The Human Atrioventricular Node: Oedipus and the Riddle of the Sphinx

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Cardiac pathologists and electrophysiologists have studied the atrioventricular (AV) node for more than 100 years, since 1906, when Tawara first described the inferior extensions of the AV node in the human heart.[1] Still, this important cardiac structure remains "a riddle wrapped up in a mystery, inside an enigma", to recall the famous Churchill quotation. Perhaps the same can be said about atrioventricular nodal re-entrant tachycardia (AVNRT): it represents the most common regular tachycardia in humans; since 1973 it has been associated with re-entry within or around the node;[2] and still, its exact circuit remains elusive.[3–5]

Apart from the seminal publication by Moe et al. on the duality of AV conduction, and that by Inoue and Becker on the inferior nodal extensions, not much human anatomical data on the detailed structure of the human AV node have been collected.[6,7] Recently, a group of eminent cardiac pathologists presented exciting new data on the structure of the human AV node and the potential implications for the AVNRT mechanism.[8] This important report provides valuable insights into cardiac pathology, and addresses several unanswered questions about the exact circuit of this fascinating arrhythmia.

We learn that considerable variation exists not only in the shape of the node, but also in the inferior nodal extensions, the potential anatomic substrate of the slow pathway. This might explain, therefore, why not all humans have AVNRT, although these structures are universal findings in the normal human heart. It seems that re-entrant tachycardia is not caused simply by the presence of inferior extensions capable of facilitating it; instead, the size and, perhaps, the orientation of these structures in the vicinity of the triangle of Koch need to satisfy particular requirements in order for the electrophysiological conditions for re-entry to occur. Unfortunately, the relevant heart specimens were not obtained from patients with clinically documented AVNRT.[8] However, the considerable variation even in the apparently normal heart suggests a clearly probabilistic phenomenon.

More importantly, we now have evidence for the anatomical substrate of the so-called 'fast pathway'. Discrete tracts that constitute insulated pathways have not been histologically demonstrated in humans, but it has been speculated that superior atrio-nodal inputs may exist, consisting of atrial myocardial cells that descend onto the node and connect via a rim of transitional cells.[9] Animal studies have demonstrated histological and electrophysiological evidence of multiple atrial inputs to the AV node.[10–13] In humans, there has been electrophysiological evidence of atrio-nodal and atrio-Hisian connections, but their role in the AVNRT circuit was not obvious.[14–16] Furthermore, histological proof of their existence was lacking. Thus, it had been proposed that the superior atrial inputs consist of loose transitional fibres, not identifiable tracts, and may play a role in fast pathway conduction in humans.[17]

It should be noted that in 1975 Anderson et al. identified an important connection of the transitional zone between atrial myocardium and compact node to the left side of the interatrial septum.[18] Anderson et al. have also recently provided solid evidence for the anatomical substrate of the fast pathway, by identifying ubiquitous connections to the compact node through the working myocardium of the atrial septum.[8] Connections were composed of ordinary myocardium. Transitional cells as forming the bridge between the septum and the body of the node were identified in only a minority of the hearts examined. The myocardial connections, and especially the last one before the node becomes insulated as the His bundle, were usually provided by the left-sided, or deep, layer of the septum, but they could also originate from the superficial, or rightward, side of the septum. These

variations may well explain the retrograde atrial conduction patterns during slow–fast AVNRT, which may display earliest activation either in the right or the left aspect of the interatrial septum.[19]

Are we close to unravelling the mysteries of the AVNRT circuit? I think that several questions remain. First, this elegant work was conducted in apparently normal human hearts. We do not know exactly what happens in patients who develop the arrhythmia. Second, the identification of this last connection was not supported by electrophysiological evidence of its significance by means of participation in the circuit. And last, but not least, conventional histology may not be sufficient to disclose the whole truth.

Staining and genotyping of connexins (Cx), i.e. the gap junctional proteins that are particularly expressed in the AV junction, have been used in order to characterise the different conduction properties of the node and its extensions. A connexin genotyping study in four human hearts has identified the right inferior extension as an area of high Cx43 expression and, consequently, faster conduction than the node and the left extension where Cx43 expression was low,[20] although the location of the presumed left inferior extension in that study was closer to the node itself rather than that of the left extension as described in pathology studies.[7,8] Nevertheless, the important message of this approach was to demonstrate the potential for different conduction characteristics of the atrial inputs to the node. Still, data are scarce, and exist only for Cx43, one of the four connexins that have been described to date.[21]

The human AV node, as well as the re-entrant tachycardia associated with it, remain enigmas. More data will be necessary for Oedipus to solve the riddle of the Sphinx. ■

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