals were stored in digital format in a desk computer (Hewlett-Packard HP 85).

For each protocol period, consecutive cycle lengths were plotted against sequence number in an interval plot (Fig. 1a). Histograms (Fig. 1b) and serial autocorrelograms, previously described in detail (2) (Fig. 1c), were also calculated for each study period.

Results

Without pacemaker interference. The distribution of the consecutive RR intervals showed the well known random pattern in all patients with atrial fibrillation (Fig. 1). Subthreshold stimulation did not alter this random ventricular response (27).

During ventricular pacing. All RR intervals longer than the artificial pacemaker intervals were abolished. RR intervals shorter than the pacemaker-induced intervals also disappeared (Fig. 2). To demonstrate these relations more clearly, RR interval plots at different pacing intervals from one representative patient are compressed and shown in Figure 3. The shortest RR intervals disappear first at a long pacing cycle; the longer RR intervals disappear at shorter pacing cycles until, at a right ventricular pacing interval of 700 ms, the RR interval range narrows down to zero and the ventricular rhythm becomes regular.

Paced QRS intervals and prevention of anterograde conduction. In all patients, >95% of the QRS complexes were ultimately pacemaker originated at right ventricular pacing intervals that were considerably longer than the duration of the prepacing spontaneous shortest RR intervals (Table 2, Fig. 4), with a few QRS complexes showing fusion and thus, presumably, preserved anterograde conduction. Further

Figure 3. Successive RR intervals (n = 500) in the same patient as in Figure 1 during right ventricular pacing: before pacing (n = 0 to 500); during pacing with a pacing interval of 1,000 ms (n = 500 to 1,000); with a pacing interval of 850 ms (n = 1,000 to 1,500); with a pacing interval of 700 ms (n = 1,500 to 2,000). At a pacing interval of 700 ms, the rhythm has become regular.

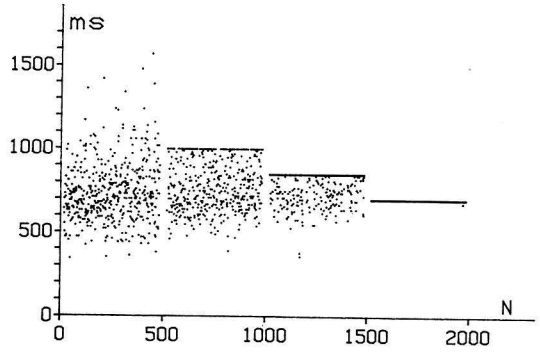

Table 2. RR Interval Before Pacing and Right Ventricular Pacing Interval (at which >95% of the spontaneous QRS complexes were eliminated) in the 13 Patients

Patient No.	Spontaneous RR Interval (ms)			95% Pacing Interval (ms)
	Shortest	Mean	Longest	
1	350	629	1,005	600
2	440	735	1,135	750
3	800	1,443	1,995	1,200
4	390	747	1,225	600
5	900	1,184	1,555	1,100
6	430	680	1,285	550
7	460	758	1,145	700
8	920	1,302	1,515	1,200
9	680	1,013	1,685	850
10	630	1,088	1,805	950
11	700	1,018	1,545	950
12	800	1,178	1,865	1,000
13	640	960	1,595	900

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shortening of the right ventricular pacing intervals resulted in preventing all anterogradely originated complexes. The right ventricular pacing cycles at which these phenomena occur vary from patient to patient and are clearly related to the ventricular intervals before pacing (Fig. 5). Sex, age, medication (such as digitalis), clinical indication for pacing or the spontaneous ventricular rate before pacing did not alter the pattern. Regularization of the ventricular rhythm was maintained for the duration of the right ventricular pacing episode.

Discussion

We have demonstrated in this study that right ventricular pacing in patients with atrial fibrillation can eliminate spontaneous RR cycles shorter than the pacing cycles. Similar observations have been reported by other investigators (6,17–23) in the presence of premature ventricular complexes, junctional or ventricular tachycardias or pacemaker-induced ventricular rhythm. To understand our data and those of others, we examined the current concepts relative to the observed phenomena and believe that they are inadequate to explain the data. The current concepts are based predominately on the presumption that anterograde conduction is interfered with by the retrogradely conducted ectopic ventricular complexes and include: prolonged refractoriness, interception of atrial impulses, slowed retrograde conduction and autonomic influences on conduction through the AV junction.

