Brain Cooling: An Economy Mode of Temperature Regulation in Artiodactyls

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Artiodactyls employ selective brain cooling (SBC) regularly during experimental hyperthermia. In free-ranging antelopes, however, SBC often was present when body temperature was low but absent when brain temperature was near 42°C. The primary effect of SBC is to adjust the activity of the heat loss mechanisms to the magnitude of the heat stress rather than to the protection of the brain from thermal damage.

In 1966, Taylor (13) discovered that when goats develop hyperthermia the temperature of the brain ($T_{\text{brain}}$) rises less than the temperature of the rest of the body core ($T_{\text{trunk}}$). The phenomenon was termed “selective brain cooling” (SBC) and was identified in many members of the order of artiodactyls, which comprises pigs, camels, deer, sheep, cattle, antelopes, and others (for review, see Refs. 1 and 10). The intuitive explanation was that SBC serves to protect the brain from thermal damage. However, this view is difficult to reconcile with the general organization of mammalian thermoregulation.

The thermoregulatory system is based on thermoreceptors in the skin and receptor-like sensors in the body core (12). In its simplest version, all afferent activity can be conceived to form an integrated signal. It is compared with a “set point” and, in case of an upward deviation of body temperature, drives heat loss mechanisms, e.g., skin vasodilation, sweating, or panting. A large fraction of all core temperature sensors reside in the brain, and it is this fraction that causes the conceptual problem with SBC: why, on the one hand, are temperature sensors capable of driving all heat loss mechanisms concentrated in the brain, and why, on the other hand, is SBC present, preventing the brain sensors from detecting upward deviations of internal body temperature? The answer requires a more detailed analysis of the distribution of temperature sensors within the body core and the mechanism underlying SBC.

Spatial distribution of core temperature sensors

In 1964, Simon and his colleagues (for review, see Ref. 12) found that the spinal cord contains temperature sensors whose selective thermal stimulation evokes all specific thermoregulatory responses, such as shivering, panting, and sweating. This marked the end of a 60-yr period in which the hypothalamus was considered the only structure capable of measuring the temperature of the body core. Later, additional, less well-defined thermosensitive sites were found in the abdomen and in skeletal muscle, and this finding raised questions regarding how the combined inputs of all trunk temperature sensors would compare quantitatively with that of brain sensors.

An answer was given by a method designed for conscious goats. Heat exchangers in the large blood vessels were used to change the $T_{\text{brain}}$ and $T_{\text{trunk}}$ independently of each other, while effector responses such as respiratory evaporative heat loss (REHL), a quantitative measure of heat loss by panting, were related by nonlinear regressions to $T_{\text{brain}}$ and $T_{\text{trunk}}$. The contour lines derived from the REHL regression are nearly symmetrical around the line of identity of $T_{\text{trunk}}$ and $T_{\text{brain}}$ (Fig. 1). The conclusion is that trunk afferents and brain afferents make approximately equal contributions to the control of REHL, if, and this is an important qualification, both regions have identical temperatures (4).

However, as mentioned before and shown in Fig. 1, $T_{\text{brain}}$ and $T_{\text{trunk}}$ do not develop along the line of identity during hyperthermia, at least not in artiodactyls in a laboratory environment. Because of SBC, $T_{\text{brain}}$ uncouples from $T_{\text{trunk}}$ near 38.8°C and rises with a much shallower slope as the heat stress increases so that, for example, $T_{\text{brain}}$ is 39.2°C when $T_{\text{trunk}}$ is 40.4°C. The implementation of SBC has two consequences. The first is that REHL is reduced from 1.2 to 0.8 W/kg at 40.4°C, i.e., the animals give up one-third of their potential heat loss. The second is that, in animals employing SBC, $T_{\text{trunk}}$ contributes much more than $T_{\text{brain}}$ toward the drive to heat loss (8).
The carotid rete heat exchanger

In artiodactyls, the arterial blood destined for the brain passes through the carotid rete at the base of the brain (Fig. 2). It consists of hundreds of small arteries, arising from branches of the carotids and after 10–15 mm joining again to enter the circle of Willis. The rete is embedded in the cavernous sinus, which carries cool blood returning via the angularis oculi vein from the evaporating surfaces of the upper respiratory tract. This is a heat exchanger of considerable capacity: in one species of antelope, Thomson’s gazelle, a 2.7°C gradient between T_{brain} and T_{trunk} was observed (14).

