Absence of selective brain cooling in unrestrained baboons exposed to heat

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Maloney SK, Mitchell D, Mitchell G, Fuller A. Absence of selective brain cooling in unrestrained baboons exposed to heat. Am J Physiol Regul Integr Comp Physiol 292: R2059–R2067, 2007.—To test whether baboons are capable of implementing selective brain cooling, we measured, every 5 min, the temperature in their hypothalamus, carotid arterial bloodstream, and abdominal cavity. The baboons were unrestrained and exposed to 22°C for 7 days and then to a cyclic environment with 15°C at night and 35°C during the day for a further 7 days. During the latter 7 days some of the baboons also were exposed to radiant heat during the day. For three days, during heat exposure, water was withheld. At no time was the hypothalamus cooler than carotid arterial blood, despite brain temperatures above 40°C. With little variation, the hypothalamus was consistently 0.5°C warmer than arterial blood. At high body temperatures, the hypothalamus was sometimes cooler than the abdomen. Abdominal temperature was more variable than arterial blood and tended to exceed arterial blood temperature at higher body temperatures. Hypothalamic temperature cooler than a warm abdomen is not evidence for selective brain cooling. In species that can implement selective brain cooling, the brain is most likely to be cooler than carotid arterial blood when an animal is hyperthermic, during heat exposure, and also dehydrated and undisturbed by human presence. When we exposed baboons to high ambient temperatures while they were water deprived and undisturbed, they never implemented selective brain cooling. We conclude that baboons cannot implement selective brain cooling and can find no convincing evidence that any primate species can do so.

SELECTIVE BRAIN COOLING IS the maintenance of the brain at a temperature cooler than arterial blood (31). In mammals with a carotid rete, the magnitude of selective brain cooling increases as core body temperature increases (33). Whether humans are capable of selective brain cooling is the subject of debate. Humans do not possess a carotid rete, the anatomical substrate enabling selective brain cooling in other mammals. But several clinical studies have assessed face fanning in the treatment of heatstroke and therapeutic hyperthermia, ostensibly because it cools the brain and attenuates neurological damage (10). Selective brain cooling is also been proposed as a physiological attribute favoring the survival of early hominids (17), and a recent theory of human evolution holds that it was the development of a superior selective brain cooling system that permitted the increase in brain size unique to the Homo lineage (19).

The cranial vasculature of modern humans shares many characteristics with other large primates, including the arterial supply to the brain and the venous drainage of the scalp (48). Because the heat produced by the brain is removed by the blood perfusing it, the vasculature is important in brain temperature regulation (44). A key element of the evidence adduced in support of human selective brain cooling is the apparent occurrence of selective brain cooling in other primates with similar vascular anatomy (11, 14). These comparisons are important because, while the brain temperature of nonhuman primates can be measured, direct measurements of brain temperature in healthy humans are nonexistent. Several research articles present evidence that, at times, the brain of monkey can be cooler than a temperature measured elsewhere in the body (21, 22), but an earlier comprehensive paper reported that monkeys do not exhibit selective brain cooling (26). All of those investigations were conducted with the primates either anesthetized or in restraining chairs. Restraint may well interfere with primate thermoregulatory mechanisms, and perhaps more importantly, may suppress any possible selective brain cooling. In artiodactyl mammals, selective brain cooling is attenuated, or abolished, by fear-associated activation of the sympathetic nervous system (14, 41).

As far as we can establish, all investigations of brain temperature regulation in nonhuman primates have been conducted on macaques or squirrel monkeys. The ecological habits and selective pressures on these primates were presumably very different from early hominids. The primate that coevolved with the hominids and faced with them the thermal challenges of leaving the canopy forests for more open, drier habitats, was the baboon (6). Extant baboons occur in open habitats as diverse as the coastal “fynbos” of the southern tip of Africa (4, 30), high-altitude mountain grasslands (9), and the dry beds of ephemeral rivers in the Namib Desert (5).

