CARDIOPULMONARY SUPPORT AND PHYSIOLOGY

SELECTIVE CONVECTIVE BRAIN COOLING DURING NORMOTHERMIC CARDIOPULMONARY BYPASS IN DOGS

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Objective: Although normothermic cardiopulmonary bypass results in improved cardiac outcome, patients do not benefit from hypothermia-mediated brain protection and thus may be at high risk for ischemic brain injury. The present study evaluated the efficacy of selective forced-air cerebral cooling. **Methods:** Sixteen dogs were anesthetized with either intravenous pentobarbital or inhaled halothane ($n = 8$ for each group). Temperatures were monitored in the esophagus (i.e., core), parietal epidural space, and brain parenchyma. Normothermic atrial-femoral cardiopulmonary bypass and forced-air pericranial cooling (to approximately 13°C) were maintained for 150 minutes. Data between groups were compared by means of repeated-measures analysis of variance and two-sample t test. Within each group, brain-to-core temperature gradients were compared to zero by means of the one-sample t test. **Results:** In pentobarbital-anesthetized dogs, after 30 minutes of cerebral cooling, temperatures in the parietal epidural space and 1 cm and 2 cm beneath the dura were $3.3^{\circ} \pm 1.4^{\circ}\text{C}$ (mean $\pm$ standard deviation), $2.6^{\circ} \pm 1.3^{\circ}\text{C}$, and $1.1^{\circ} \pm 0.6^{\circ}\text{C}$ cooler than the core temperature, respectively. At the conclusion of the study (i.e., 150 minutes), these temperatures were $4.5^{\circ} \pm 1.8^{\circ}\text{C}$, $3.9^{\circ} \pm 1.6^{\circ}\text{C}$, and $2.0^{\circ} \pm 0.9^{\circ}\text{C}$ cooler than the core temperature, respectively. Similar changes were observed in halothane-anesthetized dogs. **Conclusions:** Regardless of the background anesthetic, the magnitude of selective cerebral cooling observed in our study was larger than the 1° to 2°C changes previously reported to modulate ischemic brain injury. (J Thorac Cardiovasc Surg 1998;115:1350-7)

Improved surgical technique and myocardial protection during cardiopulmonary bypass (CPB) have significantly reduced perioperative cardiac

morbidity and mortality and overall morbidity and mortality.^{1,2} In an attempt to further improve cardiac outcome, investigators have recently evaluated "warm" or normothermic CPB (i.e., maintaining the core temperature at or near 37°C).³⁻⁶ Using this temperature management strategy, investigators have demonstrated a significant improvement in post-CPB cardiac outcome when compared with traditional "cold" CPB.^{3,6}

Despite major advances in myocardial protection, the number of deaths resulting from CPB-mediated neurologic complications appears to be increasing.^{1,7,8} This is of particular concern in patients undergoing normothermic CPB: that is, patients subjected to normothermic CPB do not benefit from cold-induced brain protection and thus potentially remain at higher risk for CPB-related brain injury resulting from focal ischemia (e.g., gaseous or particulate emboli washed into the cerebral circulation)

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and global ischemia (e.g., as accompanies severe systemic hypotension or cardiac arrest).⁵

Alterations in temperature can affect the brain's ability to survive an ischemic insult.⁹⁻¹³ Specifically, recent investigations have reported mild hypothermia (i.e., a mere 1° to 6° C decrease in temperature) can significantly improve neurologic outcome after focal or global brain ischemia.^{9, 13} The present study evaluated the efficacy of selective forced-air cerebral cooling in a canine model of normothermic CPB.

Materials and methods

All pilot and formal studies were approved by the Institutional Animal Care and Use Committee.

