Hearing Research 347 (2017) 47–55

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Review Article

Circadian regulation of auditory function

Vasiliki Basinou [a], Jung-sub Park [a, b], Christopher R. Cederroth [a], Barbara Canlon [a, *]

[a] Department of Physiology and Pharmacology, Laboratory of Experimental Audiology, Karolinska Institutet, 171 77 Stockholm, Sweden
[b] Department of Otolaryngology, Ajou University School of Medicine, 164, Worldcup-ro, Yeongtong-gu, Suwon, 16499, South Korea

ARTICLE INFO

Article history:
Received 30 March 2016
Accepted 25 August 2016
Available online 23 September 2016

ABSTRACT

The circadian system integrates environmental cues to regulate physiological functions in a temporal fashion. The suprachiasmatic nucleus, located in the hypothalamus, is the master clock that synchronizes central and peripheral organ clocks to orchestrate physiological functions. Recently, molecular clock machinery has been identified in the cochlea unravelling the potential involvement in the circadian regulation of auditory functions. Here, we present background information on the circadian system and review the recent findings that introduce circadian rhythms to the auditory field. Understanding the mechanisms by which circadian rhythms regulate auditory function will provide fundamental knowledge on the signalling networks that control vulnerability and resilience to auditory insults.

© 2016 Elsevier B.V. All rights reserved.

Contents

1. Introduction: circadian clocks

Biological clocks evolved under the influence of rhythmic environmental cues, in order to provide an internal representation of time and allow organisms to exploit temporal niches (light/dark, cold/warm, wet/dry, etc.) with all the subsequent consequences. The environmental factors that influence the function of these clocks are called zeitgebers (German for “time-giver”). Among these factors are the light-dark cycle, temperature, feeding and social interactions. The light-dark cycle is considered a major zeitgeber and probably the most significant in evolution because it

* Corresponding author. Department of Physiology and Pharmacology, Laboratory of Experimental Audiology, Karolinska Institutet, Von Eulers väg 8, 171 77 Stockholm, Sweden.
E-mail address: Barbara.Canlon@ki.se (B. Canlon).

http://dx.doi.org/10.1016/j.heares.2016.08.018
0378-5955/© 2016 Elsevier B.V. All rights reserved.

Abbreviations

ABR	Auditory brainstem response
ASR	Acoustic startle response
BDNF	Brain derived neurotrophic factor
CCG	Clock controlled genes
Clock	Circadian locomotor output cycle kaput
CRH	corticotropin releasing hormone
Cry	Cryptochrome
CT	Circadian time
DHF	7, 8 dihydroxyflavone
NIHL	Noise-induced hearing loss
Per	Period
PTS	Permanent threshold shift
ROR	Retinoid-related orphan receptors
RORE	ROR response element
SCN	Suprachiasmatic nucleus
SPL	Sound pressure level
TTS	Temporal threshold shift
ZT	Zeitgeber time

is an explicit predictor of the daily cycle, as well as the seasonal cycle (length of day fluctuations). However, the biological clock being an endogenous timing system is capable of generating biological rhythms even in the absence of environmental cues. This ability ensures that the physiological functions of an organism will continue even in temporal isolation.

When zeitgebers are not present, the biological clock sustains a rhythm of about 24 h which is called circadian rhythm (from the Latin words “circa” and “diem”, meaning approximately one day), with a corresponding circadian time (CT). In order to produce an accurate 24 h period, the clock adjusts its rhythm on a daily basis. This adjustment is mediated mainly through entrainment to the daily light-dark cycle, meaning synchronization of the circadian time to the external time (Box 1). Consequently, the clock time relies on the rhythm of the zeitgeber and is referred as a zeitgeber time (ZT).