Prolonged refractoriness. Langendorf et al. (6) proposed that the compensatory pause after ventricular premature complexes in the presence of atrial fibrillation is due to prolongation of refractoriness of the AV junctional tissue consequent to retrograde penetration by the ectopic ventricular impulse. Theoretically, this may be possible in patients with a rapid ventricular response to atrial fibrillation and the proper relations between retrograde conduction times and junctional refractoriness because the postrefractory window for successful propagation would then be quite short. However, we have been unable to model anterograde block by means of Lewis diagrams utilizing a number of realistic values for AV junctional refractoriness and retrograde conduction delays in patients with longer spontaneous RR intervals.

The studies by Moore and Spear (24) and others (25,26) demonstrate that during ventricular stimulation with intact AV conduction, anterograde conduction is facilitated by retrograde conduction rather than being blocked. For instance, Lehmann et al. (26) demonstrated that in the presence of prolonged AV conduction, concealed retrograde activation of the AV junction during ventricular stimulation resulted in normalization of the anterograde conduction by "peeling back" the AV junctional refractory periods. If the principle of "peeling back refractoriness" is applicable during atrial fibrillation as well, prolonged refractoriness of the AV junction can hardly be the principal explanation for the apparent anterograde block during right ventricular pacing as observed in our studies.

Interception of atrial impulses. Pritchett et al. (18) studied the "compensatory pause" occurring after single ventricular stimuli during atrial fibrillation and suggested that this phenomenon may be due to the "interception" of the atrial impulses. Although this mechanism may be operative when ventricular extrasystoles are delivered within a few hundred milliseconds before the expected supraventricular R wave, it does not explain the nearly complete anterograde block during atrial fibrillation and the relatively long ventricular pacing intervals.

Slower retrograde than anterograde conduction. There is no reason to assume a significantly slower retrograde conduction in patients with atrial fibrillation than in patients with sinus rhythm to explain the apparent anterograde block. In fact, even patients with complete anterograde block may have normal retrograde conduction times (28,29).

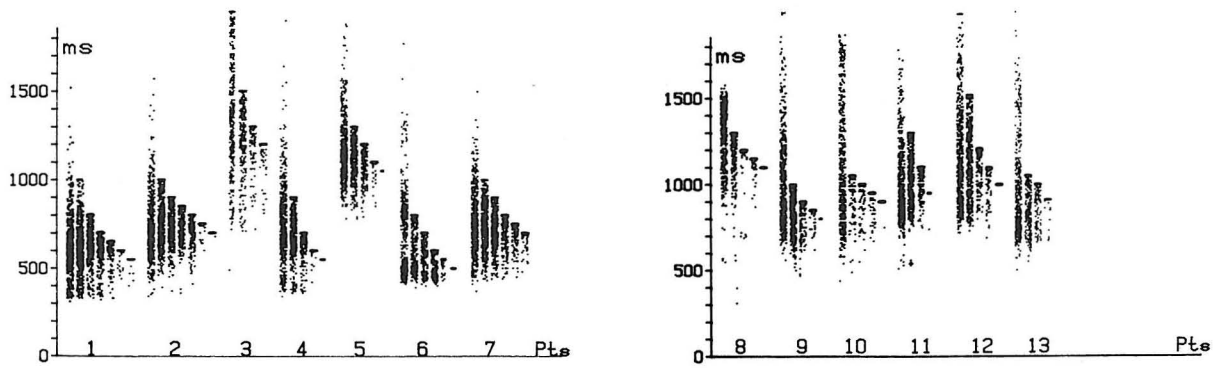

Figure 4. Compressed interval plots of episodes of 500 successive RR intervals of all 13 patients with atrial fibrillation. The nonpacing episode (first bar for each patient) is followed by three to six right ventricular pacing episodes at a progressively decreasing pacing interval. In each patient the ventricular rhythm is regularized.