Pilot studies. Before initiating our formal studies, the principal investigator (C.T.W.) designed, in correspondence with Augustine Medical, Inc. (Tom Anderson, Eden Prairie, Minn.), and evaluated the cooling efficacy of three convective helmet prototypes (i.e., soft fabric, air-diffusing coverlets, or "blankets"). Six purpose-bred hounds were studied. Background anesthetics consisted of either high-dose pentobarbital [i.e., an anesthetic known to decrease both cerebral blood flow [CBF] and metabolic rate [CMR]] or halothane (i.e., a cerebral vasodilator having little effect on CMR).

In an established canine model of normothermic CPB and brain temperature monitoring,^{14, 15} maximal forced-air pericranial cooling (i.e., cooling of the environment immediately surrounding the calvarium) was initiated and maintained for 150 minutes (Augustine Medical, Inc., Eden Prairie, Minn., Polar Air). At maximal cooling (i.e., 1000 L/min flow at 10° C), temperature measured (with the use of a flexible thermistor) at the cooling helmet was approximately 13° C. The helmet prototype producing the most efficient cooling profile was subsequently used to conduct the formal studies.

Formal studies. Formal studies were conducted in 16 purpose-bred hounds. All dogs were fasted but had free access to water for a minimum of 8 hours before the study was begun. A forelimb vein was cannulated for fluid and drug administration. After randomization, anesthesia was induced with either pentobarbital 30 mg/kg intravenously ($n = 8$) or halothane 2% to 3% inspired in an induction box ($n = 8$). Once the dog was anesthetized, the trachea was intubated and the lungs were mechanically ventilated (Siemens-Elema AB, Solna, Sweden, model 900C). A tidal volume of 15 to 20 ml/kg was used and the respiratory rate was adjusted to maintain arterial carbon dioxide tension near 35 mm Hg. The inspired oxygen fraction was adjusted to maintain arterial oxygen tension near 150 mm Hg. Inspired and end-expired concentrations of oxygen, carbon dioxide, nitrogen, and halothane were quantified with the use of a Rascal II device (Albion Instruments, Salt Lake City, Utah). Blood gases were measured by means of the alpha-stat (temperature uncorrected) technique (Instrumentation Laboratory Company, Lexington, Mass.; model BGE). Anesthesia was maintained during the preparatory period with additional intravenous pentobarbital or inspired halothane 1.0% to 1.5%. Neuromuscular block was induced and maintained with intrave-

nous pancuronium. The left femoral artery was cannulated percutaneously with a 4.25-inch 18-gauge catheter (Arrow International, Inc., Reading, Pa.) for blood pressure measurements and blood sampling.

With the use of a sagittal incision, the scalp was reflected laterally from the sagittal ridge. Bilateral parietal burr holes, 1 cm in diameter, were created 1.5 cm lateral to the midline and 3.0 cm rostral to the lambdoidal ridge. Via these burr holes, epidural temperatures were measured by inserting catheter-style thermistors (Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio, model 555) 1.5 cm rostral to the anterior margin of each burr hole. Additionally, with the use of the same burr holes, intraparenchymal brain temperatures were measured with needle thermistors (Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio, model 552) inserted perpendicular to the parietal cortex surface, to depths of 1 cm and 2 cm beneath the dura bilaterally. During the pilot studies, we observed that the distal tips of the 1 cm and 2 cm intraparenchymal thermistors were located in subcortical white matter and basal ganglia, respectively. After placement of the intraparenchymal thermistors, the burr holes were sealed with bone wax, and the portion of needle thermistor protruding beyond the dura was thermally insulated with foam tape (3M, St. Paul, Minn., Micro-foam).

Electroencephalographic activity was recorded with the use of gold cup electrodes (Grass Instrument Division, Quincey, Mass., model E-6GH) glued to the calvarium. A bifrontal and biparietal electroencephalogram was recorded with the use of a polygraph and a strip recorder (Grass Instrument Division, Quincey, Mass., model 8-10). So that insensible heat loss from the calvarium could be minimized, the scalp was reapproximated toward midline, without disrupting the trajectory of the intraparenchymal needle thermistors. Any gaps in the suture line were insulated with folded gauze sponges. Before each study, all thermistors were calibrated manually with a mercury thermometer used as a reference.