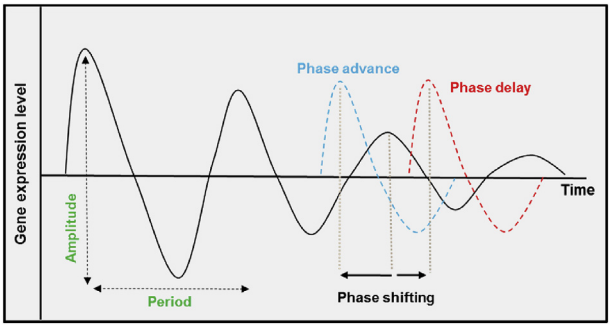
1.1. The molecular clock: how clocks tell time

Circadian rhythms are innate and are governed by genetically programmed mechanisms. The discovery of genes encoding circadian behavioral rhythms in *Drosophila melanogaster* (Konopka and Benzer, 1971) initiated an intense scientific effort to identify genes that regulate the clock machinery, known as clock genes, and led to the hypothesis that rhythms are generated at the molecular level. An autoregulatory mechanism was proposed where clock gene mRNA is translated into protein, which then translocates into the nucleus and suppresses its own transcription (Hardin et al., 1990). Reduced levels of mRNA will then lead to reduced protein and eventually increased transcription, thereby restarting the cycle. Although simplified, this model represents the basic principle of the molecular clock.

In mammals, the generation of circadian rhythms is a cellular process that involves interlocked autoregulatory transcriptional/translational feedback loops (Albrecht, 2002; Golombek and Rosenstein, 2010; Kondratov et al., 2007). At the core loop, the positive elements CLOCK and BMAL1 form heterodimers and induce the transcription of the negative-feedback elements *Period* (*Per1* and *Per2*) and *Cryptochrome* (*Cry1* and *Cry2*), by binding to E-box elements at the promoter and enhancer regions of these genes.

Box 1
Terms of Circadian Biology

Circadian rhythms: Cycles of physiology and behavior with a period length of approximately 24 h that are generated by an endogenous oscillator (as determined by the ability to free-run in constant conditions). They are characterized by their amplitude, phase and period (Graph 1).
Free-running: The ability to sustain rhythms in the absence of environmental cues. In experimental settings, free-running rhythms can be achieved by keeping an organism in constant conditions, such as constant darkness (DD) or constant light (LL) conditions.
Oscillator: An entity capable of generating rhythms (e.g a circadian oscillator generates circadian rhythms).
Peripheral Clocks: Non-SCN oscillators located in the brain or in peripheral tissues (e.g hippocampus, liver, adrenal gland, and cochlea)
Entrainment: Synchronization of a self-sustaining oscillator to a rhythmic signal. The SCN is entrained by light signals received by the retina (photoentrainment). The peripheral clocks are entrained by SCN-driven signals and some can be also entrained by external cues, including feeding and temperature. Under steady entrainment, the period of the self-sustaining oscillation conforms to that of the zeitgeber
Amplitude: The difference between the peak and the trough of the oscillation and the mean value of a rhythm (Graph 1)
Phase shift: A displacement of an oscillation along the time axis that results in an advanced or delayed rhythm (Graph 1)
Period: The time required for one complete cycle. It can be measured as the distance in time between two consecutive peaks or troughs (Graph 1).



Graph 1. Representation of a tissue gene expression rhythm. Note that the rhythm amplitude dampens over time, suggesting a loss of synchrony between individual cell oscillators (desynchrony). A resetting stimulus can synchronize the cells again and generate a new phase.

Their protein products, CRY and PER, form heterodimers that translocate to the nucleus where they inhibit the CLOCK/BMAL1 action by removing this complex from the E-box motifs of *Cry* and *Per*, and thus repress their own transcription (Fig. 1A). In an interlocking loop, the CLOCK/BMAL1 complex also activates the ROR (RORα, RORβ and RORγ) and REV-ERB (REV-ERBα and REV-ERBβ) proteins. These proteins bind to ROR response elements (RORE) within the *Bmal1* and *Clock* genes and activate or repress their expression respectively (Fig. 1B). The tight coordination of the positive and negative elements of transcription, as well as post-transcriptional and post-translational modifications, impose time delays that produce an accurate and robust cellular oscillator with a 24 h periodicity (Reppert and Weaver, 2002). Cell autonomous clocks are ubiquitously expressed throughout the mammalian body (Yoo et al., 2004). The rhythm generated by these individual oscillators at the cellular level results in a coherent rhythmic output of

Download English Version:

https://daneshyari.com/en/article/5739413

Download Persian Version:

https://daneshyari.com/article/5739413

Daneshyari.com