Although the morphology is not unique to the genus (32), baboons have conspicuously large muzzles for primates (see Fig. 1). In artiodactyls, the mammals with the most efficient selective brain cooling known (2, 41), evaporation from the large surface area in the nasal mucosa provides the heat sink for selective brain cooling. Nearly 20 years ago, Wheeler (49) asked “whether baboons, like other savanna mammals, can use the venous blood cooled in the nasal chamber to keep their brain cool,” a question that has not been answered. In an attempt to provide an answer, we have measured hypothalamic, carotid arterial blood, and abdominal temperatures of unrestrained baboons in a climatic chamber. In the expectation that if a nonhuman primate can implement selective brain cooling, it will do so when unrestrained and exposed to high ambient heat load, we subjected the baboons to environmental conditions that simulated the most extreme desert habitat that extant baboons inhabit, the ephemeral riverbeds of the Namib Desert (5).

In artiodactyl mammals, water deprivation increases the magnitude of selective brain cooling (33). Therefore, to further...
enhance the likelihood of the baboons exhibiting selective brain cooling, if they have the capacity to do so, we deprived them of drinking water for several of the days that they were exposed to the simulated desert environment. Water has been withheld from heat-stressed baboons for two days previously, without long-term sequelae (57).

MATERIALS AND METHODS

Animals. Experiments were performed on one male (mass 23 kg) and three female (masses 15–19 kg) adult baboons (Papio hamadryas ursinus), habituated to an indoor animal facility (ambient temperature 22–25°C) with a 12:12-h light-dark cycle (lights on at 0600). In the animal facility, the baboons were housed individually in a set of juxtaposed cages, were fed once daily (commercial pellets and fruit), and were given water ad libitum.

The study was approved by the Animal Ethics Screening Committee of the University of the Witwatersrand (protocol number 98/84/5).

Surgery. With the baboons under general anesthesia, we implanted three miniature thermometric data loggers (see below) and attached sensors for temperature measurement. Anesthesia was induced by intramuscular injection of ketamine (10 mg/kg, Anaket-V, Centaur Laboratories, Johannesburg, South Africa) and intravenous injection of thiopentone sodium (100 mg, Intraval sodium, Merial, Johannesburg, South Africa) and maintained with halothane (0.5–2% in oxygen, Fluothane; Astrazeneca, Johannesburg, South Africa). Respiratory rate, heart rate, and blood pressure were monitored throughout surgery. A 50-ml enrofloxacin tablet (Baytril; Bayer, Johannesburg, South Africa) was placed in surgical sites on the head. Each baboon received long-acting penicillin (3 ml im, Peni LA; Phenix, Johannesburg, South Africa) and an opiate analgesic (buprenorphine, 0.3 mg im, Temgesic; Schering-Plough, Johannesburg, South Africa). Each baboon was returned to its home cages. Temperatures were measured at three sites in each animal, in the hypothalamus, in the carotid artery, and within the abdominal cavity. For measurement of carotid arterial blood temperature, a thermistor was inserted through the skull at the bregma, via a burr hole. Examination of the carotid artery at recovery surgery revealed no occlusion or clotting along the length of the intravascular catheters, that is, the thermistor had measured the temperature of free-flowing arterial blood.

Thermometry. The miniature data loggers used for the brain and carotid arterial blood temperature measurement (StowAway XT1, Onset Computer; Pocasset, MA) had outside dimensions of ~50 × 45 × 20 mm and a mass of ~40 g, when covered in wax. Abdominal temperature loggers, with internal temperature sensors (StowAway Tidbit, Onset Computer), had outside dimensions of ~30 × 41 × 17 mm, and weighed 20 g when covered with wax. All loggers had a storage capacity of 32 kB and had been custom-modified for us to measure from +34°C to +46°C and to have resolution of 0.04°C. The scan interval of the loggers was set at 5 min. Brain and blood temperature sensors were constructed from ruggedized glass-coated bead thermistors with insulated extension leads (bead diameter 0.3 mm; ABOE3-BR11KA1033N; Thermometrics, Edison, NJ). Wax-coated loggers, with their sensors, were calibrated against a high-accuracy thermometer (Quat 100, Heraeus, Hanau, Germany) in an insulated water bath, and all had a calibrated accuracy equal to, or better than, one sampling step of the logger (0.04°C).

