Quick guide

Suprachiasmatic nucleus

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What is it? The suprachiasmatic nucleus, or SCN, is a compact, bilaterally paired cell group in the anterior–ventral hypothalamus of the brain. It lies just dorsal to the optic chiasm. Best characterized in rodents, it is less than 1 mm long and consists of about 16,000 neurons that are tiny — less 10 μm diameter — and very tightly packed.

So what's the fuss? In mammals, it is the site of an endogenous pacemaker that regulates 24 hour, circadian rhythmicity, synchronizing the phases and periods of a host of behavioral, physiological, and hormonal rhythms to the environmental light–dark cycle. The SCN also appears to function as a seasonal clock underlying the measurement of daylength. The SCN was first implicated as a master clock in 1972, independently by Robert Moore and Victor Eichler and Fred Stephan and Irving Zucker.

What's the evidence? Actually, the data are so compelling that the strength of this functional localization is unsurpassed by that of any other structure in the central nervous system. Electrical or pharmacological stimulation of the nucleus causes predictable phase shifts of overt circadian rhythms, whereas destruction of the SCN results in a breakdown of the generation of a wide array of such rhythms. Intrinsic properties of the SCN — energy metabolism, neuronal spike activity, and gene expression — show circadian rhythms *in vivo* and *in vitro*. Neural grafts of fetal SCN tissue re-establish overt rhythmicity in arrhythmic, SCN-lesioned recipients, and the rhythms restored by the transplants display properties characteristic of the circadian pacemakers of the donors rather than those of the hosts.

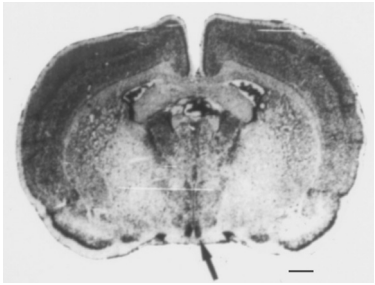

Figure 1. Location of the SCN (arrow) on a Nissl-stained coronal section of rat brain. Scale bar = 1 mm.

How does it work? It is now known that the SCN is composed of multiple autonomous single-cell circadian oscillators. Analyses of induced and spontaneous mutations, gene sequence homologies, and protein–protein interactions have identified candidate regulatory molecules and biochemical processes that are likely to constitute the basic intracellular oscillatory mechanism. It is believed that genes at the clock's core function within autoregulatory feedback loops, with nuclear proteins rhythmically suppressing the transcription of their own mRNAs. Photic input for resetting the system appears to involve a specialized retinal ganglion cell photoreceptive mechanism that functions as a 'luminance' detector. The excitatory amino acid glutamate is the primary neurotransmitter responsible for mediating the circadian actions of light in the SCN.

But how do intracellular oscillations become temporal programs? We do not yet understand how cycling molecules lead to rhythmic electrical activity, nor how individual SCN cells are assembled to create an integrated tissue pacemaker that governs circadian behaviors of whole animals. SCN neurons are known to be heterogeneous, both in their patterns of gene expression and in the topography of their afferent and efferent connections. Yet somehow they are coupled together as a network to generate a coherent read-out to the rest of the organism. Multiple output pathways are involved, including neural transmission via multi-synaptic pathways, secretion of diffusible substances by the SCN, and entrainment of extra-SCN oscillators elsewhere in the brain and body.

Why should we care? From a societal point of view, because of jet lag, shift work, sleep disorders and so on. And from a scientific one, the SCN and the circadian timekeeping system provide a remarkable opportunity to begin to understand an adaptive behavior at multiple levels of biological organization.

Insider's tip. It's not the 'super charismatic' nucleus; such adjectives should be reserved instead for some of the researchers in the field...

Where can I find out more?

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