An important feature of the system is that a carotid rete heat exchange, and hence SBC, is not mandatory. There are two routes available to the cool venous blood returning from the nasal mucosa. One is via the angularis oculi vein; if this route is taken, the arterial blood flowing to the brain will be cooled and SBC will ensue. The other route goes via the facial vein straight back to the jugular vein, in which case the cavernous sinus is bypassed and the brain is not cooled. Segments of the veins near the division contain muscular sphincters, which are richly innervated by sympathetic fibers (6). Here is a potential efferent control mechanism by which SBC can be implemented, fine-tuned, and perhaps even suppressed by switching blood flow between the two routes, but depending on what?

Independent manipulations of T_{brain} and T_{trunk} in goats have shown that it is T_{brain} that provides the exclusive thermal input into the control circuit of SBC: the combination of high T_{trunk} and low T_{brain} results in panting but no SBC, whereas high T_{brain} and low T_{trunk} are accompanied by clear SBC without any panting. Thus, in the hyperthermic range, the brain has the potential to offset its own temperature from that of the rest of the body core (8).

Environmental effects on deep body temperature of free-ranging animals in their natural environment

The account given above is based, like most of our knowledge about temperature regulation, on results of laboratory experiments in restrained animals. Although this approach has yielded valuable insights into basic thermoregulatory mechanisms, it does not mimic the natural environment. In contrast to the laboratory, animals in the natural environment are unrestrained and subject to complex thermal stressors as well as nonthermal stressors that arise, for example, from hunger, thirst, social interactions, and even predation, which confound the responses to the thermal stress, affect the heat balance, and consequently influence the resultant internal body temperature. Recent developments in data recording technology have made it possible to see what relevance laboratory results bear on the responses of free-ranging wild animals in their natural environment.

Figure 3 is based on a study on black wildebeest, a medium-sized antelope indigenous to southern Africa (5). Four animals were instrumented with temperature probes in the brain and in the carotid artery (representing T_{trunk}), equipped with data loggers, and released into freedom, which meant 110 km² of savanna-type open grassland ~1,200 m above sea level, free access to natural water sources, no natural predators, and next to no trees or other shelter. In the following 2 mo, the animals were engaged just twice, that is, when it was time to download the loggers because the memory was full; for the rest of the time, they were left undisturbed by human observers.

Figure 3, top left, contains the climatic data of the first 20-day study period. Means, minima, and maxima of air temperature (T_{air}) and solar radiation are shown as a function of the time of day. The climate (southern hemisphere spring) was characterized by cold nights and hot days. The single most important environmental factor was the radiant heat, which on average reached

![FIGURE 1. Contour lines show levels of respiratory evaporative heat loss (REHL) by panting in goats, when the temperatures of brain (T_{brain}) and trunk (T_{trunk}) were manipulated independently of each other. Symmetry of the contour lines implies that afferent temperature inputs from the brain and the trunk contribute approximately equally to heat loss, if the temperatures of both regions are equal. Contour lines are based on nearly 70 h of measurements in 3 conscious animals. Single continuous line shows means ± SE of T_{brain} plotted vs. T_{trunk} when only T_{trunk} was elevated and brain was allowed to adopt its own temperature. Due to selective brain cooling, T_{brain} rose less than T_{trunk}. Line is based on nearly 55 h of measurements in 3 conscious goats. [Redrawn from Refs. 4 and 8.]](http://physiologyonline.physiology.org/)

"There are two routes available to the cool venous blood..."
800 W/m² around noon. This constituted a potential heat load on the animals of 10 times the heat that the animals themselves produced by their resting metabolism (3). Figure 3, left, also shows T_trunk for the same period; the curves are based on average data of all four animals. Despite the large variation of the thermal environment, the circadian amplitude of T_trunk in all four animals was <0.8°C, and, in spite of the large diurnal heat load, even the maxima of T_trunk in the late afternoon just exceeded 39.5°C.