Experimental protocol. Ten days after surgery, two baboons at a time were sedated by intramuscular injection of ketamine (5 mg/kg) and transported to a climate chamber, where they were housed individually in juxtaposed cages of dimensions 0.9 m wide × 0.9 m deep × 1.2 m high, and received water and food as before. Through-out the procedure, the baboons were unrestrained in their cages. They were free to clamber around the cages and had sufficient room to adopt thermoregulatory postures (5). Their cages were cleaned once per day, at feeding time, but otherwise, the baboons were disturbed as little as possible. They were inspected regularly through a peephole, by researchers and veterinary staff. The 12:12-h light-dark cycle was maintained, with lights on at 0600 local time. Illumination at baboon height was about 100 lux when the chamber lights were on. A radio tuned to a music station was switched on, in the climatic chamber,
Foraging board for cage enrichment.

For the first 7 days in the climatic chamber, ambient temperature was maintained at 22°C. Then the animals were exposed for 7 days to a cyclic protocol simulating a desert environment. Dry-bulb temperature was held at 15°C overnight, and was increased at 0800 to 25°C, at 0900 to 32°C, and at 1000 to 35°C. Dry-bulb temperature was decreased at 1500 to 30°C, at 1600 to 23°C, and at 1700 to 15°C. For the male baboon and one of the females, mean radiant temperature was kept equal to dry-bulb temperature during the heating protocol. For the other females, to increase the midday heat load, radiant heat was applied each day from a 500-W lamp positioned 1.5 m above each animal, between 1100 and 1400, when dry-bulb temperature was 35°C. Black globe temperature, measured 1 m above the floor inside the cage, was 42°C when the lamp was on. Relative humidity was maintained at 50% throughout experiments. Wind flow in the chamber was turbulent, with speed <0.5 m/s.

On three of the seven days of the simulated desert environment, water was withheld from the baboons, and fruit removed from their diet. Drinking water was removed at 0900 and returned 51 h later, at 1200. Free-living baboons prefer to drink in the hottest part of the day (5, 29).

Data analysis. Electronic failure prevented us acquiring a usable data set from one of the female baboons, and body temperature measurements on one 22°C and one (hydrated) day from the simulated desert environment, for another of the female baboons. For that animal, therefore, we obtained 3,456 simultaneous measurements of each of hypothalamic, carotid arterial blood and abdominal temperature, evenly spaced over the day and night during the study. For the other two baboons, we obtained the full 4,032 simultaneous measurements of the temperature at each body site during the study. Those original 5-min recordings of body temperatures were used to find the overall mean and 24-h range of carotid arterial blood temperature, hypothalamic temperature, and abdominal temperature for the days when the baboons were at 22°C, when they were exposed to the desert protocol, and when they were exposed to the desert protocol without access to water. The means and ranges within each animal were compared with a 2-way repeated-measures ANOVA to determine whether temperatures at the three sites differed significantly from each other, and whether the different environmental treatments influenced them. The analysis had main effects of site of measurement (abdomen, carotid arterial blood, and brain) and environment (22°C, desert, and desert with no water). When differences were indicated by the ANOVA, a Student-Newman-Keuls (SNK) test was used to compare the three individual means or the treatments.

Following the approach of Jessen et al. (34), we analyzed the relationship between hypothalamic temperature and carotid arterial blood temperature in each animal by sorting all 5-min measurements, in that animal, into 0.1°C categories of carotid arterial blood temperature, and determining the mean, standard deviation, maxima and minima of hypothalamic temperature at each class of carotid arterial blood temperature. The frequencies at which each of the 0.1°C classes of carotid arterial blood temperature occurred also were determined. An equivalent procedure was used to compare hypothalamic temperature to abdominal temperature, and carotid arterial blood temperature to abdominal temperature.