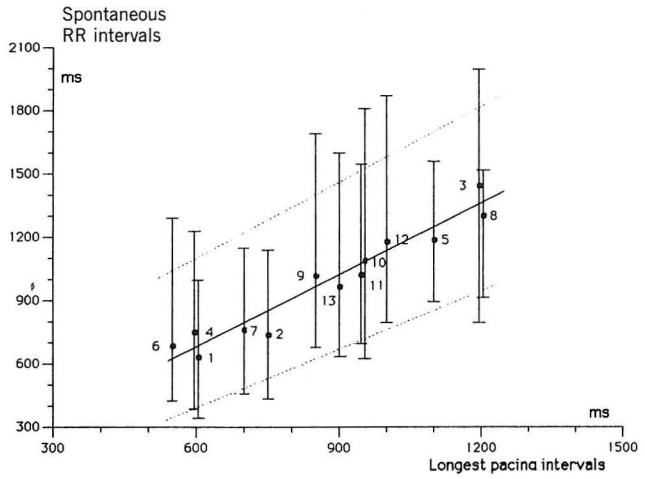

Figure 5. Relation between RR intervals during atrial fibrillation before right ventricular pacing (spontaneous) and the longest pacing cycle that eliminates RR intervals shorter than the pacing cycles. Each **vertical line** represents a patient and connects the shortest and longest RR intervals. The **dot** is the average spontaneous RR interval. The numbers correspond with the patient numbers in Tables 1 and 2.

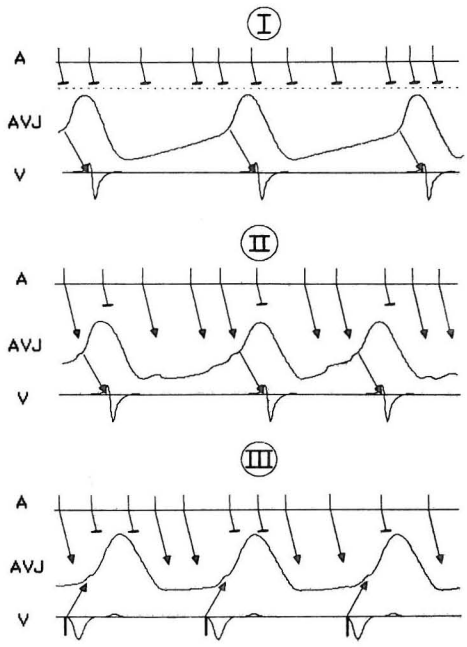

Figure 6. Schematic presentation of possible mechanisms in the atrioventricular (AV) junction during atrial fibrillation with total AV block (I), with intact AV conduction and modulation of phase 4 of the AV junctional pacemaker (II) and with potentially normal AV conduction, depolarization and resetting of the AV junctional pacemaker by concealed retrogradely conducted right ventricular impulses (III). A = assumed atrial potentials; AVJ = pacemaker action potentials in the atrioventricular junction; V = ventricular depolarizations. See text for further explanation.

Autonomic influences. Because the latency of the baroreceptor reflex effect on AV conduction is longer than the longest RR interval usually present during atrial fibrillation in the absence of AV conduction abnormality (30,31), it is unlikely that during right ventricular pacing autonomic influences could result in sufficient anterograde conduction block to eliminate all anterogradely conducted impulses. In fact, the latency of the baroreceptor effect is at least twice the length of the ventricular pacing interval at which all spontaneous complexes are abolished. Similarly, the rather short time constant or "memory" of the AV junction cannot explain the observed phenomenon (32,33).

The linear relation between the spontaneous ventricular rate just before pacing and the pacing rate (Fig. 5) at which anterograde block occurred tends to exclude autonomic influences as a contributory factor. However, this aspect of autonomic influence deserves further study.

Alternative concept. If it can be accepted that there may be some question as to the validity of the concept that the AV junction acts as a "filter" (11) for atrial fibrillatory waves and that concealed retrograde conduction of ventricular impulses may block that "filter," an alternative concept may be offered to explain our data and those of others who have reported similar phenomena.

