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plasma cell diseases, intoxication e.g. by lead, and carcinomas e.g. of the lung.

►Charcot-Marie-Tooth Disease
►Diabetes mellitus
►Thiamine (Vitamin B1) Deficiency
►Vitamin B12 Deficiency

Chronobiology

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Definition

Chronobiology is the study of biological processes with respect to time, specifically concerning the four environmental rhythms, namely tide, day, moon and season. It is not concerned with linear time-dependent processes such as aging.

Characteristics

Chronobiology refers to temporal aspects of life which have been shaped by regular, predictable and repeating structures in the environment. On earth, four geophysical time structures cycle in a predictable way: the annual cycle with its seasonally changing ►photoperiods (day length) and temperature; the lunar cycle with its changing nocturnal light levels and weak gravitational forces (that are probably irrelevant for non-tidal organisms); the daily cycle with its changing light and temperature levels; and the tidal cycle with concurrent gravitational forces leading to alternating exposure of coastal terrain to water and air. These four temporal structures have shaped biological rhythms (or biological clocks) through evolution. When shielded from their corresponding environmental cycles, all four biological rhythms are capable of oscillating with their own period which is always close to that of the environmental cycle (365.25 days, 28.5 days, 24 h and 12.5 h, respectively). Because of their moderately deviating endogenous periods, they are called circa-rhythms (circ-annual, circa-lunar, circa-dian, and circa-tidal). The environmental signals that synchronize biological clocks to the exact period of their respective environmental counterpart are called ►zeitgebers. The complex, active biological mechanism enabling this synchronization is called ►entrainment.

The biological mechanisms underlying the endogenous circannual, circa-lunar, circadian or circa-tidal clocks are the subject of intensive experimental (chronobiological) research. Most chronobiological research concerns daily and annual rhythms.

Daily Rhythms

By far the most studied biological rhythm is the ►circadian rhythm (Latin: *circa* – about – and *dies* – a day). It is an excellent example of how circa-rhythms affect living systems at all levels of biology – from gene expression, hormone secretion and physiology to complex behavior. The circadian clock represents internal time-of-day and ensures that the appropriate biological functions in cells, tissues and organs occur at the right time in relationship to other endogenous processes and to the external environment.

The signature of circadian rhythms is their persistence in constant conditions, (shielded from all zeitgebers) revealing their ►free-running period. Examples of circadian rhythms are the sleep-wake behavior in humans and other animals, leaf movement in plants, fungal spore formation, and virtually all of gene expression in cyanobacteria, to name only a few. Circadian rhythms are ubiquitous, i.e., they have been identified in organisms of all phyla, and, in each organism, they modulate all aspects of biology [1].

In spite of being built by different cellular and molecular components in different organisms (see below), circadian rhythms share basic properties. They are (i) rhythmic and (ii) self-sustained (i.e., non-dampened), (iii) with a circa 24-h period in constant conditions; (iv) circadian rhythms are both robust in their amplitude (sufficient to drive output rhythms) and precise in their period (though not exact, circadian rhythms have been shown to continue for years with deviations of only minutes [2]); (v) their period is compensated against spurious environmental changes (e.g., of temperature or nutrients); (vi) circadian rhythms can be synchronized by appropriate environmental signals (zeitgebers). This synchronization is a complex, active process called entrainment. Under natural conditions, circadian clocks are perfectly entrained to the 24-h rotation of the Earth by using the environmental changes that have shaped circadian clocks through evolution (predominantly light, but poikilotherms also use temperature) as zeitgeber signals.

Annual or Seasonal Rhythms

Similar to the day, the year also shows distinct characteristics in its temporal structure. With growing distance from the equator towards the poles, seasonal changes in day length become increasingly obvious (even at the equator, seasonal progression is apparent, for example, by different amounts of rain). Two different chronobiological strategies allow organisms to adapt their physiology and behavior to the progression of seasons: the circannual clock and photoperiodism.

