Editorial

Rate control in atrial fibrillation: role of atrial inputs to the AV node

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A vital property of the atrioventricular (AV) node is its ability to prevent excessive ventricular rates in the presence of high atrial rates, in particular atrial fibrillation, a common clinical arrhythmia during which atrial rates may be up to 600 beats per minute. The mechanisms involved have been studied for over a century, but remain incompletely understood (for reviews see [1,2]). Many factors play a role in determining the ventricular rate and irregularity in response to rapid atrial rate. The refractory period of the AV node is of major importance [3,4], related to the unique electrophysiological properties of the AV nodal cells, in which the refractory period [3,4] extends beyond the time of repolarisation of the action potential, in contrast to atrial cells [5,6]. The atrial rate is also important and has a complex relationship with the ventricular response [7]. With increasing atrial rate there is an initial corresponding rise in ventricular rate, with 1:1 conduction. However, with further increase in atrial rate the phenomenon of Wenckebach block occurs, with intermittent block of conduction to the ventricle, and there is subsequently an inverse relationship between atrial rate and ventricular response i.e. the ventricular rate decreases as atrial rate increases. This is due to the effects of concealed conduction, first defined by Langendorf in 1948, as “an impulse which affects the A–V junction by penetrating into it without traversing it” but is evident from its “influence . . . on the transmission time or on the formation of a subsequent impulse” [8]. Irregularity of atrial rhythm is also important. With regular atrial pacing the inverse relationship may be lost over ranges of atrial rate that allow a fixed ratio of conduction (e.g. 2:1, 3:1). With irregular atrial pacing, however, the inverse relationship between atrial and ventricular rate is observed at all high rates above that at which Wenckebach occurs [7]. The anatomical complexities of the AV nodal region are also relevant, with two functional inputs to the AV node, a posterior input via the crista terminalis and an anterior interatrial septal input. The direction of atrial wave front [9] and the relative timing of activation at the atrial inputs [10] may influence the patterns of AV nodal propagation. The potential role of the atrial inputs is further demonstrated in the paper by Garrigue et al. in this issue [11], which shows the importance of the differential bombardment of the inputs to the AV node in determining the ventricular response in a rabbit model of simulated atrial fibrillation.

In this paper [11], the inverse relationship between increasing atrial rate and ventricular response is confirmed, both with regular and irregular atrial pacing, and the complexity of this relationship is illustrated. Regular atrial pacing could result in irregularity of ventricular response, depending on intra-atrial block, AV nodal refractoriness, concealed conduction and atrial input activation. At critical regular atrial rates, the ventricular irregularity observed was very similar to that produced by random atrial pacing. High rate atrial pacing was used which was random but reproducible, and the same sequence of random intervals was delivered to multiple atrial sites. When the total events at both atrial inputs to the AV node were considered, the inverse relationship between atrial rate and ventricular response was confirmed but the correlation was weak with a large range of overlap e.g. a 300 ms His–His (HH) interval could result from 2 to 7 atrial input events. This indicated that more than overall atrial rate was influencing AV nodal output. The site of pacing was found to be important, although variable between preparations. The direction of the activation wavefront and the subsequent pattern of engagement of the AV nodal inputs affected the functional refractory period, as indicated by the shortest HH intervals. Pacing sites associated with the greatest discrepancies in events at the atrial inputs were those with the fastest ventricular rates. Thus, the shortest HH intervals

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occurred when the mean cycle length at either one of the inputs was longer, with a large difference between the two. Conversely, the longest HH intervals were associated with short cycle lengths at both inputs, with little difference between them. However, when the cycle lengths at both inputs were equal but relatively long, the corresponding HH intervals were short. Hence it was not simply high mean global atrial rate that slowed the ventricular response, nor concordance of input activity, but the combination of high rates and bombardment at both atrial inputs to the AV node.

