The anatomical atrioventricular node was first described by Tawara in 1906. Although some surmised the node to be the region responsible for delay between contraction of atria and ventricles, Erlanger in 1912 localized the major portion of delay to a latency at the transition between atrial and nodal fibers. Nearly a century of research on properties of the atrioventricular (AV) node has substantiated the suggestion of Hoffman and Cranefield in 1960 that the term “atrioventricular node” should be used to describe “the entire complex of fibers functionally interposed between atrial fibers proper and His bundle fibers proper” (page 132) and not just the compact node of Tawara, since nodal-like properties have been found outside the compact node. Thus, the posterior nodal extension, the compact node, a ventricular-atrial sequence would result. The location of the AV junctional pacemaker still remained a mystery.

Little progress in locating the pacemaker site causing AV nodal rhythms occurred until 1958 when transmembrane action potentials were first recorded from AV node of rabbit and dog. Spontaneous diastolic depolarization was recorded in the mid and lower node in the rabbit heart under conditions in which AV nodal rhythm occurred in vitro, and Hoffman, Cranefield, and associates described that pacemaker activity of the node was confined mainly to the lower node (called the NH region) and the His bundle, a conclusion supported by others. However, some studies in the dog AV node in vitro described automaticity in all regions of the AV node, but the location from which they came was not documented.

One of the difficulties in locating the site of pacemaker activity in the AV junction has been technical. Mapping the spread of activity is essential. This method involves registration of intra- or extracellular electrical activity at numerous sites. Obtaining detailed maps from within the electrophysiological node has been extraordinarily difficult since the extracellular signal from nodal-type cells is very small and simultaneous transmembrane potential recordings from multiple sites are nearly impossible to obtain. Therefore, application of optical mapping with fluorescent dyes to the study of AV nodal electrophysiology has been a major advance since it enables signals to be registered from many sites simultaneously. Dr Efimov, the senior author of the study by Dobrzynski et al, was among the first to apply this methodology to the AV node. Optical mapping has provided important new information on slow and fast pathway conduction and AV nodal reentry. It is, therefore, logical that the next step was to map the origin of rhythms that occurred when the dominant sinus pacemaker was eliminated (Dobrzynski et al in this issue). The activation maps for such “escape rhythms” show that the majority originate in the posterior extension of the AV node. Previous studies had shown that this region has the propensity for automatic impulse initiation in the presence of β-adrenergic stimulation, but the region was not identified as nodal.
The uniqueness of this study is not only the use of optical mapping techniques to locate pacemakers but also the simultaneous use of specific antibodies and their immunofluorescent localization to identify this region as “AV nodal” since, as discussed above, the complete extent of the electrophysiological AV node is not easily identifiable from its structural features alone. A previous study had shown in the rabbit heart that a protein, neurofilament 160, was specifically localized in the specialized conducting system. Localization of the antibody to this protein to the region extending posteriorly from the compact AV node toward the coronary sinus, which coincides with the posterior extension of the node, verifies that the region of pacemaker activity in this study is part of the AV node. The authors have also taken advantage of studies that have described the specific gap junctional protein (connexins) profile of the compact AV node to further validate that the region of impulse origin is AV node. The pacemaker region was found to be deficient in connexin43, and had both connexin45 and connexin40, very different from adjacent atrial and ventricular myocardium, both of which are rich in connexin43. The predominance of connexin45 may contribute to the slow activation of the slow pathway and its electrical isolation from adjacent atrial myocardium despite the lack of an insulating connective tissue sheath. Finally, the localization of the protein HCN4 to the compact AV node and the posterior extension where impulse origin occurred indicates the presence of the membrane channel responsible for the pacemaker current in cells in this region.

However, even after all these years that have elapsed since the first description of AV nodal rhythms in 1903 and the significant contribution of the study by Dobrzynski et al., there are still important questions about AV nodal impulse generation that remain to be answered. Unfortunately, owing to the weak optical signals that were recorded from the posterior extension during nodal impulse origin, the details of the waveforms in the initiator cells cannot be adequately discerned in this study to identify their characteristics. The study also only looked at impulse origin when the sinus node was removed (slow escape rhythms). The AV junction is an important initiator of fast arrhythmias as well. Are the sites of origin of the fast rhythms the same? The localization of HCN4 immunofluorescence to the entire compact node and His bundle connections suggests that all regions of the node may be capable of generating automaticity under special circumstances that were not reproduced in this study (AV block, sympathetic stimulation, digitalis toxicity). Nevertheless, these innovative investigators continue to contribute important new information about a fascinating and complicated region of the heart.

References

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