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Chapter

Chronobiology and Its General Perspectives

Mohammad Rayees Dar and Abdul Roof Rather

Abstract

As a significance of the earth's rotation about its axis approximately every 24 hours, most organisms on this planet are subjected to probable variations of light and temperature. A diverse range of species, from cyanobacteria to humans, evolved internal biological clocks that allow for the anticipation of these daily variations. The field of chronobiology, the study of the rhythms in plants and animals, was limited to botanists for centuries. Only recently during the last decades, the research was expanded to include animals and later even human beings. Rhythms have been recognized and associated to the fluctuation of day and night and to the succession of the seasons. Nowadays, chronobiology has developed into a multidisciplinary field in which scientists are involved in basic research as well as in applied topics.

Keywords: chronobiology, circadian rhythm, infradian, ultradian, chronophysiology

1. Introduction

Most organisms on this planet are subject to the significance of earth's rotation around its axis, approximately every 24 hours, for probable variations of light and temperature. A vast range of species, from cyanobacteria to human beings, evolved internal biological clocks that permit for the eagerness of these daily variations. Thus, physiology and functions of an organism are primarily intertwined with this geophysical cycle. An astronomer in 1729, whose name was Jean-Jacques d'Ortousde Mairan presented early impending into this evolutionary relationship between inner physiology and the geophysical cycle, he reported that daily leaf activities in heliotrope plants persist in constant darkness [1]. In 1959, another scientist whose name was Franz Halberg give emphasis to the endogenous nature of biological clocks and coined the term circadian, that refer to daily rhythms which are truly endogenously generated, i.e., rhythms having a time period of about 24 hours that continue to vary in the absence of any environmental input [2]. The term circadian comes from the Latin *circa*, meaning "around" and *dies*, "day," meaning "approximately a day." It is regulated by circadian clocks. A recognized intrinsic property of single cells has been named as rhythm making, which was determined by an intracellular molecular oscillator based on transcriptional/post translational negative response loops. Endogenous variations are synchronized to the environment under common conditions, and is usually considered that biological clock present an adaptive advantage by guarantying that internal biochemical and physiological progression of an organism's in accumulation to actions, are optimally tailored to the neighboring atmosphere [3, 4].

The study of rhythms in animals and plants was restricted to botanists for centuries but in modern times, the search could be extended to incorporate animals and later on even human beings. Rhythms have been recognized and attached to the variability of day and night and to the progression of the seasons. Currently, this study has been developed into a multidimensional field in which scientists are concerned with fundamental examination as well as in practical areas. Chronobiology, as a field of biology study, the very cyclic phenomena in living beings and their modifications that are linked to solar- and lunar-related rhythms. Such cycles are known as biological rhythms [5]. Chronobiology has it origin from Greek, comprise of two words *chromos*, meaning "time" and *biology*, which means "study of life." Terms like *chronomics* and *chronome* which are related to it have been used in some cases to explain either the pertinent molecular mechanisms involved in the phenomena of chronobiology or to explore the most assessable aspects of chronobiology, and in particular where the assessment of cycles between the living beings is required. Everyday physiology is described by chronobiology under ordinary conditions and also after the standardization or constancy. This may be, as far as possible, comprised of environmental temperature, lighting, the availability of food and other manipulable local conditions [6]. Chronobiology is an important tool of new biology rather of a new and cohesive science. Indeed, rhythmic studies in and around us provide basis for a broader transdisciplinary science which includes all branches of medicine, chemistry, biology, physics, sociology, and in particular cosmology.

