S1| (figure) – Scheme of circadian and homeostatic interaction to regulate sleep.

Diagram illustrating the key components in the generation and maintenance of the sleep/wake cycle and its relationship to mood and cognition. Mood and cognition are directly modulated by sleep and the circadian system and directly influenced by both light and social interactions 1. Sleep is regulated by two broad mechanisms involving both the 24h body clock (circadian system; known as process C) and a wake-dependent homeostatic build-up of sleep pressure (also called process S) 2. The circadian pacemaker located within the suprachiasmatic nucleus (SCN) coordinates the timing of wakefulness throughout the day and sleep during the night. This 24h rhythm interacts with the homeostatic drive for sleep, whereby the sleep pressure increases during wake and dissipates during sleep. This process has been likened to an "hourglass oscillator". The circadian and homeostatic drivers regulate the multiple neurotransmitter and brain systems involved in sleep and arousal. Sleep-wake behaviour in turn feeds back upon the circadian pacemaker and homeostat. These components are modulated by light which acts to entrain the circadian pacemaker to the environmental light/dark cycle, acutely suppress melatonin production from the pineal and acutely elevate or suppress levels of arousal. Finally, social activities such as meal times or forced awakening by an alarm clock will drive sleep-wake activity.

Core body temperature and melatonin are also important in the initiation and consolidation of sleep in humans and may be linked physiologically. The administration of melatonin has been shown to cause vasodilation of peripheral blood vessels coinciding with an increase of peripheral skin temperature and a drop in core body temperature of ~ 1°C 3. Melatonin synthesis and release is regulated by a multi-synaptic pathway originating in the SCN. Melatonin levels rise shortly after dusk, when sleep is initiated and body temperature drops and falls in anticipation of dawn. If individuals are exposed to relatively bright light (~ 2000 lux) at night, melatonin synthesis is acutely and fully inhibited. Thus, melatonin levels broadly reflect the pattern of light/dark exposure. Attempts to sleep during the declining phase of melatonin and the rising phase of core body temperature, as with night shift workers, usually results in a shorter and less well consolidated sleep episode 4. If melatonin is administered (~ 10–20 mg) during the day it can induce sleepiness and impair cognitive performance 5. Melatonin, and its synthetic agonists, can also shift the circadian timing of the sleep/wake cycle 6,7. It is noteworthy that neurons in the SCN have a high concentration of melatonin receptors and melatonin will suppress their activity in vitro 8. Receptors for melatonin are also expressed on multiple neuroendocrine cells within the hypothalamus and so melatonin has been implicated in the regulation of numerous elements of the hypothalamo-pituitary (HP) axis9.

References