SELECTIVE BRAIN COOLING DURING HYPERTHERMIA

Selective brain cooling is an attractive idea for protection of the central nervous system against fatigue (17) and potentially cellular damage. Several factors influence fatigue, but brain temperature appears to be of utmost importance for hyperthermia-induced fatigue during prolonged exercise (16). Selective brain cooling is observed in several animal species (10); however, there are no studies that support that humans themselves are capable of selective cooling of the brain; the human airway is not long enough and not connected closely enough to the arterial blood serving the brain to allow air temperature to significantly influence brain temperature. To cool arterial inflow to the brain, there needs to be applied a special apparatus or the use of specific techniques of relevance for treatment of patients during surgery or following clinical disorders.

Selective brain cooling is defined as a lowering of the average brain temperature below that of the arterial blood (19), and the idea that humans are capable of selectively cooling the brain during exercise-induced hyperthermia has arisen from the observation that tympanic membrane temperature may be reduced below the body core temperature (esophageal or rectal), if active cooling is applied to the head (3, 5, 15). Yet tympanic membrane temperature is influenced by the skin temperature of the head and largely unrelated to the temperature of the brain as evaluated by the temperature of the blood leaving the brain through the internal jugular vein (Fig. 2). Therefore, evidence for selective brain cooling based on measurements of the tympanic membrane temperature cannot be accepted.

Brain temperature depends on the metabolic rate of the brain and the amount of heat entering versus leaving the brain via the cerebral perfusion and these factors are not uniformly distributed throughout the brain (17, 21). Consequently, among different areas of the brain the temperature varies and superficial layers of the brain, especially areas close to the nasal cavities, may have temperatures marginally lower than that of
the body core as they are affected by the pulmonary ventilation (13). However, these subdural temperatures are not representative for the average brain temperature, which at rest is ~0.3°C higher than that of the body core and aortic blood (18). To reduce brain temperature, it is most effective to cool the entire body, but lowering the brain temperature may also be introduced by retrograde perfusion of the brain (2), by intracarotid injection of cooled saline (1, 6), or by a bilaterally introduced nasal balloon catheter perfused with cooled water (20). Such interventions are clinically important, e.g., following cardiac arrest and stroke, but it is questionable whether selective cooling of the brain may be achieved by “natural means” in hyperthermic humans during exercise or resting conditions with environmental heat stress.

In freely moving animals, selective brain cooling is commonly observed in species with a carotid rete (10, 14). In contrast, selective brain cooling has never been supported by any direct measurement or valid assessment of the average brain temperature in hyperthermic humans. In animals, selective brain cooling is achieved via precooling of the arterial blood on its passage through the carotid rete as this specialized complex allows for countercurrent heat exchange between the venous network and the arterial blood destined for the brain, but without a rete the ability to cool the arterial blood becomes limited (10). We observed that the temperature of the connective tissue adjacent to the internal carotid artery may be ~2°C lower than the aortic blood temperature during exercise with hyperthermia (18), and this temperature gradient would make it physically possible for arterial blood to release heat during its passage from the heart to the brain (9). However, the transit time of blood within the carotid artery is short, and the blood will not equilibrate with the thermal energy content of the surrounding tissues (7, 8). According to calculations of the cerebral heat balance, it may be concluded that the blood temperature is lowered by <0.09°C on its passage from the body core to the brain (18). This loss of thermal energy is not sufficient to lower the average brain temperature below that of aortic blood (or the body core). The brain is metabolically one of the most active organs in the body and it accounts for 20% of the resting total body oxygen consumption. At rest it has a metabolic rate of ~35 μl O₂·g⁻¹·min⁻¹ (11) corresponding to a cerebral heat production of ~0.6 J·g⁻¹·min⁻¹, and heat balance is established with a jugular venous to arterial temperature difference of ~0.3°C and a cerebral blood flow of ~0.50 ml·g⁻¹·min⁻¹ (18, 21). During exercise-induced hyperthermia, the cerebral metabolic rate increases, whereas cerebral blood flow decreases and the temperature difference between the jugular vein and aortic blood temperature is narrowed to 0.2°C. The latter may relate to the mentioned minimal precooling of the arterial blood during exercise, but it also reflects reduced removal of heat from the brain via the cerebral perfusion (18). As a consequence of the increased heat production and lowered heat removal from the brain, the cerebral temperature increases, and, as seen on Fig. 2, the jugular venous blood, and hence the brain, remains warmer than the body core.

It has been suggested that although selective-brain cooling does not take place in normothermia, it becomes relevant during hyperthermia (4). However, in the study presented in Fig. 2, the jugular venous blood temperature was in all subjects and at all times (including the period with face fanning that restored head skin temperature to normal levels) higher than the esophageal and aortic arch temperatures. This was evident although subjects reached quite high body temperatures; the highest individual core temperature was 40.1°C, with a corres- ponding jugular venous blood temperature of 40.4°C. Similarly, in baboons it has been observed that hypothalamus always remains warmer than carotid arterial blood, despite a brain temperature above 40°C (12).