The key to this extraordinary thermoregulatory performance in high solar radiation appears to lie in the insulation provided by the fur. No quantitative measurements have been made on the pelage of the black wildebeest, but in hartebeest, a member of the same subfamily and dwelling under similar conditions, the low absorptivity of the fur for shortwave radiation and the preferred orientation of the body relative to the sun reduced the effective radiative load to one-third of the potential load. In addition, the low thermal conductivity of the thick, dense pelage led to high surface temperatures, with subsequent long-wave radiative and convective losses of much of the absorbed heat (3). The insulation provided by the pelage does not protect the animals against hyperthermia resulting from diurnal activity, and, indeed, wildebeest are known to spend the middle of the day inactive. The conclusion is that well-hydrated wildebeest withstand, by a combination of perfect external insulation and appropriate behavior, even extreme external heat loads without developing significant degrees of hyperthermia. Similar observations were recently made in springbok, a smaller antelope living in the same habitat (11).

Figure 3, right, shows the relationship between T_trunk and T_brain throughout the same 20-day period, during which the animals were left undisturbed by the experimenters. Figure 3, bottom right, shows the frequency histogram of 0.1°C classes of T_trunk. Means, minima, and maxima of T_brain were calculated for each class of T_trunk; they are shown in Fig. 3, top right. The data, therefore, represent the interrelationship of the two temperatures under natural conditions. The line connecting the means of T_brain intersects the line of identity near 39°C; this is the mean threshold of SBC. It agrees well with what had been observed previously in tame artiodactyls in the

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However, as the frequency histogram shows, the free-ranging animals spent almost all of their time below this threshold. Above the threshold, two zones can be discerned. Between 39.2 and 39.8°C $T_{\text{trunk}}$, the class means of $T_{\text{brain}}$ remain stable at 39.2°C, whereas, for classes of $T_{\text{trunk}}$ above 39.8°C, the means of $T_{\text{brain}}$ rise steeply again. Another noteworthy point is the large variability of the $T_{\text{trunk}}$-$T_{\text{brain}}$ interrelationship: over the 38–39.5°C range of $T_{\text{trunk}}$, which encompasses the temperatures normally adopted by the animals, $T_{\text{brain}}$ could be either higher or lower than $T_{\text{trunk}}$. Similar observations were made when the effects of arousing stimuli on SBC were recorded in sheep (1). The conclusion is that there was little evidence for a tight thermal control of SBC in free-ranging animals in their natural environment. The animals just showed a tendency to employ SBC if they experienced, rarely in their everyday activities, mild hyperthermia. On the other hand, SBC also was implemented, on occasion, in the normothermic range of $T_{\text{trunk}}$, which points to a nonthermal component in the control of SBC.

**SBC during exercise hyperthermia**

The animals had to be recaptured to download the loggers. The capture was done by darting the animals from a low-flying helicopter, the standard procedure for translocation, vaccination, and treatment of larger animals in African wildlife parks. It involved a high-speed chase of some minutes’ duration and resembled the activity of an antelope pursued by a predator. During and after the chase, both $T_{\text{trunk}}$ and $T_{\text{brain}}$ rose precipitously, exceeding 42°C in one animal. The symbols in Fig. 3, top right, reflect the highest $T_{\text{brain}}$ and the corresponding $T_{\text{trunk}}$ that occurred during the severe hyperthermia of a chase, the animals abandoned SBC. Similar observations have been made in free-ranging springbok: SBC often occurred at low $T_{\text{trunk}}$ when the animal was resting or moderately active, and SBC was abandoned during spontaneous bouts of high activity despite high $T_{\text{trunk}}$ (11).

