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FRONT MATTER: COMMENT

Brain control of body temperature: Central command vs feedback

Comment on: Blessing W, Ootsuka Y. Timing of activities of daily life is jaggy: How episodic ultradian changes in body and brain temperature are integrated into this process. Temperature 2016; 3:371-83; http://dx.doi.org/10.1080/23328940.2016.1177159

In his landmark *Physiological Reviews* article of 1929[1] Walter Cannon defined homeostasis as the coordinated physiological mechanisms that maintain the physical and chemical properties of the internal environment, i.e. the extracellular fluid that surrounds all cells in the body. This in turn was based on the principle, first enunciated by Claude Bernard, that the constancy of the internal environment is essential for the survival of organisms. Modern physiology textbooks typically begin with a discussion of the principles of homeostasis, and often explain these as analogous to physical feedback control systems. Thus, the body system maintaining body temperature is often likened to a thermostat that maintains a constant room temperature. According to this scheme, the body detects deviations in temperature from some desired constant setpoint, and then generates physiological changes that return the temperature to the setpoint.

The difficulty with this scheme, as pointed out by Blessing and Ootsuka[2] in their article "Timing of activities of daily life is jaggy: How episodic ultradian changes in body and brain temperature are integrated into this process" published in this issue, is that continuous measurements of temperature in the body core or brain show that changes in body temperature frequently occur that cannot be explained by feedback regulation around a constant setpoint. For example, as illustrated in Figure 2 in their article, there are distinct episodes, occurring on average every 1–2 hours, in which the body and brain temperature of a rat is increased by 1°C or more for periods ranging from a few minutes to about 30 minutes, even under conditions where the rat is in a quiet environment with controlled ambient temperature, and with ad libitum access to food and water. The increases in temperature were accompanied by increases in the temperature of brown adipose tissues (BAT) of even greater magnitude, indicating that they occur as a direct consequence of sympathetically mediated BAT thermogenesis. The episodes of increased temperature are part of a patterned coordinated physiological response, since they are accompanied by increases in arterial pressure, heart rate and somatomotor activity, and are interspersed with rest periods. The somatomotor and autonomic changes are preceded by an increase in EEG theta power, suggesting increased engagement with the environment, and typically are followed by increases in eating.[2,3] Such episodic events that occur more frequently than once every 24 hours are referred to as "ultradian" events, to distinguish them from circadian events that occur once every 24 hours.

The coordinated ultradian physiological responses must be driven from the brain, i.e., by central command. Similarly, the immediate coordinated somatomotor and autonomic changes that occur at the onset of exercise, or which are triggered when an animal detects a predator or prey, are also driven by central command.[4] At the same time, reflex compensatory mechanisms that depend upon feedback from peripheral receptors are also an essential part of physiological regulatory systems that ensure the survival of animals in the face of environmental threats or internal challenges. Furthermore, reflex mechanisms and central command are not necessarily independent. For example, during exercise central command signals from the forebrain reset the baroreceptor reflex, such that arterial pressure continues to be reflexly regulated, but around a higher level which is physiologically more advantageous during exercise.[4]

As Day has pointed out in an insightful review,[5] Cannon[1] in explaining the concept of homeostasis clearly distinguished between the physiological factors that are critical for cell survival (e.g. nutrient availability, oxygen content, pH, ion concentration and temperature) and those variables that help to maintain these critical factors, such as arterial pressure or ventilation. Thus there is no conflict between Cannon's concept of homeostasis and the changes in arterial pressure or ventilation that may accompany different behaviors. On the other hand, the episodic ultradian changes in body temperature that occur as part of an animal's daily life, even when there is no change in ambient temperature, do not conform with the traditional view of homeostasis, as Blessing and Ootsuka have pointed out. Instead, the ultradian episodes of coordinated behavioral and physiological changes that include an increased body temperature represent an additional mechanism by which an animal increases its probability of survival.

The article by Blessing and Ootsuka also describes 2 other very interesting features of ultradian events. First, the timing of these events is random, which means that a predator cannot predict when such an event may occur. Secondly, there is a considerable time lag (~5 min) between the increase in EEG theta power that initiates each episode and the subsequent changes in body temperature, arterial pressure and somatomotor activity, and an even longer time lag (~15 min) before the onset of eating. Such long time lags indicate that there must be a non-neural signal or signals that link the increase in EEG theta power to the subsequent physiological and behavioral components of each episodic event. The nature of these signals, and the brain circuitry that mediates the stereotyped physiological and behavioral responses, are fascinating questions that require further studies.

The idea that physiological and behavioral changes occur in an episodic ultradian fashion is not new – it was first described in the 1920s, as Blessing and Ootsuka[2] point out. Their article, however, clearly explains the importance of this phenomenon. In addition, the article also describes sophististicated analytical methods that will help other investigators to perform quantitative studies of ultradian episodes. I hope that future textbooks will provide a more complete explanation of the regulation of body temperature and other physiological variables by putting greater emphasis on central command mechanisms, in addition to homeostatic mechanisms.

References

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Roger A. L. Dampney
School of Medical Sciences (Physiology) and Bosch Institute
The University of Sydney, NSW 2006, Australia
roger.dampney@sydney.edu.au