

Suprachiasmatic Nucleus (SCN)

The Suprachiasmatic Nucleus is a small pine cone shaped, about a cm in length, region in the brain, situated above the optic chiasm (hence its name) in the brain's midline, inside the hypothalamus in its anterior. This region of the brain uses around 20,000 neurons, and several hormonal functions to govern a 24 hour cycle in the human body. Thus it controls what are called circadian rhythms and acts as the primary clock of the human body while providing a vague sense of what time of the day it is cognitively. Humans have a natural periodic rhythm for many biological processes. Indeed such behaviour is observed in most organisms but the genes involved in these biological clocks seem to have developed independently for each kingdom. In the animal kingdom these genes are related across a wide spectrum of animals. In mammals the Suprachiasmatic Nucleus (or SCN) is the control centre for all the biological clocks. Some of the periodic activities of mammals controlled by the SCN are length and time of sleep, hormone levels, activity, body temperature, digestive functions etc. Thus, damage to the SCN leads to damage to the periodicity of these activities.

What are Circadian Rhythms?

Circadian Rhythms are biological processes that display the biological period of about 24 hours. These rhythms are triggered by outside stimuli, for example in humans like the sunrise sunset cycle triggering photoreceptors in the eyes. Circadian Rhythms are found in almost all organisms including plants, fungi, and bacteria aside from animals and in each a different biological system controls it. In mammals these are controlled by the SCN.

The SCN works in conjunction with other tissue based timekeepers in the human body, these are subordinate to the SCN and their oscillations are synchronized with those of the SCN. As mentioned the SCN receives its inputs from the human eyes, in particular, from the photosensitive ganglion cells in the retina. These ganglion cells contain a chemical called Melanopsin which is sensitive to the blue region of visual light frequency. The SCN is connected to the retina having the ganglion cells by a tract called the retinohypothalamic tract.

The SCN has two parts, the dorsal and the ventral. The dorsal has a 24 hour period regardless of light input to the eyes, thus it will continue to work even in constant darkness. The ventral gets the input from the eyes and thus distinguishes night from day. Thus by giving eyes light during the night regularly and depriving during day time the ventral can be trained to reverse its cycle. In chronobiology this period matching training exercise of the ventral part of the SCN is called entrainment. After entrainment the cycle persists, and to change it again the inputs need to be reversed for significant time. Improper entrainment can cause health problems.

Research on the SCN is done through experiments on mice and reptiles like lizards. These experiments have found the way SCN controls the temperature cycles and other behavioural patterns. In the animal kingdom vertebrates can be classified into two, endothermic vertebrates and ectothermic vertebrates. Ectothermic vertebrates like frogs and lizards are very sensitive to external heat sources which severely change their body temperature, whereas endothermic vertebrates like humans have a relatively stable internal temperature which is primarily determined by internal controls. This also has effects on the SCN. In endotherms like mice or humans external heat sources may reset some peripheral oscillators in the body but never the main SCN. But in ectothermic vertebrates like frogs and lizards the SCN itself will get reset by changes in external temperatures.

Control of the SCN and Gene Expression Cycles

One of the factors that control the circadian rhythms inside the components of the SCN is a process of transcription and repression of proteins binded to specific DNA sequences by various transcription factors characterized by a basic helix-loop-helix-PAS. This protein family is encoded by a gene called CLK or CLOCK (Circadian Locomotor Output Cycles Kaput). In the circadian pacemaker the CLK gene acts as an activator of elements involved in downstream circadian rhythms. Many gene expression cycles are involved in the SCN, primarily those like CLK or Period2. Neurons in the SCN also fire their action potentials in a 24 hour period. We still do not exactly know how the neuron firing sequence is connected to the gene expression cycles involved. There are connections between the neural period and genetic transcription cycles inside the neurons of the SCN and the biological macro properties of such connections are discovered primarily through experiments related to thermoregulatory mechanisms. For example the temperature control of a mouse experiencing hypothermia is different when it experiences the cold in light or dark. In the dark the mouse will be able to control its fall in its internal temperature using its SCN. Since the SCN is controlling both the periodic processes in the body and the internal temperature, one can affect the other through both gene controlled and neural mechanisms. Similar tests have been done on lizards and birds though the degree of control of SCN over thermoregulatory processes in cold blooded animals is still not completely understood.

As stated before we do not know how the CLK transcription process controls the neural firing period of the SCN in humans, but we do know how it does that in the fruit fly. And as the CLK of mammals is a homolog of the CLK of the drosophila we can assume similar processes are involved. In the fruit fly the circadian rhythm inside its neurons are controlled by two process loops. In the first loop the CLK and CYC (cycle) gene expressions drive the transcription of their repressor genes PER (period) and TIM (timeless). PER and TIM proteins accumulate in the cytoplasm and move inside the nucleus of the neurons in the night, and deactivate their own transcriptions letting the transcription of the other two continue. This transcription and translation has a 24 hour period. In the other loop the VRI (vrille) and PDP1 are initiated by CLK and CYC. PDP initiates transcription of CLK and represses transcription of VRI. All of this forms a “heterodimer” called CLK-CYC which has an expression mechanism with a negative feedback mechanism in a 24 hour period. As mentioned all of these genes have homologs in mammals. Though the SCN is present primarily in higher animals, the gene expression resulting in the SCN is the same for most animals and does the same task. The CLK gene in mammals is essentially a homolog of a similar gene found in the fruit fly. Similarly the TIM gene found in the fruit fly is also found in humans and mutations in TIM lead to an inability to reset the SCN clock using light input as described previously. The periodic activity of the neurons of the SCN leads to the periodic activities of the SCN which sets the rhythm for all the timekeepers of the body.

New research has shown that SCN genes and neurons, aside from timekeeping, may have some other functions as well. The timekeeper gene expressions like CLK may have involvement in processes outside the neurons of SCN as well.

Summarizing the SCN controls a lot of periodic processes and is a primary factor in the generation of circadian rhythms which it achieves through periodic gene transcription cycles in its neurons and periodic neural firing in addition to external stimuli through the retina. Using these processes the SCN acts as the primary timekeeper of the body.