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Neural Influence of Cardiac Electrophysiology

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Cardiac electrophysiology is influenced by a spectrum of regulatory mechanisms. Their combined feedback mechanisms influence the electrophysiological processes of every heartbeat to ensure effective response of the cardiovascular system to the demands of the organism. Of these regulatory mechanisms, those maintained at the neural level have been extensively studied but our understanding of the brain – heart interaction is still far from perfect and surely not complete. In particular, while electrophysiologic abnormalities have been reported in patients with different pathologies and abnormalities of the central nervous system,[1-4] only speculations exist on the details of the mechanisms causing these abnormalities.

Some of these central neural and cardiac abnormalities share their basis in cellular electrophysiology. A number of ion channels are important for the function of both

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the brain and the heart [5-7]. Consequently, there are known congenital channelopathies that lead to syndromes with both cardiac and central neural manifestations.

In this issue of the Journal, Hayashi et al report an impressive observational study in patients with epilepsy but without apparent heart disease.[8] Compared with a matched control group, they found more frequent fractionation or slurring of the terminal portion of the QRS complex and, somewhat unexpectedly, marginally albeit statistically significantly shorter QTc interval in the epilepsy patients. This report contributes a valid addition to the mosaic of electrophysiologic abnormalities due to pathologies of the central nervous system. At the same time, since the report by Hayashi et al is a large clinical observational survey, they can only speculate on the underlying mechanisms leading to the observed electrocardiographic differences. The clinical implications of the observed findings are even more limited. Of the two arrhythmic deaths that Hayashi et al observed during the study period, an early repolarization pattern was seen only in one case. It seems therefore seemly to discuss the investigative options that might be proposed for future clinical studies of this kind and that might perhaps advance our understanding of the core mechanistic processes.

Considering the brain-heart interaction, it is not entirely obvious whether QRS fragmentation and the shortened QT interval and other signs of shortened and early repolarization are consistent manifestation of the same process. While early repolarization might share some so-far unknown congenital channelopathy link with epilepsy [9], QRS fragmentation is more likely a reflection of structural and/or functional defects at the level of ventricular myocardium rather than at the level of ionic processes of individual myocytes. It is certainly worthwhile trying to elucidate any links between these cardiac levels and the mechanisms and consequences of the central nervous pathology.

Hayashi et al appropriately relied on the consensus definition of QRS fragmentation and slurring.[10] This consensus definition is binary in the sense of yes/present – no/absent. While such a binary classification is appropriate for clinical assessments, it is not necessarily helpful for detailed physiologic studies since it does not allow any quantification of the degree of the abnormality. Quantifying early repolarization patterns on a continuous numerical scale would be more helpful. We can hope that

interested biomedical engineering groups would soon propose an appropriate methodology so that it can be evaluated in existing ECG collections. Indeed, during the "old days" of signal-averaged electrocardiography, techniques were proposed to quantify abnormalities well within the bulk of the QRS complex.[11,12] While these techniques relied on the high signal to noise ratio due to signal averaging, it seems plausible to adapt their principles to the analysis of individual QRS complexes especially if obtaining the recordings with modern good quality equipment as used by Hayashi et al.

Having a numerical quantifier of early repolarization patterns would be also very helpful in borderline cases. For instance, we note in Figure 3A by Hayashi et al that they observed minimal QRS disturbance (likely well below the thresholds suggested in the consensus document) in some, but not all QRS complexes of lead I while detecting obvious fractionation of lead aVL. It can be debated whether the observation in aVL (which is only a simple algebraic combination of leads I and II that appear to be much less or not at all affected) signifies the same abnormality as in other, say, lateral precordial leads.

We also understand that Hayashi et al evaluated only paper printed electrocardiograms. While this did not compromise their observational study, it would be ideal in future studies if digital recordings were analyzed by objective means independent of visual personal interpretations. Keeping ECG recordings in digital formats of recorded voltage values in individual leads (rather than as only scanned print images) in hospital information systems is now becoming a norm and should be encouraged also for future research purposes. Such recordings could eventually be processed by analytical techniques that are still to come. Studies of heart rate variability have long benefitted from novel processing of historical records of digital tachograms and there are no reasons why morphological analyses of 12-lead ECGs should not follow the same model.

Once morphological ECG abnormalities are quantified on a beat-to-beat basis, the conjecture by Hayashi et al on the autonomic background of the observed abnormalities might also be addressed more directly. Spectral analyses of beat-to-beat fluctuations have long been used to differentiate between the different modulation frequencies that correspond to the feedback control of parasympathetic and

sympathetic regulation. Similarly, numerical quantification of ECG abnormalities would allow studies in patients in whom imaging results of the extent of myocardial scarring and fibrosis are available. This would, among others, not only allow elucidating of whether epileptic seizures lead to histological myocardial abnormalities but also suggest more refined risk factors of sudden unexplained death in epilepsy patients. Assessment of risk in other patient groups would likely benefit equally.

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