Point:Counterpoint: Humans do/do not demonstrate selective brain cooling during hyperthermia

POINT: HUMANS DO DEMONSTRATE SELECTIVE BRAIN COOLING DURING HYPERTHERMIA

Selective brain cooling (SBC) is defined by the International Union of Physiological Sciences (11) as “a lowering of the brain temperature either locally or as a whole below arterial blood temperature.” Since the first observations of SBC in hyperthermic, nonhuman mammals (1, 14, 25), there have been efforts to resolve the physiological mechanisms underlying this response (3, 12, 19, 27). It is still hotly debated whether SBC also exists in hyperthermic humans. This contribution is first to give evidence confirming SBC exists in humans, second to outline the mechanisms underlying SBC, third to counter arguments suggesting that SBC is absent in humans, and finally to present a physiological rationale for human SBC.

Evidence of Human SBC

The first evidence of human SBC was in passively heated (5) or exercising (4) humans whose tympanic (Tty) dropped below esophageal (Tes) temperature after face fanning. As reviewed by Cabanac (3), SBC has been repeatedly demonstrated in hyperthermic humans. Recent results in neurosurgical patients with both face fanning and continuous ventilation of the upper airways resulted in cooling of parenchymal brain tissue (10). Although this moderate intervention showed similar reductions in Tes (10), suggesting no SBC, both extubation as well as elevated breathing rate and depth in postoperative neurosurgical patients confirmed the existence of human SBC by giving significant lowering of cribriform plate temperature (16). With a more aggressive cooling cap treatment, Liu and colleagues (13) found evidence of human SBC during a ventriculostomy. Brain temperature was lowered to 33–35°C in 2 h and maintained at this level over 3 days while rectal temperature (Tre) remained between 36.5 and 37.5°C (13). Employing a novel nasopharyngeal coolant spray, Castrén and colleagues (7) observed a 1.5°C drop of Tty within 60 min in cardiac arrest patients before their return to spontaneous circulation. Collectively these studies give evidence confirming the existence of human SBC.

Mechanisms of SBC

Three predominant mechanisms of human SBC include: 1) direct surface heat loss on the cranium, 2) drainage of cooled cutaneous blood from the scalp and face, to allow a countercurrent heat exchange between the intracranial plexus of venous sinuses and internal carotid artery, and 3) thermal hyperpnea-induced heat exchange between the upper airways and the internal carotid artery.

Direct surface cooling. During forced convection, at different submaximal exercise intensities, total direct surface cephalic heat loss in humans was ~200–250 W (21). At an exercise intensity of 150 W (Fig. 1A), the majority of this direct head heat loss was latent or insensible (21). The resulting rise of Tcv was slower than that of Tcw throughout these exercise sessions and this demonstrated a “heat sink” that was directly involved in cranial heat balance and SBC in hyperthermic humans.

Surface cooling and countercurrent heat exchange. Following surface cooling of the cranium during hyperthermia (6), the cutaneous blood drains from the cranial subcutaneous venous plexus to the intracranial plexus of venous sinuses through valveless, bidirectional emissary veins and microscopic anastomoses (Fig. 1B). This cooled venous blood drains to the cavernous sinus and other intracranial venous sinuses to give a countercurrent-induced temperature reduction of the main cranial arterial blood supply in the internal carotid artery.

Thermal hyperpnea. An elevation of human body temperatures has been demonstrated in numerous studies to give a thermal hyperpnea or hyperthermia-induced (as reviewed in Ref. 27). The physiological need for this response remained obscure in hyperthermic humans who mainly employ sweating.
and surface evaporative cooling to regulate their core temperature. In contrast to humans, several mammals employ thermal panting or thermal tachypnea as a primary heat loss mechanism during body warming (22). Respiratory evaporative cooling from their upper airways and nasal cavity cools mucosal venous blood that is drained into the intracranium to provide SBC (12, 19). In humans, thermal hyperpnea provides a parallel avenue of heat loss that contributes to SBC. Mariak and colleagues (16) and others groups (7, 13) directly demonstrated that increases or decreases in upper airway ventilation gave proportional changes of intracranial temperatures and confirmed that thermal hyperpnea provides a third avenue of heat loss for human SBC.

Counterpoints to Human SBC

Tympanic and intracranial temperatures. The use of T<sub>Ty</sub> has been debated as to its validity as an index of human intracranial temperature (12, 19, 20). When properly measured, T<sub>Ty</sub> is a good “global index” of directly measured human intracranial temperature (17). Different groups (15, 18) have demonstrated pronounced intracranial radial temperature gradients that decrease from the third and fourth ventricles to the brain meninges. Taking into account the heat loss from the head (Fig. 1A) and these radial temperature gradients, it appears untenable only to assess human SBC from extracranial aortic arch to and these radial temperature gradients, it appears untenable.

Carotid retre mirabile. Some have suggested (12, 19, 20) that without carotid retre that there is no countercurrent heat exchange in the cavernous sinus and, consequently, human SBC is not possible. Several other mammals, including the rabbit and horse, lack a carotid retre but clearly demonstrate SBC (3). Consequently, lack of a carotid retre does not preclude the existence of SBC in humans or other mammals.

Intracranial blood flow during hyperthermia. Recently, blood flow velocity in the human middle cerebral artery (MCA) was shown to be reduced during hyper- relative to normothermic temperatures (2, 20). The assumption of these results (2, 20) is that the MCA does not dilate during hyperthermia (23). An alternative explanation is that the MCA, and possibly other cerebral arteries and arterioles, dilate during hyperthermia and give increased cranial perfusion (9, 26). Poiseuille’s Law (Q = ΔP·πr<sup>4</sup>/8ηl) for resistance to flow in blood vessels shows a 20% decrease in cerebral blood velocity corresponds to a blood vessel radius increase of only 5%. To maintain a constant arterial-venous temperature difference (20), with increased cranial perfusion, a substantial cranial surface cooling is needed and it is evident (Fig. 1A). It remains to be explained how MCA velocity, and presumably cranial perfusion (2, 20), is reduced in hyperthermic humans if mean arterial blood pressure is maintained (2) and MCA caliber remains constant.

Physiological Benefits of SBC

Recent clinical studies confirm that a rapid cranial cooling gives neuroprotection following traumatic brain injury and during cardiac arrest (8). It is evident, however, from telemetry studies of wildebeest cranial temperatures (12) that a physiologically and psychologically stressed, hyperthermic animal appears to abandon SBC. In contrast, resting but hyperthermic animals appear to selectively cool their brains. By selectively cooling the hypothalamus, humans or mammals sweat or pant less and consequently conserve body fluids. Both neuroprotection and body fluid conservation during hyperthermia are important physiological benefits of SBC.

Conclusions

During hyperthermia, avenues of human SBC include direct cranial surface heat loss, drainage of cooled subcutaneous venous blood to intracranial venous plexuses to give a countercurrent heat exchange with internal carotid artery blood, and upper airway respiratory cooling that helps lower internal carotid artery blood temperature. Recent studies reaffirm the existence of SBC in hyperthermic humans and novel clinical interventions in traumatic brain injured and cardiac arrest patients are providing a venue to further explore the mechanisms underlying this beneficial physiological response.

REFERENCES


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Fig. 2. Esophageal, tympanic, arterial, and jugular venous temperature responses during cycling (n = 7) with a normal core temperature response (A: control) and during a similar exercise bout with progressive hyperthermia (B). Standard deviations are omitted for simplicity, but were in the range of 0.1–0.3°C. Reprinted from Nybo et al. (18) with permission.

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...