Core temperature was measured with a flexible vinyl thermistor (Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio, model 401) placed in the esophagus to the level of the right atrium. Thermistor position was confirmed by palpation at the time of thoracotomy.

Preparation for CPB was achieved by modifying previously described techniques.¹⁴ In brief, dogs were placed in the right lateral decubitus position, and a left anterolateral thoracotomy was performed in the fourth intercostal space. Heparin (Elkins-Sinn, Cherry Hill, N.J.) 300 U/kg was administered intravenously before cannulation. A single-stage venous cannula (C. R. Bard, Inc., Murray Hill, N.J., 34F) was inserted into the right atrial appendage. Then, so that insensible heat loss from the thoracic cavity could be minimized, the skin margins of the thoracotomy were reapproximated with multiple perforating towel clips. Arterial cannulation was achieved by inserting a 16F catheter (Sherwood-Davis & Geck, St. Louis, Mo.) into the right common femoral artery. Femoral cannulation was selected to prevent cerebral hyperperfusion associated with inadvertent cannula tip malalignment. A membrane oxygenator-heat exchanger (Medtronic, Inc., Minneapolis, Minn., Maxima), open venous reservoir,

Table I. Control physiologic variables

Variable	Halothane	Pentobarbital
Weight (kg)	22.9 ± 2.6	22.0 ± 2.1
Pao ₂ (mm Hg)	151 ± 9	151 ± 9
Paco ₂ (mm Hg)	36 ± 1	35 ± 2
pH	7.42 ± 0.02	7.43 ± 0.02
MAP (mm Hg)	107 ± 16	95 ± 9
Hemoglobin (gm/dl)	15.2 ± 2.6	14.1 ± 1.8
Temperature (°C)		
Esophageal	38.0 ± 0.1	38.0 ± 0.1
Epidural	38.0 ± 0.2	37.9 ± 0.1
1 cm beneath dura	38.1 ± 0.2	38.1 ± 0.2
2 cm beneath dura	38.2 ± 0.1	38.2 ± 0.2

Values are mean ± standard deviation ($n = 8$ per group). There were no significant differences between groups. *Pao₂*, Arterial oxygen tension; *Paco₂*, arterial carbon dioxide tension; *MAP*, mean arterial blood pressure.

serial arterial filter (Pall Corporation, Fajardo, Puerto Rico), and standard roller pump were used to provide nonpulsatile perfusion. The pump prime consisted of an electrolyte solution (Plasma-Lyte solution, 1000 ml, Baxter Healthcare Corp., Deerfield, Ill.).

Once the preparatory period was complete, the anesthetic dose was adjusted to achieve a steady state. Specifically, barbiturate-anesthetized dogs received incremental pentobarbital in doses of 1 to 5 mg/kg intravenously to achieve and maintain electroencephalographic burst suppression; anesthesia in dogs receiving halothane was maintained at 0.87% end-expired (1.0 minimum alveolar concentration). Additionally, the cooling helmet was carefully placed around the head and neck to avoid movement of the intracranial needle thermistors and accidental hemorrhage in the heparinized dog. Before CPB, core and cranial temperatures were maintained at 38.0° C by means of convection-based surface warming techniques (Augustine Medical, Inc., Eden Prairie, Minn., Bair Hugger). Fine regional temperature control was attained with supplemental heating lamps and pads. The ambient room temperature was maintained near 22° C during the entire study period. Before and during CPB, (1) the oxygen fraction and total gas flows were adjusted to maintain the arterial oxygen tension greater than 100 mm Hg and arterial carbon dioxide tension near 35 mm Hg and (2) sodium bicarbonate was given intravenously as needed to maintain the base deficit at less than 2 mEq/L. Before CPB, the systemic mean arterial blood pressure (MAP) was allowed to spontaneously equilibrate in halothane-anesthetized dogs. Although baseline values were relatively large, no attempt was made to pharmacologically decrease MAP because it remained within the range of autoregulation.¹⁶ In contrast, pentobarbital-anesthetized dogs received an intravenous infusion of phenylephrine (i.e., a systemic vasoconstrictor that does not directly affect cerebral vascular tone or CBF¹⁷) 80 µg/ml to produce an MAP similar to that of the halothane group. During CPB, the MAP was maintained near 75 mm Hg in both groups by means of a phenylephrine infusion as needed.