Finally, it should be considered that the described human studies were conducted in a laboratory with an air temperature of 20°C where hyperthermia was provoked by exercise in water-impermeable clothing, which impaired evaporative heat loss. This implies that the air inhaled by the subjects and the average skin temperature of the head during the period with facial fanning and cooling of the head was much lower than it would be if subjects are exposed to environmental heat stress in a natural setting. Since the average brain temperature remains higher than that of the body core during these conditions, it seems unlikely that humans demonstrate selective brain cooling under any natural circumstances.

REFERENCES

REBUTTAL FROM WHITE, GREINER, AND MCDONALD

Below are our responses to two of the three main arguments presented by Nybo and Secher (7). Their third argument is addressed in our Point contribution, where it was already given that several animals demonstrate SBC without a carotid rete and consequently this countercurrent heat exchanger is not a prerequisite for SBC (1).

Comparison of cranial temperatures in anesthetized humans demonstrated an excellent relationship exists between tympanic (T_{ty}) and directly measured brain temperatures (3). Mariak and colleagues (3) concluded that of the externally accessible body temperatures, “T_{ty} gives the best approximation of average cerebral temperature,” and this result was also supported by a separate group with direct measures of brain temperatures (6). With face fanning of normo- or hyperthermic, nonanaesthetized patients, evidence showed intracranial subdural temperature changes on the convexity of the brain were highly and significantly correlated (r = 0.91, P < 0.05) with T_{ty} changes (5). The facts clearly illustrate T_{ty} is a valid index of human intracranial temperature. It follows we agree with Nybo and Secher’s (7) view that T_{ty} does not follow the external jugular temperature. This is expected for any human extracranial/thoracic temperature that remains above cranial temperatures during hyperthermia (1).

With direct measures of cribiform plate temperatures, human SBC was indisputably demonstrated with only small increases in rate and depth of breathing (4). Recent evidence (reviewed in Ref. 2) with cooling caps, enhanced upper airway cooling, and continuous ventilation of the upper airway each confirm the existence of SBC in humans.

Nybo and colleagues (7, 8) describe cranial heat balance using a black box approach. The heat balance equation they employ (10) includes variables for cranial heat production, cranial blood velocity/flow, and aortic arch to external jugular vein temperature gradients. Although this model appears to support cranial heat balance, at rest it is dependent mainly on heat loss by cranial perfusion (10); during passive or active hyperthermia it is a flagrant oversimplification. During hyperthermia, cranial thermo-regulatory heat loss responses are initiated and these include eccrine sweating, cutaneous vasodilatation, and thermal hyperpnea. These thermoregulatory responses elevate cranial surface evaporative (9), convective/conductive (1), and respiratory heat loss (9). These thermoregulatory responses contribute to the centrifugal decreases of intracranial temperature from the brain ventricles to the subdural space (6). Together the evidence strongly supports that there is significant heat loss from cranial surface that needs to be considered in any cranial heat balance model and in the description of the mechanisms of SBC in hyperthermic humans.

REFERENCES


REBUTTAL FROM NYBO AND SECHER

White et al. mention three mechanisms for selective brain cooling that all represent potential routes for cerebral heat dissipation. However, heat removal through the skull is very limited and both at rest and during exercise with and without hyperthermia the main part of the metabolic heat produced in the brain is released via the venous blood leaving the brain (4, 7, 8). Therefore, the brain temperature is mainly dictated by the cerebral metabolic rate, the cerebral blood flow, and the temperature of the arterial blood. As discussed in the Counterpoint in this debate, ventilation-induced pre-cooling of the carotid blood may increase from rest to exercise, but it should be considered that heat removed via this mechanism is restricted to −0.1 J·g⁻¹·min⁻¹ compared with a total cerebral heat production of −0.6 J·g⁻¹·min⁻¹. Furthermore, our previous evaluation of the cerebral heat balance reveals that <5% of the heat produced by the brain may be removed through the skull (7). White et al. question this assessment of the cerebral heat balance—specifically the reduction in cerebral blood flow during exercise-induced hyperthermia. Yet it has to be acknowledged that the reduction in the perfusion of the brain during exercise with heat stress has been verified by independent techniques (5, 6) and it is well known that cerebral blood flow declines when hyperventilation reduces the arterial P_{CO2} as observed during passive and exercise-induced hyperthermia (3, 9).

When special cooling devices are applied (1) it is possible to create significant cooling of the brain, but in “natural settings,” i.e., resting or freely moving humans the rate of heat loss through the aforementioned mechanisms is limited. It would require unphysiological flow rates and/or temperature gradients.