The proportion of time that the animals spent with the hypothalamus cooler than the carotid arterial blood, the hypothalamus cooler than the abdomen, and the abdomen cooler than the carotid arterial blood was calculated for each animal, in each environment, by counting the number of 5-min observations of body temperature in which that condition was met, and expressing that count as a percentage of the total number of 5-min simultaneous observations of body temperatures.

The effect of rate of change of body temperature on the relationship between carotid arterial blood and hypothalamic temperatures also was assessed. First, the rate of change in carotid arterial blood temperature from one sample to the next (that is, the rate of change in temperature over 5 min) was calculated for the entire data set, for each animal. The difference between hypothalamic and carotid arterial blood temperature for each sample then was calculated, and plotted as a function of the rate of change in carotid arterial blood temperature during the previous 5 min. The relationship for each animal was analyzed using linear regression procedures.

RESULTS

Four days of the original record for one animal, showing the three body temperatures recorded every 5 min during the simulated desert protocol with additional radiant heat, are shown in Fig. 2. Water was removed at 0900 on the second day and returned at 1200 on the fourth day. There was a nychthemeral cycle to each of the temperatures, with a diurnal peak and a nocturnal plateau lasting about 9 h. Withholding water during

![Fig. 2. Nychthemeral changes in hypothalamic, carotid arterial blood and abdominal temperature in an unrestrained female baboon. Five-min simultaneous recordings of body temperatures at the three sites are plotted against time of day, for four days over each of which the ambient temperature was cycled between 15°C at night and 35°C in the middle of the day. In this baboon, radiant heat was added between 1100 and 1400 on each day, raising black globe temperature to 41°C. Water was withheld from 0900 on the second day until 1200 on the fourth day.](http://ajpregu.physiology.org/)

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desert simulation led to an increase in the daily maximum of each of the temperatures. Hypothalamic temperature always was higher than carotid arterial blood temperature (discussed in more detail later), while abdominal temperature tended to be between the other two temperatures.

There was a significant effect of site of temperature measurement on the daily mean body temperatures \( (F_{2,4} = 18.0, P = 0.01) \), no effect of environment \( (F_{2,4} = 2.3, P = 0.2) \), with no interaction \( (F_{4,8} = 1.1, P = 0.4) \). Further analysis of the effect of site, with SNK, showed that the mean hypothalamic temperature was significantly higher than both mean carotid arterial blood temperature and mean abdominal temperature \( (P = 0.01 \text{ and } P = 0.01, \text{ respectively}) \) and the latter two temperatures did not differ significantly from each other \( (P = 0.25) \). There was a tendency for the range of the nycthemeral rhythm of body temperature (maximum minus minimum daily temperature) to increase when the baboons were exposed to heat and deprived of water \( (F_{2,4} = 4.9, P = 0.08) \), but the increased range was the same for each of the three sites of temperature measurement \( (F_{2,4} = 1.3, P = 0.4) \).

