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EDITORIAL

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How is the circadian rhythm of core body temperature regulated?

The circadian rhythm of core body temperature (CBT) is a well-documented physiological phenomenon. Already in 1842, Gierse [6] had shown that his own oral temperature revealed a maximum temperature in the early evening and a minimum in the early morning hours with a maximum-minimum range of 0.9 °C. It had been assumed for a long time that muscular activity (exercise) and digestive processes were the most important factors for generation of the CBT rhythm [8]. Aschoff and his colleagues systematically explored the causes of this rhythm [1, 2]. He showed that the circadian rhythm of CBT is determined both by changes in heat production and changes in heat loss, and concluded that heat production undergoes a circadian rhythm which is phase advanced by 1.2h with respect to the circadian rhythm of heat loss, i. e. when heat production surpasses heat loss, CBT increases – transport of heat needs time.

Therefore, when we want to explain changes in CBT we need to know the relationship between heat production and heat loss. Under resting conditions, heat production depends mainly on the metabolic activity of inner organs such as liver, intestines, kidneys, heart in the abdominal/thoracic cavity, and the brain, together producing ca. 70 % of the entire resting metabolic rate of the human body [3]. However, this "core" heat is generated in only 8 % of the body mass with a surrounding skin surface of only about 0.3m^2 (surface to volume = 0.1) [3]. The proximal skin surface is not ideally shaped: too flat for good heat transfer to the environment. This means, that even in a comfortable thermoneutral environment, heat has to be transferred from the core to parts of the body with better heat transfer capacities, namely to the extremities (surface to volume coefficient e. g. of fingers = 2.2) [3]. These distal parts of the body have ideal (round) surface shapes for good heat transfer properties to the environment. Blood is the main medium for transporting heat from the core to distal skin regions (convectively), driven and distributed by the cardiovascular system. The human body consists therefore of two compartments, the heat producing core, and the heat-loss regulating shell [3]. CBT (especially in the brain) is homeostatically regulated, and the shell is poikilothermic and therefore largely dependent on environmental conditions. The shell serves as a kind of thermal protector for the core. When the air is cold, the shell is large, whereas in a warm environment it is small [3]. This autonomically regulated mechanism of shell size occurs via constriction or dilatation of peripheral blood vessels, mainly of smooth muscles in arterioles, as well as smooth muscles in arteriovenous anastomoses in distal skin regions [7]. There is substantial evidence indicating that homeostatic control of CBT is mediated by a hierarchically organized set of neuronal mechanisms, with the anterior hypothalamic/preoptic areas at the top of the hierarchy [16]. In addition to the homeostatic principle, a rostral projection from the circadian pacemaker (localized in the suprachiasmatic nuclei) to the preoptic areas serves the circadian modulation of CBT [14].

Changes in shell size also take place when the underlying endogenous circadian CBT rhythm is regulated. This has been studied under controlled environmental conditions [9], where external influences (masking) are minimized, in the so-called constant routine protocol [13] (e. g. constant room temperature, 22 °C; humidity, 60 %; light, < 8 lux, constant bed rest in supine body position, no sleep allowed, food and fluid intake in small isocaloric portions at equal intervals). It has been shown that distal skin temperature rises in the evening, whereas heat production, proximal skin temperature

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and CBT decline – in the morning the inverse happens [9] (see figure, right panel). The circadian rhythm in heat production (measured by indirect calorimetry), as well as heart rate (a correlate of heat production), is phase advanced with respect to CBT and heat loss, as shown originally by Aschoff [2]. A crucial role for the heat loss effector system in the evening appears to be the nocturnally secreted pineal hormone melatonin. Melatonin initiates not only distal vasodilatation, but also sleepiness [11]. After lights off, and even before sleep onset, an additional phenomenon can be observed. Both distal and proximal skin temperatures increase rapidly to a similar level, due to relaxation (withdrawal of the sympathetic vasoconstrictor tonus) [12] (see figure, left panel). This means there is a complete loss of the core/shell principle during sleep. However, this increase in skin temperatures does not lead to efficient heat loss, because cardiac output is decreased in parallel – CBT declines very slowly under temperate environmental conditions [12].

