Commentary

Temporal Variation of Cardiovascular Diseases: An Internal Biological Rhythm Disruption May Play a Role?

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"*Whoever wishes to investigate medicine properly, should proceed thus: In the first place to consider the seasons of the year, and what effects each of them produces for they are not all alike, but differ much from themselves in regard to their changes*"… Hippocrates wrote in 400 B.C.

A growing body of evidence has accumulated showing that fall and especially winter months represent a high-risk temporal frame for occurrence of various cardiovascular diseases. Fares[1] reviewed the existing knowledge of seasonal patterns of 12 foremost cardiovascular diseases, such as deep venous thrombosis, pulmonary embolism, aortic dissection and rupture, stroke, intracerebral hemorrhage, hypertension, heart failure, angina pectoris, myocardial infarction, sudden cardiac death, ventricular arrhythmia, and atrial fibrillation. Moreover, the author discussed the potential underlying concurring factors. Classically, these rhythms have been ascribed to fluctuations in extracardiac factors, such as environmental temperature, blood lipids, coagulation factors, physical activity hormones, vitamin D, air pollution, and infections.[1]

The recent growing interest for chronobiology, branch of biomedical sciences devoted to the study of biological rhythms has opened new horizons. Biological rhythms exist at any standard of living organisms and according to their cycle length, may be divided into: (a) Circadian (period of ~24 h), (b) ultradian (period < 24 h), and (c) infradian (period > 24 h, such as, for example, months and seasons). Biological rhythms are driven by a principal circadian clock or master clock, located in the suprachiasmatic nucleus. Moreover, peripheral clocks have been identified in almost all organs of the human body, including cardiomyocytes, vascular smooth muscle cells, endothelial cells, and cardiomyocytes.[2] In addition of the above quoted seasonal variation, the onset of the leading cardiovascular events events seems to be time-of-day-dependent in humans, peaking near the sleep-to-wake transition (i.e., early morning).[3] The crucial role of cellular biological clocks is driving circadian rhythms to adapt the organism to further needs in an anticipatory manner, so providing selective advantage.[4] However, it has been recently shown that external or internal disruption (dyssinchrony) of circadian control may result in overt diseases.[2]

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The hypothalamic master clock is entrained by light, and alterations in light/dark cycle conditions can have profound effects on both central and peripheral clocks. The rate of resynchronization of cellular clocks following a shift in the light/dark cycle is tissue/organ specific, with a rapid resynchronization of the master clock, followed by peripheral clocks. The re-entrainment of clock gene oscillations within the rat heart requires some days following a reversal of the light/dark cycle,[5] so that the heart is out of synchrony with its environment for 3-7 days following such an alteration. The possibility that a molecular circadian clock intrinsic to the cardiomyocyte, may contribute to cardiovascular disease secondary to a rhythm dyssinchrony,[2] driven by either

external and internal cues, and represents an innovative way of thinking about cardiovascular diseases.

References

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