In each of the baboons there was a bimodal distribution of carotid arterial blood temperature \( (Fig. 4, D–F) \), each mode reflecting the diurnal and nocturnal plateaus evident in Fig. 2, with a relatively rapid transition between the two. All three baboons exhibited carotid arterial blood temperatures ranging from below 37°C to above 39.5°C, with that of the baboon subjected to additional radiant heat reaching 40.5°C \( (\text{female 1}) \). Over the entire range of carotid arterial blood temperature, and with remarkably little variability, hypothalamic temperature was proportional to, and higher than, carotid arterial blood temperature \( (Fig. 4, A–C) \). The lines showing minimum hypothalamic temperature at each class of carotid arterial blood temperature never are below the line of identity, that is, hypothalamic temperature never was cooler than carotid arterial blood temperature. The 95% confidence intervals of the slopes of regression lines fitted to the relationship between hypothalamic temperature and carotid arterial blood temperature for the three baboons \( (\text{for all animals } P < 10^{-6}, r^2 = 0.98 – 0.99) \) indicate that there was no evidence for selective brain cooling. For baboon \( \text{female 1} \), in Fig. 4, A and D, the regression line was parallel to the line of identity (slope 1.00), and for the other two baboons, the slopes were slightly, but significantly, greater than one \( (1.02 \text{ and } 1.04) \), that is, hypothalamic temperature increased more per unit increase in carotid arterial blood temperature as carotid arterial blood temperature reached the upper limit of its distribution.

Although hypothalamic temperature always exceeded carotid arterial blood temperature, it did not always exceed abdominal temperature \( (Fig. 5) \). For the female baboons, hypothalamic temperature was sometimes below the concurrent abdominal temperature, and at high abdominal temperatures, it was up to 1°C below abdominal temperature in \( \text{female 1} \) \( (Fig. 5A) \), the baboon that reached the highest temperatures. At all body temperatures, the relationship between abdominal temperature and carotid arterial blood temperature was variable. For example, at an abdominal temperature of 38°C, the carotid arterial blood temperature of \( \text{female 1} \) could be as low
as 37.1°C or as high as 38.2°C. The 95% confidence intervals of the slopes from regression analysis indicate that the lines relating hypothalamic temperature to abdominal temperature (for all animals \( P < 10^{-6}, r^2 = 0.92 - 0.96 \)) were significantly less than 1 for two of the three baboons (0.97 and 0.98), and equal to 1 for the third (1.00). Those relating carotid arterial blood temperature to abdominal temperature (for all animals \( P < 10^{-6}, r^2 = 0.92 - 0.97 \)) had slopes significantly less than one for all three baboons (0.92, 0.98, 0.99). Thus, at the higher body temperatures, the abdomen became progressively warmer than the arterial blood.

Hypothalamic temperature sometimes (2.3 ± 2.3% of the time) was lower than abdominal temperature, and the percentage of the time that it was lower did not change with heat exposure or water deprivation (\( F_{2,4} = 0.27, P = 0.8 \)). Abdominal temperature was higher than carotid arterial blood temperature most of the time (81 ± 4% of the time), and the proportion of time that it was higher did not change with heat exposure or water deprivation (\( F_{2,4} = 3.1, P = 0.15 \)).

To test the hypothesis that some of the variability in the difference between hypothalamic and carotid arterial blood temperature was the result of a thermal lag during blood temperature changes, we correlated the rate of change in carotid arterial blood temperature between two subsequent 5-min samples with the difference between the hypothalamic and carotid arterial blood temperatures at the second sample. For each baboon, there was a significant relationship between these variables (for all animals \( P < 10^{-6}, r^2 = 0.06 - 0.10 \)) with a negative slope (−1.30, −1.42, and −1.73 for the three animals). The regression for one female baboon is illustrated in Fig. 6. The regression line shows that when carotid arterial blood temperature was increasing, hypothalamic temperature increased at a slower rate, resulting in a reduction in the difference between hypothalamic and carotid arterial blood.
temperature. Conversely, when carotid arterial blood temperature was decreasing, hypothalamic temperature decreased at a slower rate, resulting in an increase in the difference between hypothalamic and carotid arterial blood temperatures. While the negative association was significant, the coefficient of variability ($r^2$) of the linear regressions revealed that 10% or less of the variance in the elevation of hypothalamic temperature was associated with the rate of change of the temperature of blood entering the brain.