Similar to the circadian clock, a circannual clock represents internal time-of-year and ensures that the appropriate biological functions in cells, tissues and organs occur at the right time in relationship to both other endogenous functions and to external time-of-year. Similar to the case of the circadian clock, alterations in light and dark are the predominant zeitgeber that entrain ►circannual rhythms – in this case, alterations in changing photoperiod. Circannual clocks can run free when photoperiod is kept constant, slightly deviating from 365.25 days (some circannual clocks only show a free-run in a specific constant photoperiod of, for example, 10 h light and 14 h darkness, LD10:14 [3]).

While the entrained circannual program ensures continuous adjustment of immunological, metabolic and behavioral processes to seasonal environmental changes, photoperiodism opens a once-a-year window, which is called the critical photoperiod, triggering a (photoperiodic) response. In most plants and animals, this response is related to reproduction. The mechanisms that detect this critical photoperiod involve the circadian system as an internal reference (abnormal photoperiodic timing is typical for ►circadian clock mutants [4]). The sensitivity to certain critical photoperiods requires a previous sensitization by, for example, short days. Hamsters provide an impressive example for a photoperiodic response, as they rapidly enlarge testes and become reproductive following exposure to days with photoperiods over 12 h [5].

Compared to the circadian program, we know far less about the anatomical structures, genes and molecular mechanisms which form the basis of both circannual rhythmicity and photoperiodism.

Molecular Chronobiological Mechanisms

Genetics has been broadly applied to describe the circadian clock mechanism, an approach pioneered in the lab of Seymour Benzer. Mutant screens have revealed a complex network of so-called ►clock genes – genes that, when mutated or deleted, change at least one of the six fundamental properties of circadian rhythms (see above). Clock genes, involved in generating the circadian rhythmicity at the cellular level, form a transcriptional-translational negative feedback loop. Activators control the production of gene transcripts leading to proteins which undergo a progressive modification (mainly phosphorylation) and eventually feed back to inhibit their own transcription. In the cyanobacterial system, circadian oscillations have been definitively shown to depend on rhythmic phosphorylation and dephosphorylation of a set of proteins, a process which even persists in a test tube [6]. It is not clear how this may relate to eukaryotic molecular clocks.

Clock genes have been identified in model genetic organisms from all phyla. Interestingly, animals, plants, fungi and bacteria all feature distinct gene sets, which nonetheless function similarly on the molecular level. This suggests that these are species-specific adaptations to their environment, rather than evidence of a primordial, common clock.

Human Chronobiology

One of the easiest ways to understand chronobiology is to recall common human daily behaviors. For example, the human ►sleep-wake cycle occurs once per 24 h when entrained but runs free (with a circa 24-h period) when shielded from zeitgebers. There is, however, a tremendous difference in *when* sleep occurs in different individuals. The temporal differences in these so-called chronotypes are not restricted to sleep, but extend to other clock-controlled processes, such as melatonin or cortisol production. Within a population, the frequencies of different chronotypes show an almost normal distribution, reflecting that chronotype is a multi-genic, highly complex trait. Chronotypes result from individual differences in entrainment characteristics due to a variety of reasons: within the population there are polymorphisms or mutations in clock genes [7]; the late-to-bed, late-to-wake teenager is well known to all of us, and it reflects a systematic effect of development on the circadian clock [8]. From childhood to adolescence, the clock entrains progressively later, a trend that reverses – at the population level – at around the age of 20; there are gender differences in chronotype also, at least until the age of menopause, with females typically being earlier chronotypes than males; exposure to strong or weak zeitgebers also determines when the clock is entrained within the daily cycle. People who work outside in broad daylight are generally earlier chronotypes than office workers [8]. Thus, genes, environment, age and gender all contribute to chronotype.

The implications of chronotype are manifold. If chronotype, for example, is not incorporated into medical practice, results of tests or the efficacy of treatments may differ merely due to the patient's chronotype. Chronotype is also a quality of life issue. The more discrepancy between internal and external time (e.g., between an individual's circadian timing and his or her work hours), the more sleep debt accumulates during the work-week, culminating in a chronic "social jetlag." The larger this social jetlag, the more likely an individual is to be a smoker, indicating that a chronic jetlag acts as a stressor [8].