Laboratory experiments have yielded a somewhat different picture. In exercising reindeer, the onset of SBC was shifted to higher levels of $T_{\text{trunk}}$ in comparison to rest (9). In a Thomson’s gazelle, a 2.7°C gradient between $T_{\text{brain}}$ and $T_{\text{trunk}}$ was observed in a single experiment. However, the animal was tame, had been habituated to observers, had received 3–4 months of training, and was running on a circular race track at ~60% of its top speed (14). What is presumably absent in animals exercising in a laboratory is the emotional stress associated with high levels of activity in a natural environment.
The mechanism by which the facilitation or inhibition of SBC takes place can be conceptualized as follows (Fig. 2). The adrenoceptors of the angularis oculi sphincter are of the α-type, and the sphincter normally is relaxed, whereas the facial vein sphincter has β-receptors and is normally contracted (6). Thus low sympathetic activity in the fibers to the veins will allow flow of cool venous blood to the cavernous sinus, and the degree of SBC is potentially large, depending on the thermal inputs provided by $T_{\text{brain}}$; high $T_{\text{brain}}$ generates low activity in these fibers. Conversely, higher sympathetic activity associated with low $T_{\text{brain}}$ will constrict the angularis oculi sphincter, dilate the facial sphincter, and direct the cool venous blood away from the cavernous sinus.

However, the activity of the fibers leading to both vessels is likely to be enhanced, irrespective of $T_{\text{brain}}$, if there is general sympathetic excitation. Thus, even in a severely hyperthermic animal, the angularis oculi sphincter can be closed and SBC can be suppressed, for example, during strenuous exercise. In this case, the thermal drive to SBC is overridden by a general nonthermal activation of the sympathetic system. Thus SBC is possible only in the absence of general sympa-

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**FIGURE 4.** High sympathetic activity inhibits brain cooling and increases heat loss. Left: an animal, resting or moderately active during low-level environmental heat stress (top), employs selective brain cooling (SBC, middle). SBC largely prevents brain temperature ($T_{\text{brain}}$) sensors from detecting the rise in body temperature. Consequently, respiratory evaporative heat loss (REHL) is predominantly driven by trunk temperature ($T_{\text{trunk}}$) sensors, and its increase with rising body temperature is attenuated (bottom). Right: during high sympathetic activity (top), SBC is suppressed, and $T_{\text{brain}}$ rises in parallel with $T_{\text{trunk}}$ (middle). REHL is now driven by $T_{\text{trunk}}$ and $T_{\text{brain}}$ sensors, and increases with a steeper slope (bottom).
thetic excitation, such as that generated by intense physical activity and, particularly, by emotional stress; then it is fine-tuned by $T_{\text{brain}}$. This leads to an apparent dilemma regarding the widely accepted assumption that the purpose of SBC is to protect the allegedly vulnerable brain from thermal damage (2). On the one hand, fighting, chasing, or being chased are the only conditions in which larger, euhydric, nondomestic animals in the wild work hard enough to develop substantial hyperthermia. On the other hand, all three conditions are certainly associated with high levels of sympathetic activity, which are incompatible with the development of SBC. The consequence is that, in nondomestic and free-ranging animals in their natural environment, severe exercise and significant SBC appear mutually exclusive. Thus SBC as a protective mechanism for the brain becomes a rather unlikely proposition.

**SBC as a means of adjusting the activity of heat loss mechanisms**

The facilitation of SBC during rest and its inhibition during strenuous exercise fit in with the general organization of the thermoregulatory system. SBC inhibits panting and saves water. In arid environments, water is a scarce commodity, and utilizing water for evaporative cooling may be more disadvantageous than allowing body temperature to rise, in particular, if the environment-induced rise is limited due to the combined benefits of fur, larger body mass, and behavior. It makes sense for animals in arid habitats to inhibit evaporation during rest or moderate activity to save water. This is accomplished by SBC: the increase in REHL per °C rise of body temperature is reduced, since the brain temperature sensors are largely uncoupled from rises in body temperature (Fig. 4).

During strenuous exercise, however, which normally will occur only in life-threatening situations, it is imperative for animals to activate their heat loss mechanisms to their full capacities. Abandoning SBC, allowing $T_{\text{brain}}$ to rise, and thereby activating $T_{\text{brain}}$ sensors would serve this purpose well and permit increasing REHL to the maximum possible at the given body temperature. Figure 4 makes this point for REHL, since quantitative data are available; however, qualitatively similar relationships between body temperature and skin blood flow were observed when situations with and without SBC were compared (7).

Thus the implementation of SBC during moderate hyperthermia and its inhibition during severe hyperthermia adjust the activity of all heat loss mechanisms to the magnitude of the heat stress.

**References**