Though the influence of brain thermal inertia on the variance of the elevation of hypothalamic temperature above carotid arterial blood temperature contributed only a small part to that variance, regression analysis (like that in Fig. 6) allows us to eliminate that contribution mathematically. The $y$-intercept of the regression represents the predicted elevation when the rate of change of carotid arterial blood temperature is zero. That equilibrium elevation of hypothalamic temperature above carotid arterial blood temperature averaged 0.51°C for the three baboons, but the 95% confidence intervals of the intercept for the three animals did not overlap. Consequently, at equilibrium, hypothalamic temperature exceeded carotid arterial blood temperature by a significantly different amount in each baboon, ranging from 0.39°C in female 1 and 0.45°C in female 2, to 0.71°C in the male.

**DISCUSSION**

To test the hypothesis that baboons can use selective brain cooling, we have measured brain temperature in the hypothalamus of healthy, conscious, and unrestrained baboons. We believe this is the first time that such measurements have been made in any primate. We reduced the human exposure of the baboons to the minimum compatible with maintaining their welfare in a climatic chamber. The measurements were possible because we employed, for the first time in primates, techniques we have developed to measure body core temperatures, including brain temperature and carotid arterial blood temperature, with implantable miniature data loggers. Baboons were chosen for this study because they are primates that are exposed naturally to aridity and high ambient thermal load on the open plains of Africa, because they evolved sympatrically with early hominids on those plains, and because the arterial supply to their brain and the venous drainage from their scalp is similar to humans (48). The suggestion has also been made (49) that the large muzzle of the baboon may provide an evaporative heat sink for selective brain cooling. We subjected the baboons initially to a benign thermal environment and then to an environment designed to simulate the most extreme conditions of heat and aridity that baboons have been reported to survive naturally, namely, the conditions of the canyon of the ephemeral Kuiseb River of the Namib Desert (5). The implanted thermometric data loggers allowed us to measure, with accuracy of 0.04°C, the temperatures in the hypothalamus, in the free-flowing blood of the carotid artery, and in the abdomen, every 5 min. We obtained more than 3,400 concurrent measurements of those three temperatures in each animal.

Selective brain cooling is defined as the “lowering of brain temperature, either locally or as a whole, below arterial blood temperature” (31). In artiodactyl mammals the anatomical substrate for selective brain cooling is the carotid rete/cavernous sinus complex, where arterial blood destined for the brain loses heat to venous blood returning from evaporative surfaces in the upper respiratory tract. The circumstances in which those animals are most likely to use selective brain cooling are those of high thermal load, hypohydration, and absence of stress from human observers (41). Our baboons, in those circumstances, never exhibited selective brain cooling (Fig. 4), even though the brain temperatures of all three baboons reached 40°C, easily exceeding the threshold at which species with a carotid rete begin to implement selective brain cooling (41). Whatever the time of day, and whatever the conditions to which the baboons were exposed in the climatic chamber, the hypothalamic temperature was higher than the temperature of arterial blood leaving the heart by 0.5°C, on average, over the entire range of arterial blood temperatures that baboons experienced. The elevation of brain temperature above arterial blood temperature arises because the perfusing blood removes the heat produced locally in the brain (43), necessitating a gradient from brain to blood. The highest body temperatures we recorded in the baboons were brain temperatures. One conclusion that can be drawn from our results and the fact that baboons inhabit the Namib Desert is that selective brain cooling is not a prerequisite for desert habitation in mammals.

Though our baboons never exhibited selective brain cooling, their hypothalamic temperatures were below abdominal temperature for about 2% of the time. That phenomenon cannot be interpreted as thermal protection of the brain, since it occurred even when the baboons were at their coolest (Fig. 5, A and B). The only thermal protection afforded to the brain was that afforded to all organs cooled by the perfusion of arterial blood, namely cooling of the venous blood returning to the heart, with consequent cooling of arterial blood leaving the heart. That cornerstone of thermoregulatory responses to heat (8) was evident in the relationship between carotid arterial blood temperature and abdominal temperature (Fig. 5, D–F), which exhibited a slope significantly less than 1. At low body temperatures, carotid arterial blood and abdominal temperatures were similar, but at high temperatures, the carotid arterial blood was cooler than the abdomen. Abdominal organs are the main source of endogenous heat in resting animals, and their
metabolic heat is removed by the perfusing blood. Because the highest body temperatures occurred when the baboons were exposed to an ambient temperature of 35°C or higher (Fig. 2), cooling must have been predominantly evaporative. Evaporative cooling in baboons, as in humans, occurs mainly as surface cooling via sweating (23, 28).

