



UNIT-I

Manipulation and disruption of biorhythms in homeostatic and natural ecosystem

Chemical Bioregulation in Physiological functions

Course No. – VPY- 609

Credit Hrs. – 3+0=3

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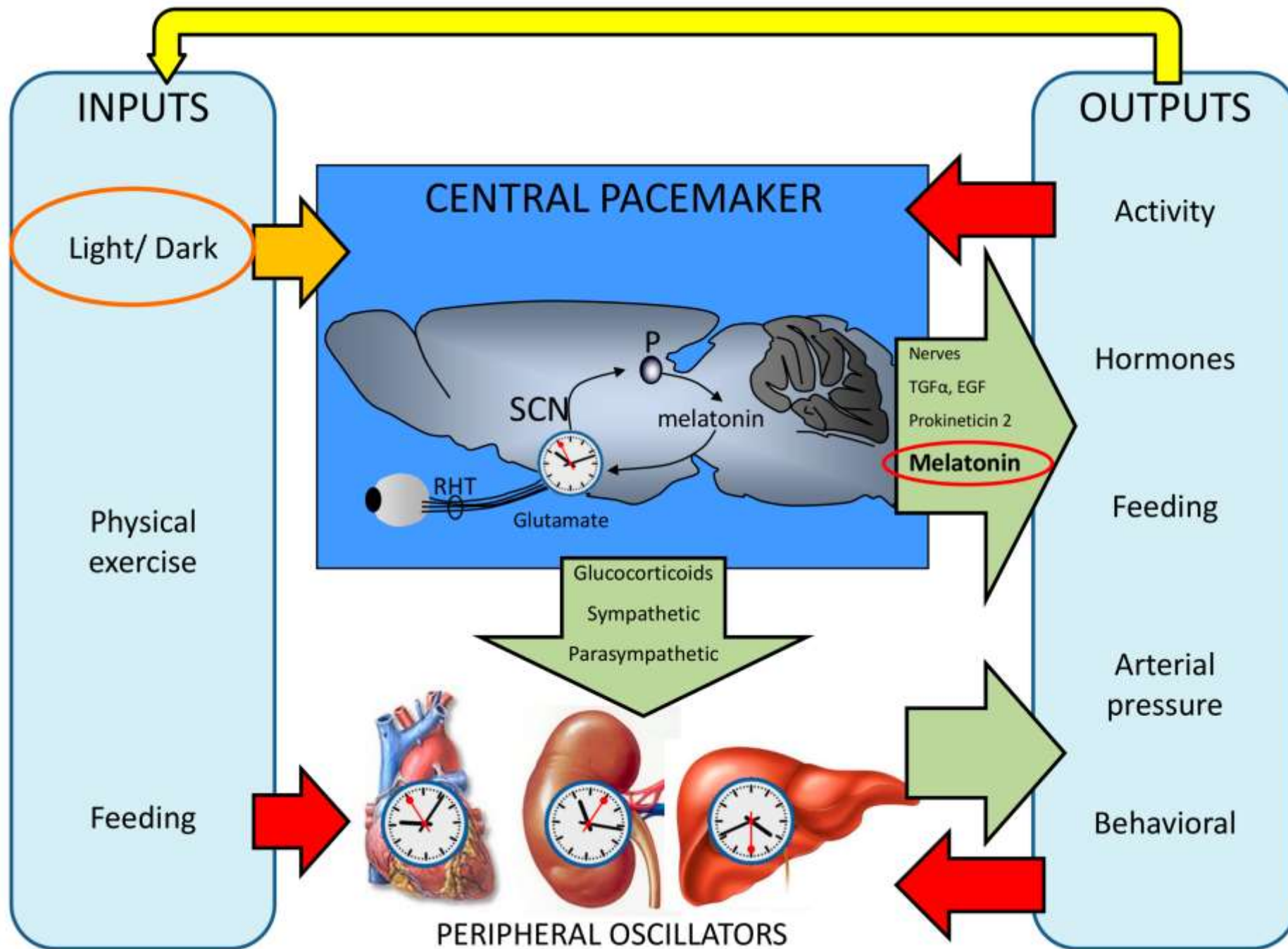
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Overview

- The physiological activity is organized around the daily cycle of activity and sleep. During the active phase, energy expenditure is high and food and water are consumed, organs need to be prepared for the intake, processing and uptake of nutrients.
- During sleep, energy expenditure and digestive processes decrease and cellular repair takes place. The ANS and hormones (melatonin and corticosterone) are used to transmit signals from hypothalamic and brain stem nuclei to the body in order to prepare it for the daily changes in activity, food intake and rest. Hypothalamic structures receive information from the suprachiasmatic nucleus (SCN), the biological clock; this nucleus transmits 24 h time information synchronized by the light dark cycle. It is known that neurons of the SCN, even *in vitro*, maintain a 24 h rhythm of electrical activity and neurotransmitter release. Via the secretion of its neurotransmitters, the SCN transmits rhythmicity to hypothalamic structures to the brain and to the rest of the body. An example is the secretion of corticotrophin releasing hormone and thus the secretion of ACTH, which is modulated by the SCN via vasopressin projections to the dorsomedial hypothalamus and subsequently to the paraventricular nucleus. The ANS, the SCN influences peripheral organs such as liver, adrenal gland, heart and even fat tissue for daily adjustment such that the physiology of the body responds optimally to support activity or sleep and to keep it coupled to the external cycles.



➤ Animal models provide experimental and controlled conditions for further understanding the mechanisms of circadian disruption. A strategy used frequently to induce circadian disturbance is exposing rodents to constant shifts in the onset and offset of light. Shifts of 6–8 hours are scheduled once to several times per week and for as long as 3 to 6 months. Shifting the LD cycle resembles the condition of transmeridian traveling and is accepted as a good model for frequent exposure to jet lag. Phase shifts, especially when the LD cycle is advanced, imply a gradual resetting of physiological and behavioral rhythms. The speed of re-entrainment after a 6 h phase advance differs among the functional systems. While general activity and the skeletal muscle achieve complete adjustment after 6–10 days core temperature, lungs and the liver adjust faster, leading to a loss of synchrony. Depending on the frequency of the shifts and the duration of this treatment, some groups have reported disruption of behavioral and physiological rhythms, while others do not observe significant effects. In a long term, frequent LD shifts alter cognitive functions and neurogenesis in the hippocampus, they result in a weak immune response and accelerated tumor growth in the liver after exposition to a cancer promoter.

➤ Other models of circadian disruption expose rodents to short days of 20–22 h, which are incongruous with the normal endogenous 24 h period. This short photoperiod challenges the capacity of circadian system to adjust and to produce a circadian desynchrony. Under such conditions, rodents exhibit two components of activity, one free-running under a long period and the second component entrained to the 22 h LD cycle. In the SCN, this protocol produces a disruption of neuronal activity, where the dorsal SCN reflects the free-running rhythm while the ventral SCN reflects the LD synchronized rhythm. Rodents housed under these conditions developed dissociation of the sleep-wake cycles from the core temperature as well as changes in metabolic hormones. In the brain, circadian-disrupted mice exhibit decrease of dendritic length and decreased complexity of neuronal dendritic trees in the prelimbic prefrontal cortex, associated with reduced cognitive flexibility and altered emotional responses.