Protection of the brain against heat damage

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Abstract In homeothermic animals, metabolic heat production in the brain is higher than in other tissues. However, cerebral tissue is susceptible to heat. Several animals have mechanisms that selectively cool the brain during hyperthermia (i.e., selective brain cooling [SBC]). Carotid retes have been well documented in artiodactyls (hoofed animals) and felids (cats) as mechanisms of SBC. SBC has also been found in some species without carotid retes, such as horses and squirrel monkeys. However, the presence of SBC in humans remains controversial. Brain temperature cannot be directly measured in healthy subjects; therefore, tympanic temperature has been used to estimate brain temperature. However, tympanic temperature is reportedly affected by facial skin temperature. We recently investigated the effect of facial fanning on tympanic and esophageal temperature in normothermic and hyperthermic humans. The results showed that tympanic temperature is not affected by the facial skin temperature under normothermic conditions and that facial fanning may induce SBC under hyperthermic conditions. Regional differences in thermal comfort are present over the body surface in humans, i.e. humans prefer a cool head in the heat and a warm abdomen in the cold. Therefore, preference for a low facial temperature may activate SBC. Several recent studies have demonstrated that whole-brain temperature can be measured noninvasively with proton magnetic resonance spectroscopy. The existence of a thermal gradient within the brain has been suggested. Studies measuring whole-brain temperature will reveal the details of human SBC.

Keywords : brain temperature, hyperthermia, sweat, skin blood flow, behavioral thermoregulation

Introduction

Metabolic heat production in the brains of homeotherms (warm-blooded animals) is higher than in other tissues¹⁾. However, the brain is particularly susceptible to heat²⁾. Some animals have mechanisms that selectively cool the brain during hyperthermia (i.e., selective brain cooling [SBC]). Humans reportedly also have an SBC mechanism, but it remains controversial. In this review, we discuss SBC in animals and humans. We first review earlier studies of SBC and then summarize our knowledge of SBC in humans.

Evidence and mechanisms of SBC in mammals and birds

SBC is defined by the International Union of Physiological Sciences (IUPS) as the “lowering of brain temperature, either locally or as a whole, below aortic (arterial blood) temperature”³⁾. Since the first observations of SBC in hyperthermic cats and goats^{4,5)}, a number of studies on

SBC have been published. SBC has been well documented in animals that have a carotid rete - for example, artiodactyls and felids. According to Jessen⁶⁾, a carotid rete exists at the base of the brain and consists of hundreds of small arteries. Carotid retes arise from the branches of the carotids and merge again to enter the Circle of Willis. The rete is embedded in the cavernous or pterygoid sinus, which receives cooler blood from the mucosal surfaces of the nose. This system is optimized for efficient heat exchange: the large total surface area of the rete arteries can decrease the temperature of arterial blood and the temperature of the whole brain by 2°C or more.

SBC has been observed in dogs, which have a rudimentary carotid rete⁷⁾. SBC has also been documented in some species that lack a carotid rete, such as pigeons⁸⁾, rabbits^{9,10)}, horses^{11,12)}, and squirrel monkeys¹³⁾. Several animals use thermal panting or thermal tachypnea as a heat loss mechanism during body warming^{11,14-17)}. Respiratory evaporative cooling from the upper airways and nasal cavity cools blood in the mucosa that drains into the intracranium to provide SBC. Although horses do not pant, SBC can be suppressed by a tracheostomy¹¹⁾. Thus

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indicating that heat loss from the airways contributes to SBC in horses as well. It has been reported that horses use their guttural pouches to cool the internal carotid artery during exercise¹²⁾. In pigeons SBC is induced by an ophthalmic rete, which functions similarly to the carotid rete: evaporation from the eyes and upper respiratory tract cools venous blood in these areas, which is drained into the ophthalmic rete, cooling the arterial blood supply to the brain⁸⁾. Fuller and Baker observed SBC in squirrel monkeys where, during heat exposure, facial cooling enhances SBC. They speculated that the cooled venous blood from the face, which drains into the intracranial, may be involved in SBC in squirrel monkeys. In rats, the presence of SBC is controversial; positive results obtained during external heat exposure¹⁸⁾ contrast with negative observations during exhaustive exercise¹⁹⁾.

SBC has been considered a mechanism to protect the brain from heat damage. However, several studies have introduced another concept. Kuhnen and Mercer²⁰⁾ have reported that increased sympathetic activity during exercise suppresses SBC in reindeer. Jessen et al.²¹⁾ investigated SBC in black wildebeest in their natural environment and reported that SBC was suppressed during helicopter chases even though brain temperature was near 42°C. If SBC protects the brain from thermal damage, it should be maintained during exercise or flight. Hetem et al. measured the brain and carotid blood temperatures in Arabian oryx (*Oryx leucoryx*) in the deserts of Saudi Arabia, and reported that SBC is enhanced in Arabian oryx compared to other species of the same genus exposed to similar ambient temperatures, but less aridity²²⁾. This suggests that greater SBC may occur in arid environments. Another study demonstrated that dehydrated sheep exhibit greater SBC than when euhydrated²³⁾. In addition, SBC prevents evaporative cooling and reduces water loss in goats during heat stress²⁴⁾. These studies have introduced a new concept that SBC may be a means for preventing dehydration in mammals and birds.

Human SBC

The presence of SBC in humans has also been speculated but remains hotly debated²⁵⁻²⁸⁾. Nybo et al.²⁹⁾ measured temperature in the jugular vein and in the aorta of humans under hyperthermic and normothermic conditions, during exercise, and reported that the temperature of jugular venous blood is always higher than aortic blood, even during a 5-minute facial fanning. Based on these results they concluded that humans are unable to establish SBC. Moreover, other groups also reported a lack of evidence to support human SBC under hyperthermic conditions, during exercise, or hot water immersion measuring the interspike intervals of auditory evoked potentials, which reflects brain stem temperature^{30,31)}. However, Cabanac and Caputa^{32,33)} demonstrated that during facial fanning, the tympanic temperature, which is an index of brain

temperature, is lower than the esophageal temperature in hyperthermic humans during exercise or hot water immersion. Based on these results, they suggested that facial fanning induces SBC in hyperthermic humans.