After a 20-minute stabilization period, normothermic CPB (with flows of 100 ml/kg per minute) and maximal

forced-air pericranial cooling (i.e., approximately 13° C) were initiated simultaneously and maintained for 150 minutes. Mechanical ventilation was terminated after the onset of CPB. During CPB, anesthesia was maintained with either (1) incremental doses of intravenous pentobarbital in an amount sufficient to maintain electroencephalographic burst suppression or (2) 1.0% halothane added to the CPB circuit. Resulting brain temperatures were recorded, and brain-to-core temperature gradients were calculated by subtracting the core temperature from regional brain temperature (derived by averaging right and left values at each brain temperature monitoring site).

At the completion of the study, dogs were put to death with high-dose pentobarbital (Fort Dodge Laboratories, Fort Dodge, Iowa, Sleep Away) and discontinuation of CPB.

Data analysis. Baseline physiologic variables were compared between groups (halothane vs pentobarbital) by means of the two-sample *t* test. Brain-to-core temperature gradients were calculated by subtracting core from regional brain temperature (derived by averaging right and left values at each brain temperature monitoring site). Within each group, brain-to-core temperature gradients were compared to zero by means of the one-sample *t* test. The 30-minute and 150-minute time periods were determined a priori to represent the approximate timing of aortic cannulation and aortic crossclamp release, respectively. Both time periods have been reported to be associated with large embolic loads^{18,19} and, thus, potential brain ischemia. The effect of anesthetic agent (halothane vs pentobarbital) was evaluated by means of a two-factor repeated-measures analysis of variance model with brain-to-core temperature gradient as the dependent variable, anesthetic agent as an independent cross-classification factor, and time as the repeated factor. Separate analyses were performed for each temperature monitoring site. Two-sample *t* tests, comparing temperature gradients for halothane versus pentobarbital at 30 minutes and 150 minutes, were used to supplement these analyses.

Results

Groups were well matched for all systemic physiologic variables at the start of (Table I) and throughout the study period.

In pentobarbital-anesthetized dogs, all brain temperatures began to decrease immediately after the start of selective cerebral cooling (Fig. 1). This trend continued throughout the 150-minute study period (Fig. 1). At all times, forced-air cooling resulted in brain-to-core temperature gradients of the superficial brain loci that were greater than gradients in deeper brain loci. For example, after 30 minutes of cerebral cooling, temperatures in the parietal epidural space and 1 cm and 2 cm beneath the dura were 3.3° ± 1.4° C (mean ± standard deviation), 2.6° ± 1.3° C, and 1.1° ± 0.6° C cooler than the core temperature, respectively ($p < 0.001$ for all intracranial sites) (Table II). At the conclusion of the study

Fig. 1. Brain-to-core temperature gradients in pentobarbital- or halothane-anesthetized dogs undergoing simultaneous normothermic CPB and forced-air cerebral cooling. Temperature of forced air was approximately 13° C. Core temperature was assessed with the use of a flexible vinyl thermistor placed in the esophagus to the level of the right atrium. Regional brain temperatures were measured with thermistors placed bilaterally: (1) in the epidural space, (2) 1 cm beneath the dura, and (3) 2 cm beneath the dura. Resulting brain-to-core temperature gradients were calculated by subtracting core from regional brain temperature (derived by averaging right and left values at each brain temperature monitoring site). Thus a negative value denotes that the cranial measurement site was cooler than the core temperature.