Basic principles of thermodynamics dictate that the temperature of an organ, where the blood reaches thermal equilibrium with the tissue of that organ before leaving it (15), will be determined primarily by the temperature of the blood entering the organ, its flow rate, and the metabolic heat produced by the organ. If the temperature of the blood entering the organ changes, for physical reasons it will take some time for the organ’s temperature to follow, and the faster the change of temperature, the greater will be the phase lag. In their pioneering paper on primate brain temperature, Hayward and Baker (26) cautioned against physiological misinterpretations of internal temperature differences that could be the result of thermal lag. We believe that failure to take account of the lag has induced some researchers to see selective brain cooling in species when none exists (42). We analyzed the consequences of the thermal lag in the brains of our baboons (Fig. 6) and identified an unequivocal, but small, contribution of the lag to the variance of the temperature difference between the hypothalamus and carotid arterial blood. If arterial blood temperature was increasing, the subsequent difference between the brain and blood temperature was smaller. The majority of the variance in that difference remains unexplained and presumably resides in instability of the relationship between brain metabolic heat production and cerebral blood flow (37). Because the instability occurred across the range of hypothalamic temperatures, and irrespective of the external environment, it is unlikely to have arisen from brain heat transfer directly to the environment, or to extracranial blood.

Although no one previously has reported brain temperature in an unrestrained nonhuman primate, brain temperatures have been measured in primates restrained in chairs. As far as we can establish, the first such measurement was hypothalamic temperature in a single, chronically restrained, rhesus monkey (24). Whenever brain temperature and carotid arterial blood temperature have been measured in the same animal (25–27), brain temperature, just as in our baboons, always exceeded carotid arterial blood temperature, and changes in brain temperature paralleled those in carotid arterial blood temperature, with some lag. To the best of our knowledge, therefore, selective brain cooling never has been observed in a primate. Our finding that baboons never implemented selective brain cooling is important for primate ecological physiology, but perhaps more pertinent is the possibility that the physiology of the baboon can inform us regarding the physiology of the human.

Reviews that endorse the ability of both human and nonhuman primates to selectively cool the brain (11, 14) cite the papers of Fuller and Baker (22) and Fuller (21) as evidence. In those papers, hypothalamic temperature was compared with colonic temperature measured 60 mm from the anus, not to arterial blood temperature. We now have confirmed for baboons what already was known for sheep (36), namely, that temperatures measured in the abdomen cannot be used as surrogates for arterial blood temperature. As Baker et al. (3) pointed out, “rectal temperature in a monkey has a variable and unpredictable relationship to central arterial blood temperature”. In our baboons, which never exhibited selective brain cooling, hypothalamic temperature sometimes was lower than abdominal temperature, and the likelihood of hypothalamic temperature being lower than abdominal temperature increased as body temperature rose. Consequently, manifesting a hypothalamic temperature below colonic temperature at high ambient temperature (22) provides no proof that a squirrel monkey can implement selective brain cooling.

Selective brain cooling has physiological advantages, not, as conventionally thought, in protecting the brain during hyperthermia, but in conserving water, by switching heat loss from evaporative to nonevaporative avenues (33, 41). Such a process potentially would benefit baboons in the arid, hot, open plains of Africa, which they inhabit. While baboons, like humans, lack the carotid rete present in artiodactyl mammals (16, 20), there are other potential means of achieving selective brain cooling (43). These are other means of 1) cooling of arterial blood en route to the brain, 2) cooling of the brain by entry of cool venous blood from the overlying skin, and 3) cooling of the base of the brain by evaporation in the upper airways.