Chronobiological studies include comparative anatomy, physiology, genetics, molecular biology and behavior of organisms within biological rhythms mechanics but are not limited to these areas. Other aspects include epigenetics, development, reproduction, ecology and evolution. Chronobiology is an interdisciplinary field of study and research, which interacts with medical and other research fields such as sleep medicine, endocrinology, geriatrics (branch of medicine that focuses on health promotion, prevention and treatment of disease and disability in life), sports medicine, space medicine and photoperiodism [7–9]. The factual biology of chronobiology rests in the wide variety of procedures that are controlled by the circadian clock. Even though this biology plays an essential role at the level of the whole organism, it derives, finally, from clock-driven fluctuations in physiology, and quite often in gene expression, that come about at the level of individual cells. For many essential biological processes the differences of the timing and space in natural activity in living beings takes place, for example, in animals (cellular regeneration, eating, hibernating, sleeping, mating, migration, etc.), in plants (photosynthetic reactions, leaf movements, etc.), and in microbial organisms such as fungi and protozoa. These essential processes have even been found in bacteria, mainly in the blue-green algae. Circadian rhythm is the most dynamic rhythm in the field of chronobiology, an approximately 24-hours cycle revealed by biological processes in all the above mentioned organisms [10].

Based on routine cycles during the 24-hour day, the circadian rhythms can further be classified as: (a) diurnal, daytime activity of an organism, (b) nocturnal, nighttime activity of the organisms, and (c) crepuscular, organisms which are active at the dawn and dusk hours. The control process of circadian rhythms is defined as endogenous, and other biological cycles may be controlled by exogenous signals. While multi-tropic systems may flair rhythms driven by the circadian clock of one of the members (which may also be predisposed or reorganized by external factors) [11].

Other important cycles studied, include (a) infradian rhythms are longer than a day, for example, the reproduction or annual cycles of migration in many plants and animals or menstrual cycles in humans, (b) ultradian rhythms are shorter than

24-hours, for example, 3-hour growth hormone production cycle, 4-hour nasal cycle and/or 90-minute REM cycle, (c) tidal rhythms are roughly 12.4-hour transition from high to low and vice versa and are usually seen in marine life, (d) lunar rhythms follow the lunar month (29.5 days) and is related to the modulations of the level of tides across the lunar cycle [12], and (e) gene fluctuations have different activity cycles for acrophase (the period during which the process is more active) and bathyphase (when the process is less active). How high or low the process gets is measured by the amplitude. Some genes are more expressed during certain hours than other hours, e.g., cortisol, melatonin, etc. [13].

2. Chronobiology subdivisions

Some subdivisions of chronobiology are:

1. Chronophysiology: the fiction of "baselines" in an imaginary homeostasis is replaced by chronophysiology through dynamic parameters and competent feedbacks and feed forwards in organisms by feed sideward in a collateral hierarchy of living things and of external-internal interactions. As far as, time analysis is concerned the same stimulus has different effects at various predictable stages of a rhythm's timescale [14]. Responses in the form of data can then be quantified by using reference values, for example, parametric and nonparametric sum of blood pressure and heart rate variability over time, of people of different gender, age and ethnicity in health [3, 4].

2. Chronohygiene: it is meant through pre-habilitation, which means it detects elevation of risk by analysing a variation of rhythm characteristics before and after deviations in the average. Thus, before pathology becomes overt and symptomatic by a conventional approach relying on a normal range, it recognizes an increase in the risk of disease and covert pathology, e.g., by monitoring the circulation parameters of body such as blood pressure and heart rate of an individual in time, combining it with chronobiological data examination, it detects certain unfavorable collections of sequential variables early before hypertension occurs. Pre-habilitation deals with the enhancement of health by means of prophylactic interference with a purpose of decreasing the risk of diseases, it relies on the procedures like as the scheduling of food intake [6]. Exercise, on the other hand, must not be scheduled to induce involuntary circadian blood pressure over swing. Likewise, prayer, meditation, self-hypnosis and other procedures employed could explore any kind of influence by the time structures of the organism and its environment. Meanwhile, socio environmental-organism interactions like those in close association with the about 10-years solar activity cycle (SAC) and/or extreme magnetic storms have effects that may ultimately lead to a space weather report and to corresponding preventive research. Gene studies and genome research which has found connections between genes and diseases may be complemented by the genome mapping with various characteristics such as the circadian periods, amplitudes and phases both in the more readily assessed 24-hour synchronized state and under the conditions of desynchronization or multiple synchronization [3, 4].