(i.e., 150 minutes), these temperatures were $4.5^{\circ} \pm 1.8^{\circ}$ C, $3.9^{\circ} \pm 1.6^{\circ}$ C, and $2.0^{\circ} \pm 0.9^{\circ}$ C cooler than the core temperature, respectively ($p < 0.001$ for all intracranial sites) (Table II).

Similar changes were observed in halothane-anesthetized dogs (Fig. 1). For example, after 30 minutes of cooling, temperatures in the parietal epidural space and 1 cm and 2 cm beneath the dura were $2.3^{\circ} \pm 0.6^{\circ}$ C, $2.0^{\circ} \pm 0.8^{\circ}$ C, and $0.7^{\circ} \pm 0.4^{\circ}$ C cooler than the core temperature, respectively ($p < 0.001$, $p < 0.001$, and $p = 0.002$, respectively) (Table II). After

150 minutes of cerebral cooling, these temperatures were $3.8^{\circ} \pm 2.3^{\circ}$ C, $3.4^{\circ} \pm 2.4^{\circ}$ C, and $1.5^{\circ} \pm 1.7^{\circ}$ C cooler than the core temperature, respectively ($p = 0.002$, $p = 0.005$, and $p = 0.034$, respectively).

From repeated-measures analysis of variance, the brain-to-core temperature gradients in the parietal epidural space and 1 cm and 2 cm beneath the dura were significantly associated with time ($p < 0.001$ for all three sites). Brain-to-core temperature gradients were not significantly different between anesthetic agents ($p = 0.23$, $p = 0.48$, and $p = 0.27$ for epidural,

Table II. Brain-to-core temperature gradients during normothermic CPB

Time	Pentobarbital (n = 8)		Halothane (n = 8)		<i>p</i> [†]	95% CI [‡]
	Mean ± SD	<i>p</i> [*]	Mean ± SD	<i>p</i> [*]		
30 min						
Epidural	−3.3 ± 1.4	<0.001	−2.3 ± 0.6	<0.001	0.09	−2.1 to +0.2
1 cm	−2.6 ± 1.3	<0.001	−2.0 ± 0.8	<0.001	0.34	−1.7 to +0.6
2 cm	−1.1 ± 0.6	<0.001	−0.7 ± 0.4	0.002	0.11	−1.0 to +0.1
150 min						
Epidural	−4.5 ± 1.8	<0.001	−3.8 ± 2.3	0.002	0.19	−2.9 to +1.4
1 cm	−3.9 ± 1.6	<0.001	−3.4 ± 2.4	0.005	0.64	−2.7 to +1.7
2 cm	−2.0 ± 0.9	<0.001	−1.5 ± 1.7	0.034	0.50	−1.9 to +1.0

*One-sample *t* test comparing mean brain-to-core temperature gradient versus zero.

†Two-sample *t* test comparing mean brain-to-core temperature gradient for pentobarbital versus halothane.

‡Ninety-five percent confidence interval for the difference in mean brain-to-core temperature gradient between anesthetic agents (pentobarbital minus halothane).

1 cm, and 2 cm sites, respectively), and there was no evidence of a significant time-by-agent interaction ($p = 0.76$, $p = 0.94$, and $p = 0.84$, respectively).

There were no significant differences in brain-to-core temperature gradients between groups.

Discussion

The present study demonstrated that, regardless of the background anesthetic, forced-air pericranial cooling significantly decreased brain temperature, independent of core temperature. Further, the magnitude of selective brain cooling observed in our study was larger than the 1° to 2° C change (see below) previously reported to modulate ischemic neurologic injury.