Chronobiology Concerns all of Biology

Because chronobiology has an impact on broad aspects of an organism's biology, it represents a scientific specialty similar in scope to development or reproduction. Circadian rhythms are a fundamental property of all organisms (with few exceptions). The concept of selective advantage due to increased fitness is inherent to evolutionary theory. The adaptive advantage of biological clocks lies in the benefit of being able to anticipate environmental changes. The activity of animals is frequently restricted to certain times of day, and straying outside of these domains can increase the risk of predation, for instance [9]. Sessile organisms such as plants and fungi also benefit from prediction of temperature, nutrient, or humidity changes. The fitness concept was recently substantiated in vitro using cyanobacteria, showing that a circadian oscillation with a period similar to the environmental one is more successful [10]. Similar adaptive advantages hold for all circa clocks, whereby organisms prepare for seasons, tides or nocturnal light levels.

References

1. Roenneberg T, Merrow M (2005) Circadian clocks – the fall and rise of physiology. Nat Rev Mol Cell Biol 6:965–971
2. Richter CP (1968) Inherent 24-hour and lunar clocks of a primate – the squirrel monkey. Comp Behav Biol 1:305–332
3. Gwinner E (1986) Circannual rhythms. In:Farner DS (ed) Zoophysiology, vol. 18. Springer Verlag, Berlin, p 154
4. Nunes MV, Saunders DS (1999) Photoperiodic time measurement in insects: a review of clock models. J Biol Rhythms 14(2):84–104
5. Elliott JA, Bartness TJ, Goldman BD (1989) Effects of melatonin infusion duration and frequency of gonad, lipid, and body mass in pinealectomized male siberian hamsters. J Biol Rhythms 4:439–455
6. Nakajima M, Imai K, Ito H, Nishiwaki T, Murayama Y, Iwasaki H, Oyama T, Kondo T (2005) Reconstitution of circadian oscillation of cyanobacterial KaiC phosphorylation in vitro. Science 308:414–415
7. Toh KL, Jones CR, He Y, Eide EJ, Hinz WA, Virshup DM, Ptacek LJ, Fu YH (2001) An hPer2 phosphorylation site mutation in familial advanced sleep phase syndrome. Science 291(5506):1040–1043
8. Roenneberg T, Kuehnle T, Juda M, Kantermann T, Allebrandt K, Gordijn M, Merrow M (2007) Epidemiology of the human circadian clock. Sleep Med Rev 11 (6):429–438
9. DeCoursey PJ, Krulas JR (1998) Behavior of SCN-lesioned chipmunks in natural habitat: a pilot study. J Biol Rhythms 13:229–244
10. Yan OY, Andersson CR, Kondo T, Golden SS, Johnson CH, Ishiura M (1998) Resonating circadian clocks enhance fitness in cyanobacteria. PNAS 95(15): 8660–8664

Chronobiotics

Definition

A biological compound that can alter parameters (phase, period or amplitude) of circadian oscillators, or their responsivity to other inputs, thereby changing the phase relationship between circadian rhythms and local time, or the rate at which circadian rhythms are resynchronized following a shift of local time (e.g., transmeridian jet travel).

►Circadian Rhythm
►Human Circadian Timing System

Ciliar Body

Synonyms

Corpus ciliare; Ciliary body

Definition

Ciliary body of the eye. Contraction of the circular ciliary muscle results in relaxation of the lens ligament (zonal fibers), so that the lens can follow its inner elasticity and thicken. This increases its refractive power, needed for focusing on close objects. If conversely, the ciliarymuscle is relaxed, the eye is distant accommodated.

►Eye

Ciliary Ganglion

Synonyms

►Ganglion ciliare; ►Ciliary ganglion

Definition

Parasympathetic ganglion, some 2 cm behind the eyeball. The postganglionic fibers innervate, inter alia, two intraocular muscles:

- Ciliarymuscle (accommodation)
- Sphincter of pupil muscle (adaptation)

►Nerves

Ciliary Neurotrophic Factor (CNTF)

Definition

►Neurotrophic Factors