

REVIEW ARTICLE

The medical interpretation of new research data related to the function of the biological clock of the liver; starting from the basis of the chronobiologists' work

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ABSTRACT

Liver keeps a central role among the abdominal organs that are multiply connected with the central nervous system via a complicated network of nerves and molecular pathways. The biological clock of the liver is a rather complicated collection of molecular and cellular clocks and belongs to the internal biological clock system of the human organism, according to the chronobiology theories. However, recently, the existence of the CRF family neuropeptides inside the liver images the biological clock in full colour and dimensions. Changes that can now be watched, in the function of the liver clock, will update the existing series of theories and offer new prospects, interesting for clinical therapeutics. What is more interesting for medical doctors from the fields of hepatology and hepatic surgery, beyond from what basically concerns physiologists and biologists, is to determine the alterations of the biological clock of the liver in aging, in patients with cancer as well as degenerative diseases. The function of the biological clock of the liver in life threatening conditions and in the post-operative period after hepatectomy, is currently under reconsideration. The connection of the theories of the brain-liver axis and the liver biological clock is suggested in this article. This is a review of the articles published during 2008, indexed in Pubmed database, and refer to the biological clock of the liver. The only limitation was that the articles used were not interpreted by medical doctors in their primary publication form, and were not yet reviewed in published review articles.

Key words: liver, biological clock, chronobiology, liver cancer, neuropeptides, CRF, urocortin.

INTRODUCTION

The biological clock of the liver is a classical theory, and is part of the biological clock of the human organism. It expresses the internal timekeeping

mechanism coordinating a circadian rhythm in human liver and affects almost all physiologic processes in a cyclic rhythmic correspondence, like a clock. Such a vital organ like liver, which is necessary for survival, should be expected to detect everything happening in the organism and automatically trigger physiologic processes to keep us alive. Unfortunately much of liver's research was lost from the attention of medical doctors, in many publications that are exclusively written by basic researchers, as chronobiologists, in articles that the biological clock of the liver is concerned. Medical knowledge and interpretation is necessary for the evaluation of the thousands of data coming from basic research laboratories, and there is a great need of co-operation among researchers of different specialties, because otherwise, medical doctors will always have to write articles that will interpret the uninterpreted or partially interpreted results of basic researchers.

In the book titled "Signalling pathways in liver diseases", Hitochi Okamura' presents the biological clock of the liver in a special chapter based on research published from 1975 to 2003. What we, medical doctors, learn from this invaluable chapter is the following:

A. Internal clocks and circadian rhythms are characteristics of many organisms and do not occur in humans only.

Medical interpretation: Clock systems are necessary for the maintenance of life since when a protective physiologic mechanism is found in humans, mammals and lower organisms, like drosophila and zebra fish, this means that this mechanism is bound to survival. So there is a need for further research of this mechanisms characteristics in critically ill patients, in aging and in patients with cancer, where this mechanism may be altered.

B. The liver biological clock is comprised of the cell clocks of hepatocytes. The hepatocytes' clocks regulate the liver regeneration, and explain the adjustment of liver clocks to their environmental cues.

Medical interpretation: Almost all liver diseases are characterized from altered liver regeneration and do have a connection with the biological clock of the liver. Acute and chronic hepatitis, liver sepsis, post-hepatectomy condition cause disruption of the cellular liver clock functions, and any

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