Brain injury after CPB. Patients undergoing CPB-facilitated cardiac operations often have postoperative alterations in neurologic and neuropsychologic function.^{1,2, 5, 7, 8, 18, 19} For example, Mills¹⁹ reported neuropsychologic deficits (i.e., cognitive changes) in 60% to 80% of patients 1 week after coronary artery bypass grafting (CABG) and in 20% to 40% of patients 8 weeks after CABG. He¹⁹ also identified major neurologic deficits (i.e., fatal cerebral injury, stroke, seizures) in up to 6% of patients after CPB. Similarly, in a prospective multicenter study, Roach and associates⁸ evaluated the effect of elective CABG on neurologic outcome in 2108 patients. They reported that 6.1% of patients had major neurologic deficits associated with a (1) fivefold to tenfold increase in in-hospital mortality, (2) twofold to fourfold increase in average length of postoperative hospital stay, and (3) threefold to sixfold increase in discharge to a

skilled-nursing facility or rehabilitation center.⁸ Taken together, neurologic injury is probably the most common source of morbidity and the second most frequent cause of death after cardiac surgery.^{1,7, 8, 19}

Etiology of CPB-related brain injury. CPB-related brain injury is believed to be caused by showers of air and particulate emboli washed into the cerebral circulation (i.e., multifocal ischemia) and low flow states (i.e., global ischemia accompanying severe systemic hypotension or cardiac arrest).^{18, 19}

Changes in temperature management during CPB. Traditionally, hypothermic CPB has been used to protect vital organs, including the brain, from ischemic injury during cardiac surgery. In contrast, a current trend is normothermic CPB.³⁻⁶ Studies evaluating the effect of this temperature management strategy have reported significant improvements of cardiac outcome after cardiac operations.^{3, 6} However, lack of hypothermia-mediated brain protection may predispose this patient population to ischemic brain injury. For example, Martin and associates⁵ compared patients undergoing CABG with moderate hypothermia and those exposed to normothermic CPB. They reported a threefold increase in "total neurologic events" (including stroke) in patients exposed to normothermic CPB.

In response to this limitation (i.e., worsening of neurologic outcome after normothermic CPB), we evaluated a novel, noninvasive approach of providing brain protective therapy while permitting core temperature to remain at normothermia. Selective, rather than whole-body, cooling has the theoretic advantage of providing brain protective therapy

while avoiding adverse changes in systemic physiology (i.e., cardiac arrhythmias, myocardial ischemia, decreased myocardial contractility, coagulopathy, leftward shifting of the oxyhemoglobin dissociation curve, and impaired function of the immune system).²⁰

Hypothermia-mediated brain protection. Recently, numerous studies have demonstrated that mild (i.e., 1° to 6° C) increases or decreases in brain temperature during or immediately after ischemia can significantly worsen or improve, respectively, neurologic outcome after ischemia.¹¹⁻¹³ The most dramatic examples of modulation of ischemic brain injury by small alterations in brain temperature have been reported by Wass,¹¹ Warner,¹² and their colleagues. The former investigators discovered that temperature changes of either 1° or 2° C significantly altered functional and histologic outcome in a canine model of complete cerebral ischemia.¹¹ The latter authors discovered that a change in brain temperature of 1.2° C significantly altered functional and histologic outcome in a rat model of focal cerebral ischemia.¹² Consistent with the animal literature, several groups of investigators have reported a correlation between temperature and neurologic outcome in human beings.⁹ For example, when comparing patients experiencing an ischemic stroke, Reith and colleagues⁹ demonstrated that initial stroke severity, infarct size, functional outcome, and mortality were significantly better in individuals who were mildly hypothermic at the time of hospital admission than in patients who were normothermic. In contrast, fever significantly worsened the neurologic outcome and the mortality rate.⁹ Specifically, for each 1° C increase in body temperature, the relative risk of a poor neurologic outcome increased by a factor of 2.2.⁹

Mechanisms of brain protection by small changes in temperature. The physiologic basis by which small temperature changes produce significant alterations in postischemic neurologic outcome has not been fully elucidated. Proposed mechanisms include alterations in (1) CMR, (2) membrane stability (including the blood-brain barrier), (3) membrane depolarization, (4) temperature-induced ion homeostasis (including calcium fluxes), (5) neurotransmitter release or reuptake (e.g., glutamate or aspartate), (6) enzyme function (e.g., phospholipase, xanthine oxidase, or nitric oxide synthase activity), and (7) free radical production or endogenous scavenging.¹³