3. Chronotherapy: it refers to timing treatment in order to maximize the effects at the same time minimizing the undesired effects. Seeking possibilities, the treatment is timed to marker rhythms for each of the desired effect and for each of the undesired effect. Chronotherapy utilizes a set of different

parameters for cases like cancer, including physical markers, ranging from a chemical tumor marker or a tumor temperature and/or the bone marrow's integrity hematological gauges, and to gauge cardiotoxicity, vascular parameters among others. The chronobiologically interpreted ambulatory blood pressure monitoring may provide information regarding the need for treatment of vascular variability disorder along with its timing. This information could be about the confirmation of the desired as well as undesired effects and this may avoid the status quo with misdiagnosed vascular variability disorder [3, 4].

4. Medical chronobiology: being an emerging field of medicine, its prime concern is with two important issues (a) chronopathology deals with the effect of circadian rhythms and the indices of disease; and (b) chronopharmacology deals with the study of the circadian variability of efficacy and toxicity of various treatments for a wide variety of medical conditions [15].

In chronopathology additional biological systems and disease conditions are reflected on, it has turn out to be evident that many conditions, not all, have an expected circadian variation in activity or severity. For example, blood pressure is lowest at 3:00 am; epidermal mitosis is maximal at midnight. The same seizes to be true for disease states: asthma is bad at early morning, and cerebral hemorrhage hit the highest point in the evening. Asthma at night is likely one of the most studied medical disorders in which there are perfect chronobiological stages. More is the climax of incidence of biological variables and disease conditions, more efficient treatment techniques can be developed.

In the field of chronopharmacology, not only pharmacological agents handle natural rhythms, but the sufficient range of medicines along with their timing of administration and other therapies such as irradiation may have reflective effects upon their value and toxicity. By the management of drug at the suitable time of the day, the therapeutic benefits may be maximized and the toxic side effects may be minimized. Circadian rhythms have been verified in rate of metabolism and inactivation, along with differences in blood volume and extracellular fluid volume, ensuing in variable degrees of attenuation of the drug, susceptibility of the target organs to the circulating drug.

All included with the consequence of circadian difference in reply to a precise prescriptions and treatments. There is credible indication of the suggestion of taking into consideration time of the circadian rhythm in management of drug from clinical areas such as use of anesthetics and antiepileptic drugs, cancer chemotherapy, and steroid administration. Some specific examples of circadian variation are: (a) evening medication with diltiazem is more effective than other dosage schedules, and (b) constant intravenous infusion of heparin has a maximum anticoagulant effect between 4:00 and 8:00 am, with a minimum effect at noon, indicating that the laboratory control studies should be performed at fixed times. Very small work has been carried out on the circadian considerations of drugs operated in the treatment of sleep disorders till now as narcolepsy is an exceptional example of a sleep disorder. At present data is not available to help in planning the timing of medicine to maximize therapeutic outcomes and minimize toxicity of the drug. This concept presents a demanding novel prospect for research of drug therapy in sleep disorders.

Chronomolecular biology is itself a very vast area of study, which actively discuss the mechanisms, approaches and beyond as biological clocks. Pertinent to it, chronobiology in its broader aspect are the findings that infradians—such as half-weekly, weekly, circaparasemiannual, half-yearly, para-annual, transyearly, yearly and even transtridecadal modulations of the circadian rhythm characteristics—are

now represented as having significant relations in disease and health. Infradians and some ultradians may be tied to the circadian system, as may be the development of a roundworm in the laboratory. In recent decades, chronobiology has exposed the truth of a temporal regulation system that synchronizes all body systems to environmental cycles, such as the day-night cycle. Hence, it is at present known that living organisms react proactively to environmental rhythmicity and for that reason prepare actively.

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