The potential importance of the atrial inputs to the AV node has been shown previously. Janse demonstrated in 1969 that the interatrial septum was a less effective input to the rabbit AV node, with 2:1 conduction block at rates that were able to conduct 1:1 when delivered at the crista terminalis [9]. Effects of the relative activation of the inputs during simulated atrial fibrillation [12] or in response to atrial premature beats [10] in the rabbit heart have previously been reported by Mazgalev and co-workers. The patterns of AV nodal propagation were complex depending on whether there was summation with enhanced conduction or annihilation with block. The effects of high rates at both AV nodal inputs [11] may be due to increased collision and annihilation producing concealed conduction and ventricular slowing, whereas slower activity at either or both inputs may increase the likelihood of summation and conduction. However, the importance of the atrial inputs is disputed and others have not found significant effects of pacing at the atrial inputs, whether separately or together [7,13], when using perfused whole rabbit hearts rather than superfused AV nodal/atrial preparations [9–12]. In the whole heart, the AV nodal response during high atrial rates appeared to depend more on the atrial rate than on alterations in the site and timing of activity at the inputs. However, the complexity of the responses and the sensitivity of the ventricular response to changes in the timing at the inputs [11] may in part explain these discrepancies.

In humans, recent evidence about the roles of the atrial inputs to the AV node has come from experience with catheter ablation of these regions. The reentry circuit of AV nodal reentry tachycardia has a ‘slow’ pathway that has shorter refractoriness and can be ablated in the region of the anterior input [14,15]. The return limb of the circuit is a ‘fast’ pathway, with longer refractory period, which can be ablated at the region of the anterior input [14]. Whether ablation is targeting discrete nodal pathways or the atrial inputs is a subject of continuing debate. Recent anatomical evidence has identified posterior nodal extensions [16], which may correspond to the ‘slow’ pathway [17]. In atrial fibrillation, the technique of AV nodal modification aims to reduce the rate of ventricular response by ablating in the region of the posterior input [18,19]. This may be related to ablation of the slow pathway thereby increasing the refractory period of the AV node and thus reducing ventricular rate [18]. However, results with this technique have been variable [19] and there is evidence that AV node modification may be independent of complete slow pathway ablation [20] and that in half of patients there is damage to the compact AV node [21].

The study by Garrigue et al. [11] does not provide a simple explanation for the mechanism of AV nodal modification by which ablation of the posterior input would result in reduced ventricular response, since the opposite might be expected if the discrepancy between activity at the inputs were increased. The authors hypothesise that ‘ablation might change the dynamic interaction between both atrial inputs resulting in a higher level of concealed AVN conduction’. The same group has studied the role of input modification in their rabbit model of simulated atrial fibrillation [22]. Posteroanterior intra-atrial block could lead to ventricular rate slowing related to a reduction in the rate of AV nodal bombardment, without elimination of the AV nodal slow pathway (since the shortest HH intervals were unchanged). It may be that the slow and fast pathways are discrete structures within the AV node that remain intact even after ablative procedures, and that the ventricular response during AF depends on the complex interaction of propagating wavefronts at the AV nodal inputs.

Our understanding of AV nodal function, and the role of the atrial inputs, continues to increase but remains incomplete. The debate over the mechanisms underlying the responses attributable to concealed conduction may now be less, with decremental conduction [23] or modulated pacemaker activity [24] giving way to electrotonic modulation [2] as the likeliest most important factor. The effects of sub-threshold activation may be of particular relevance to the mechanism underlying the influence of the atrial inputs to the AV node, with summation or annihilation of activity. Simulated atrial fibrillation has shown that such responses may be highly complex [11], but atrial fibrillation in humans may be even more so, with multiple directions of wavefronts, and the possibility of multiple atrial inputs to the AV node [25]. However, the advent of novel techniques such as high-resolution optical recordings of electrical activity, which can demonstrate three-dimensional conduction through the AV node [26], give reason for optimism that the complexities of AV nodal propagation will be further clarified.

References