Proposed mechanisms of human SBC

Although humans do not have a carotid rete and do not pant, perspiration occurs primarily on the forehead and back³⁴⁾. This high rate of perspiration on the forehead region facilitates heat loss.

In addition, a specific circulatory response occurs when humans become hyperthermic. Under normothermic conditions, blood flow through the emissary veins moves outward from within the intracranial to the face or scalp; however, under hyperthermic condition during passive body warming or exercise, blood flow is redirected and moves from the face and scalp into the intracranial. Hence, cooled blood from the skin drains into the intracranial. This mechanism is considered to induce a countercurrent heat exchange between cooled venous blood and arterial blood to the brain in the internal carotid artery³⁵⁻³⁷⁾.

An increase in blood flow to the head skin during hyperthermia may also contribute to human SBC. Under hyperthermic conditions during exercise, central blood flow decreases^{38,39)}; however, head skin blood flow increases⁴⁰⁾. Sato et al.⁴¹⁾ have demonstrated that during exercise, blood flow increases through the external carotid artery immediately in contrast to a reduction in the internal carotid artery. This change results in a large increase in cutaneous blood flow on the head. In addition, the increase in forehead skin blood flow is greater than skin blood flow at the chest, forearm, thigh, and back during exercise⁴⁰⁾. A large increase in blood flow to the head skin during hyperthermia should facilitate heat dissipation from the head area.

Heat loss from the upper airways is also a proposed mechanism of human SBC. Mariak et al.⁴²⁾ determined human intracranial temperature in conscious patients during and after upper respiratory bypass under mild hyperthermic conditions, and reported that extubation from the upper respiratory bypass resulted in an immediate decrease in intracranial temperature at the basal aspect of the frontal lobes. Vasodilation of the nasal mucosa has been observed in passively heated humans⁴³⁾. Moreover, Hirata et al.⁴⁴⁾ have shown that oral respiration induces a higher tympanic temperature than nasal respiration during exercise. These results support the proposal that heat loss from the upper airways is one of the sources of human SBC.

Human SBC and behavioral thermoregulation

The body temperature of homeotherms is regulated by both autonomic effector responses (e.g., vasodilation of the skin and sweating) and behavioral responses. Behav-

iorally, animals seek preferable thermal environments and change postures. "Thermal comfort" is important for behavioral thermoregulation in that it drives an individual to search for the best thermal environment.

Regional differences in thermal comfort over the body surface are present in humans^{45,46} and may also contribute to human SBC. During mild heat exposure, local cooling is most comfortable when applied to the face. Conversely, during mild cold exposure, local warming of the trunk area produced a strong comfort sensation. These preferences would induce humans to cool their heads in the heat and maintain the warmth of the trunk area in the cold. In most studies of proposed human SBC, the effects of brain cooling have been observed during facial fanning^{32,33}. By contrast, SBC occurs without head cooling in many animals. Preference for a low facial temperature and behavioral thermoregulation (e.g., facial fanning) in the heat may contribute to human SBC.

Tympanic temperature as an index of brain temperature

Brain temperature cannot be measured directly in healthy humans; therefore, tympanic temperature has been used to estimate brain temperature. However, the use of tympanic temperature as an index of human intracranial temperature is still debated⁴⁷⁻⁴⁹. Shiraki et al.⁵⁰ have reported that tympanic temperature is affected by facial skin temperature during facial fanning, and did not reflect intracranial temperature measured at the lateral ventricle and white matter above the ventricle of a 12-year-old boy after surgery. On the contrary, other studies have reported that skin temperature has no effect on tympanic temperature^{47,51}. Sato et al.⁵¹ described an accurate method for measuring tympanic temperature. In that study the subjects gently inserted a probe into their ear canals, when the probe-sensor came in contact with the tympanic membrane, slight discomfort is experienced and a scratching noise was heard. The ear probe was then readjusted until the highest stable value was obtained, which was very close to esophageal temperature, after which the ear was covered with a soft rubber pad. In this manner, they reported that tympanic temperature is not affected by skin temperature during head cooling. In addition, Mariak et al.⁴⁹ have reported that tympanic temperature reflected intracranial temperature changes during facial fanning when brain temperature was measured at the subdural space in 14 adult patients after neurosurgery.

We recently investigated the effect of facial fanning on tympanic and esophageal temperatures in normothermic and hyperthermic humans. Under normothermic conditions, forehead skin temperature decreased during facial fanning; however, tympanic temperature did not change with decreased forehead skin temperature and, in fact, remained the same as esophageal temperature. Only under hyperthermic conditions was a difference between tympanic and esophageal temperatures observed. After facial

fanning, tympanic temperature was lower than esophageal temperature (unpublished data). These results suggest that tympanic temperature is unaffected by skin temperature under normothermic conditions and that facial fanning may induce SBC under hyperthermic conditions.

Future prospects

Several recent studies have demonstrated that whole-brain temperature can be measured noninvasively with proton magnetic resonance spectroscopy^{52,53}. The existence of a thermal gradient within the brain has been suggested^{42,54}. Therefore, further studies measuring whole-brain temperature will reveal the details of human SBC.

Conclusions

Human SBC remains controversial. However, our recent study suggested that facial fanning may facilitate human SBC. Further investigations measuring whole-brain temperature will reveal the details of human SBC.

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