One possible mechanism might be that the AV junction acts as an automatic focus (34,35), its pacemaker function being electrotonically modulated by disorganized atrial fibrillatory waves (36–38) in a random fashion, resulting in a random ventricular response. During right ventricular pacing, retrogradely conducted and well organized impulses could depolarize and reset this focus and thus suppress its automaticity (39). Overdrive suppression would necessitate a pacing cycle slightly shorter than the intrinsic cycle of the AV junctional pacemaker.

However, if during right ventricular pacing there were no suppression of AV junctional automaticity, and the modulating effect of the atrial fibrillatory waves remained the same, the right ventricular pacing cycles would relate to the shortest RR intervals before right ventricular pacing. Pacing cycles that eliminate all anterograde conduction will then have to be shorter than, but can be nearly as long as, the shortest spontaneous RR interval (thus without right ventricular pacing) plus the retrograde and anterograde conduction times.

Evidence from several sources supports the alternative concept we offer. Cohen et al. (40), using sophisticated computer techniques, studied the genesis of RR interval fluctuations during atrial fibrillation and could only simulate these rhythm patterns by means of a phase 4 mechanism of pacemaker cells in the AV junction. They suggested that fibrillatory impulses affect the slope of phase 4 of those cells until depolarization occurs. It is of interest that this concept is experimentally supported by the observations of Mazgalev et al. (11), demonstrating phase 4 modulation of AV junctional action potentials by atrial fibrillatory waves.

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Other supporting evidence is that neither in humans nor in animals with spontaneous atrial fibrillation has AV conduction been absolutely demonstrated. Although His bundle potentials precede the ventricular complexes and show the same irregularity as the QRS complexes in the surface ECG, for obvious reasons it has not been possible to identify any atrial fibrillatory wave that actually causes a particular His spike similar to the coupling that can be demonstrated during atrial flutter and atrial tachycardias (41).

An even more persuasive argument for the fact that the AV junction may have to act as a pacemaker can be derived from signal analysis in atrial fibrillation. Until now, it has been generally believed and accepted that an atrial excitation wavefront during atrial fibrillation could affect and actually depolarize the AV junction (node) in more or less the same fashion as does an impulse originating from the sinus node or other forms of organized atrial electrical activity. Studies of Puech et al. (42), however, and signal analysis of the atrial electrogram during atrial fibrillation (43) suggest that atrial excitation may not possess the necessary characteristics to depolarize the AV node. Atrial fibrillatory waves would then have a modulating effect on the AV junctional pacemaker.

In Figure 6 this assumed mechanism is schematically presented. Part I demonstrates the intrinsic AV junctional rhythm with a proximal block preventing atrial impulses from reaching the site of the pacemaker. Part II of Figure 6 represents electrotonic modulation of phase 4 of the AV pacemaker causing either shortening or lengthening of the inherent interval as shown in Part I. In Part III it is assumed that the AV pacemaker is being depolarized and reset by the ventricular impulses while automaticity is suppressed. The essence of our concept is that, during atrial fibrillation, the AV junction behaves as an unprotected pacemaker electrotonically modulated by randomly spaced and chaotic atrial impulses.

Conclusions

Our observations and reasoning make it plausible that during atrial fibrillation there may be AV junctional automaticity that is electrotonically modulated by the chaotic electrical activity of the atria resulting in a random ventricular response rather than a simple filtering mechanism of randomly spaced atrial impulses in the AV node (2–4). This reasoning calls to mind Mackenzie's original concept (44) that during atrial fibrillation (atrial paralysis as it was called by Mackenzie) the irregular ventricular activity is caused by a nodal rhythm.

If during atrial fibrillation the AV junction does act as a nonprotected pacemaker randomly modulated by the fibrillating atria, the following observations can be easily explained: 1) the random ventricular rhythm (2); 2) the so-called compensatory pause after ventricular extrasystoles (6,17,18); 3) RR interval durations after ventricular pacing during atrial fibrillation (17,18,23,45); and 4) the occurrence of what appears to be anterograde block during right ventricular pacing (20).

Future clinical and experimental investigations may either confirm or deny the existence of an AV junctional pacemaker electrotonically modulated by randomly spaced and chaotic atrial fibrillatory waves.

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