

Circadian Rhythms

by Richard H. Hall, 1998

Suprachiasmatic Nucleus

Circadian rhythm is the term used to describe the physiological and behavioral twenty-four hour cycle that most organisms experience. This, of course, includes the sleep/wake cycle, but includes many other factors, which vary as well (e.g., hormonal levels, eating, and drinking). In fact, in some ways our lives are simply rhythms within rhythms. As we've already discussed there is a regular ninety minute cycle that characterizes the sleep of most humans, and, interestingly, there also appears to be a similar approximately ninety minute cycle that we go through during waking called the **basic rest activity cycle**. In terms of circadian rhythms, research with humans and other animals indicates that our bodies are tuned internally to cycle in this manner. However, it is also true that external cues can dramatically influence this cycle. The most obvious example of such external cues is light, which, for most of us, serves to "reset" this cycle each morning.

The brain area that appears to play a central role in circadian rhythms is the **suprachiasmatic nucleus (SCN)** in the hypothalamus. The most direct evidence that supports this comes from animal studies in which the lesioning of this small nucleus completely disrupts the normal sleep wake cycle. Further, these lesions do not decrease the amount of sleep that an animal experiences, just the cycle. Lab animals with such lesions sleep at random times for varying lengths of time. The fact that light has been found to increase SCN activity is further evidence that this nucleus plays an important role in circadian rhythms.

Figure 1 illustrates important inputs to the SCN. Not surprisingly, there is a direct pathway between the SCN and the **retina** in the eye. There is also a pathway between the **lateral geniculate nucleus (LGN)** in the thalamus and the SCN. The lateral geniculate nucleus is an important point in the main visual pathway that goes from the eyes to the primary visual cortex in the occipital lobe. Somewhat surprisingly, the pathway that connects the LGN and SCN appears to play a particularly important role in sensitivity to non-light circadian cues such as loud noises.

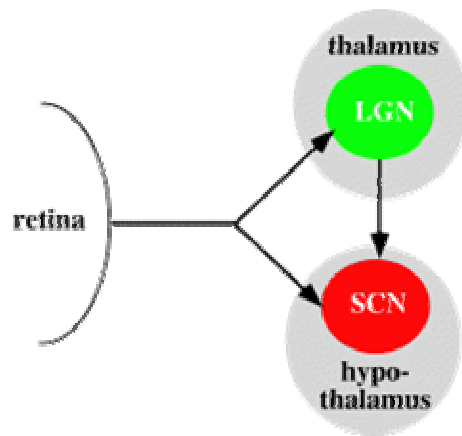


Figure 1. Important Inputs to SCN

Cellular Clocks

Given that the SCN plays such an important role in circadian rhythms, we would suspect that it contains some sort of mechanism for recording the passage of time. Further, we might expect that such a mechanism would be the function of some sort of intricate neural circuitry. Although there is a lot of evidence that such a mechanism exists, the research indicates that this mechanism is actually contained within individual neurons within the SCN. For example, glucose metabolism of cells in the SCN in prenatal rats exhibits a circadian cycle, despite the fact that these neurons have very few neural connections. In addition, individual cells from the SCN that have been kept alive in a culture medium, still display electrical activity indicative of circadian rhythms.

One possible explanation for the working of these cellular clocks is illustrated by fruit fly neurons. These neurons contain two proteins, PER and TIM. The synthesis of these proteins is initiated by genes which direct mRNA to leave the cell nucleus and, in turn, direct the synthesis of PER and TIM proteins by ribosomes. The reason that this process is offered as an example of a mechanism sensitive to circadian rhythms is that the protein synthesis varies with the light and dark cycle. When there is little or no light the PER and TIM proteins combine and, in a feedback loop, they suppress the activities of the PER and TIM genes, thus, their buildup acts to suppress their own production. However, during periods of light, the TIM protein is immediately destroyed upon synthesis, so it cannot combine with PER and disrupt protein synthesis. When it becomes dark again, the proteins begin combining again, and the process starts over. (This process is illustrated in Figure 2). Such a mechanism could, presumably, serve as a dark/light signal as represented by the synthesis, or lack of synthesis, of these proteins.

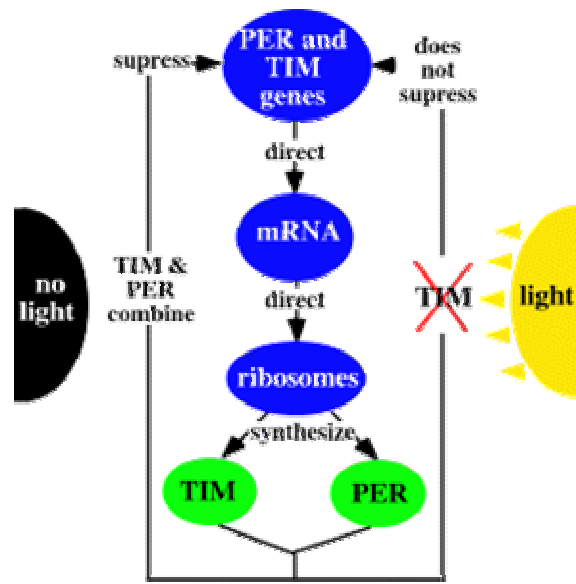


Figure 2. Effect of Light on PER and TIM