

Circadian Rhythm Control

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The retina might be the response to circadian rhythm disturbances.

The daily alternation of light and dark is undoubtedly the most reliable time signal, and it is therefore not surprising that most organisms have developed precise synchronization mechanisms that allow them to adapt and anticipate to changes day- night establishing a physiological rhythms that cover a 24-hour period: the daily rhythms are an universal feature of the living systems [1-2]. Dysfunction of circadian rhythms due to environmental factors (shift work, jet-lag) or genetic mutations contribute to the development of many diseases, such as sleep disorders, poor mood and irritability, feelings of fatigue or exhaustion, early aging, frequent infections, bipolar disorder, depression and schizophrenia, as well as the risk of cancer, obesity, high cholesterol levels, and cardiovascular disorders [3-5]. In mammals, including humans, the master circadian pacemaker is located in the suprachiasmatic nuclei located in the anterior hypothalamus (SCNH) [6]. SCNH controls a variety of biological processes, coordinating daily physiological and behavioral cycles such as sleep-wake and food intake and physiological constants such as body temperature, alertness, heart rate or hormones secretion. Many body organs and tissues can generate circadian rhythms independently of the SCNH, are called peripheral circadian oscillators [1,7,8], and among these peripheral circadian oscillators, the retina represents a special case, since it appears to be quite independent of the SCNH and may influence the circadian rhythms generated by the SCNH [7,8]. Ambient light is detected by three types of ocular photoreceptors, rods and cones in the external retina, and retinal photosensitive ganglion cells (pRGCs) that use the melanopsin photopigment. pRGCs send direct projections to many regions of the brain to regulate non-imaging responses to light, transmitting light information directly to the SCNH where the neurotransmitter glutamate is released [9-10]. Therefore, the retina plays an essential role in the circadian organization, since it is the only source of light stimulation to the SCNH. It has been proposed that the retina may also contribute to global circadian organization, since changes in circadian rhythm in locomotor activity have been observed after photoreceptor degeneration or bilateral enucleation [11-13]. Previous studies have established a link between the peptide hormone vasopressin and altered circadian rhythm [14,15]. Recently, a sub-population of RGCs that directly communicate with the SCNH has been discovered in rats using the neuropeptide vasopressin as mediator (VP-RGCs) [16]. These cells are projected directly into the SCNH, and the expression of Fos transcription factor (involved in the regulation of vasopressin synthesis) was significantly higher in VP-RGCs after light stimulation. Vasopressin released by light stimulation increases the response of SCNH neurons to light, further supporting the action of vasopressin on circadian rhythms [14-16]. Jet-lag occurs when you travel across multiple time zones: symptoms derive from the temporal misalignment between body's internal clock and local time (external solar time): vasopressin pathway could be a pharmacological target for jet-lag treatment and shift work. In our minds opens the exciting possibility of being able to re-establish our biological clock by modifying vasopressin signal with eye drops.

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