Determinants of brain temperature. It has been theorized that brain temperature results from three major factors: CBF (i.e., heat flux between the brain and core), CMR (i.e., endogenous heat production), and heat exchange with the environment.^{13, 21} The significance of each “compartment” has previously been reviewed.¹³

In our study, we pharmacologically altered two of the temperature “compartments” (i.e., CBF and CMR). In the setting of normothermic CPB, we did not observe anesthetics possessing differing effects on CBF and CMR to have a significant effect on brain temperature. This probably indicates that the efficacy of forced-air pericranial cooling was sufficient to overwhelm any differences in brain temperature that may have resulted from the differing pharmacologic profiles of the two anesthetics. We also noted that brain temperature decreased, beginning with the outermost brain layers. This phenomenon has been clearly documented in subjects having either nonischemic^{21, 22} or ischemic²³ brains.

Limitations. We did not quantify changes in brain temperature associated with pharmacologic alteration in CBF or CMR. This may be viewed as a potential study design limitation. However, it was not our intent to quantify changes of brain temperature associated with alterations in each “compartment.” Rather, we simply observed the overall effect of forced-air cooling on brain temperature in dogs anesthetized with two anesthetics having divergent effects on cerebral physiology. Within each group, we observed significant decreases in brain-to-core temperature gradients, indicating that selective forced-air cooling was effective in each group. We did not detect a significant difference in brain-to-core temperature gradients between groups. However, with only eight animals in each group, we cannot make definitive conclusions with respect to differences between anesthetic agents.

In interpreting our results, one should consider several anatomic and physiologic features of the dog model. In our study, the dog model was chosen because its mass and thickness of cranial fat approximated the human condition as well as any nonprimate species. However, the temporalis muscles in the dog are thick, and the calvarium deviates from a spherical shape, thus biasing our study toward a negative result. Potentially offsetting these factors are the facts that the dog brain is smaller than the human brain. Additionally, dogs share with cats, but not human beings, a vascular mechanism that, during panting (i.e., spontaneous ventilation), protects

the brain against overheating during hyperthermia.²⁴ Specifically, evaporative heat loss associated with air exchange in the mouth, nose, and upper airways results in cooling of an intracranial arteriovenous countercurrent heat exchanger known as the rete mirabile.²⁴ The rete mirabile is a vascular network formed by division of the carotid artery into a fine network of arterioles surrounded by the cavernous sinus. In studies evaluating changes in brain temperature in spontaneously ventilating dogs (without tracheal intubation), this may threaten the validity of the resulting data. However, in our studies, mechanical ventilation was terminated at the onset of the study period (i.e., during normothermic CPB). Thus, evaporative heat loss from respiratory mucosa would be negligible, rendering the rete relatively inactive. As evidence for this, the rete (which is small in the dog) is designed to cool the deep brain structure in preference to the superficial brain structures. In our studies, the superficial brain structures were cooler than the deep structures, reflecting that forced-air surface cooling, not the rete mirabile, was predominant in inducing brain-to-core temperature gradients.

Summary

The magnitude of selective brain cooling observed in our study was larger than the 1° to 2° C changes previously reported to modulate ischemic injury. Additionally, the effectiveness of selective cerebral forced-air cooling was observed in both treatment groups and was not associated with differences in brain temperatures resulting from the different pharmacologic profiles of halothane versus pentobarbital. When these observations are extrapolated to human beings undergoing normothermic CPB, we speculate that selective convective brain cooling may enable clinicians to simultaneously improve both cardiac (i.e., resulting from normothermic CPB) and neurologic (i.e., resulting from non-invasive hypothermia-mediated brain protection) outcomes after cardiac operations. In addition to its potential applicability in patients undergoing cardiac operations, we speculate that selective forced-air cerebral cooling may be of benefit in other groups of patients, including those having a stroke or undergoing extracranial cerebrovascular surgery (e.g., carotid endarterectomy).

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