Baboon brains derive their blood, as does the human brain, from the internal carotid and vertebralbasilar arteries (35, 48). These vessels, as described for rhesus monkeys, provide “a direct uninterrupted major vascular pathway from the intrathoracic vessels to the circle of Willis” (26). The internal carotids, but not the vertebralbasilar arteries, pass through the cavernous sinuses, venous lakes fed, in part, by veins draining the nasal mucosa and the skin of the head. Venous blood in the cavernous sinuses is therefore potentially cooler than the arterial blood. But the internal carotids curve, without ramification, through the sinuses (35), a configuration that does not allow sufficient heat transfer for appreciable cooling of the carotid arterial blood (55). Outside the sinuses, the trajectories of both the internal carotids and the vertebralbasilar arteries take them antiparallel to the veins draining the superficial tissues of the head and neck, hypothetically, offering a mechanism for countercurrent cooling of the arterial blood. Heat transfer analysis shows, though, that the conformation is such that the influence of these veins on arterial blood temperature is negligible (15, 44). One analysis (56) claimed that the temperature of carotid arterial blood could drop by more than 1°C in the human neck. Although that degree of arterial cooling may be possible if the venous blood was at 19°C (as assumed), such low temperatures have never been reported, and in one of the few direct measures of jugular temperature in humans, it exceeded carotid arterial blood temperature (45).

Brain cooling by venous blood from the head skin need not occur via heat exchange with arterial blood, but could occur directly if emissary veins were to carry the blood through the skull into the brain, a mechanism proposed for hyperthermic humans (12). Baboons, like humans, have emissary veins (48). That proposal invokes a direction change of emissary blood flow during hyperthermia, to enter rather than leave the cranial cavity. Careful Doppler measurement of flow velocity in several emissary veins of healthy hyperthermic volunteers, with their faces fanned, in contrast to the study of Cabanac and Brinrel (12) failed to detect such a direction change; flow always was outward (18). Even if relatively-cool blood did enter the cranium via emissary veins, that blood would influence the temperature of only the most superficial layers of the
brain in humans (7, 50) and in nonhuman primates (26). So, even though the blood flow to the skin of the head increases about three times in hyperthermic baboons (23), that blood can have little or no direct effect on deep brain temperature.

The final hypothetical way by which the baboons could implement selective brain cooling is via evaporation in the upper airways, and conductive cooling of adjacent brain tissue. Such a mechanism also has been proposed for humans (39, 52). However, heat transfer analysis again shows that the capacity of such a mechanism for human brain cooling is negligible (54), a conclusion confirmed by direct measurement of brain temperature during ventilation of the upper airways of brain-injured patients (1), and by analysis of time-dependent latencies in brain stem evoked potentials in healthy volunteers breathing dry air at −1°C (40). Thus, on the basis of evidence from human and other nonhuman primates, contrary to Po-chron (46), the cranial morphology of baboons does not host a selective cooling system for the brain. That conclusion is supported by our observations, which show that baboons cannot control brain temperature independently of carotid arterial blood temperature.

The absence of selective brain cooling in hyperthermic baboons, especially when they were deprived of drinking water, and its absence in reports about other nonhuman primates, seriously undermines the notion that humans can implement selective brain cooling (10, 14). Measurement of brain temperature in healthy hyperthermic humans has not been attempted. The notion that humans have access to selective brain cooling has been proposed along three lines: 1) by inference, from the presence of supposed selective brain cooling in nonhuman primates (11, 14), 2) by experiments that often use tympanic membrane temperature as a surrogate for brain temperature in humans (13, 47, 51, 53), and 3) by direct measurement of brain temperature in patients with brain pathology, having craniostomies for therapeutic reasons (38). Our results directly refute that the first line of argument showing that hyperthermic baboons do not exhibit selective brain cooling. We cannot find convincing evidence that any primate species does so.

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