The environmental conditions (temperature, air movement, humidity, sunshine, microclimate under clothing, bedding etc.) are the important determinants of heat loss. Heat exchange with the environment occurs by means of conduction, convection, radiation and evaporation. The "overall" dry heat loss is proportional to the body surface and the difference between skin and ambient temperatures, whereas heat loss by evaporation is proportional to the difference of water vapor pressure of skin and air. Under sedentary thermoneutral conditions, about 20 % of total heat loss occurs by insensible perspiration, the passive evaporation from the surface of the body of water that has diffused through the skin, plus water lost as water vapor from the lung [15]. As the environmental temperature rises and exceeds an upper critical temperature threshold (ca. 31 °C), dry heat loss is progressively reduced, and the dependency upon evaporative heat loss by sweating increases. The sweat rate increases when CBT rises, while mean and local skin temperature acts as a multiplier of the central control signal [15]. In humans, the sweating mechanism is well developed, and the tolerance to heat is high. In all situations, induction of sweating requires increased skin blood flow in advance. Therefore, it is reasonable to assume that the initial threshold for sweating underlies a parallel circadian modulation as the vasomotor responses to increased CBT, with highest thresholds in the evening and lowest thresholds early in the morning [17]. However, we have to keep in mind that sweating does not occur under sedentary temperate environmental conditions. In the evening, when the threshold for sweating drops and distal and proximal skin temperatures increase when lights are turned off, sweating can easily be induced. In fact, sweating at the beginning of sleep has often been observed [18]. In a subject with congenital generalized anhidrosis (CGA), a normal circadian pattern of CBT (measured under room temperature conditions of 24 °C), could be observed also after lights off [5]. Even though heat loss was not measured, it would seem that under temperate environmental conditions, subjects with CGA regulate their circadian CBT rhythm with a normal functioning vasomotoric effector system (dry heat loss is not impaired). If CGA subjects were tested at higher room temperatures (e. g. in the summer) the vasomotoric control of heat loss alone would not be sufficient, and thus, the nocturnal decline of CBT would be reduced. In fact this has been described in a single case report, where a subject with CGA slept in a warm environment (32 °C) on a higher CBT level, which led to interrupted sleep, reduced amount of rapid-eye-movement (REM) sleep and altered REM/nonREM-sleep cycles [4]. Further studies using different room temperatures and expanded physiological measures, including skin temperatures, heart rate, and sleep electroencephalographic recordings are required under stringently controlled constant routine conditions. Such studies could elucidate the influence of heat load on sleep and in addition could lead to improved therapeutic strategies for subjects with CGA.

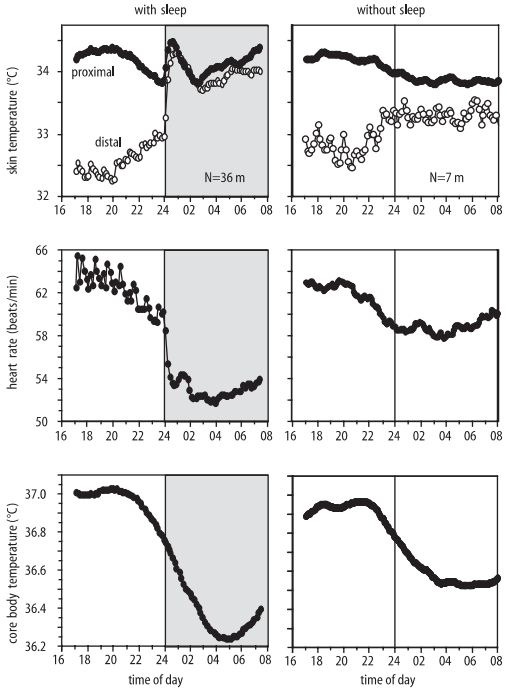

Fig. Time course of distal and proximal skin temperatures, heart rate, and core (rectal) body temperature (CBT) in two protocols where sleep was permitted (left panel) or not (right panel). Note: distal and proximal skin temperature increased in parallel after lights out – however, without sleep, proximal skin temperature followed the CBT rhythm. Heart rate and CBT dropped to a lower value during sleep (redrawn from [10]).

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