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Direct cooling of the human brain by heat loss from the upper respiratory tract

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MARIAK, Zenon, Matthew D. White, Janusz Lewko, T. Lyson, and P. Piekarski. Direct cooling of the human brain by heat loss from the upper respiratory tract. J. Appl. Physiol. 87(5): 1609–1613, 1999.—This study is the first report on human intracranial temperature in conscious patients during and after an upper respiratory bypass. Temperatures were measured in four subjects subdurally between the frontal lobes and cribiform plate (Tcr) and on the vault of the skull (Tsd). Further measurements were taken in the esophagus (Tes) and on the tympanic membrane. Reinstitution of airflow in the upper respiratory tract under conditions of mild hyperthermia gave a rapid drop in Tcr of 0.4–0.8°C. In three patients the intracranial temperature at the basal aspect of the frontal lobes fell below Tes. Thus local selective cooling of the brain surface below that of the trunk temperature was shown to occur. Intensive breathing by the patients after extubation for a 3-min period produced a cooling at the site of Tcr measurement at a rate of up to 0.1°C/min, and this response could be evoked on demand. The results support the view that cooling of the upper airway can directly influence human brain temperature.

brain temperature; respiratory heat loss; selective brain cooling; human

EVAPORATIVE HEAT dissipation from the outer surface of the head, face, and upper respiratory tract is known to be a significant source of heat loss during whole body hyperthermia (15, 19). It would seem reasonable to expect that this heat loss influences brain temperatures, although the manner and extent to which this is achieved have been the subject of long-standing controversy. One view suggests that it is not only heat loss from the head but also cooled venous blood from the entire body surface that lower the temperature of circulating blood, which, in turn, cools all thermogenic tissues including those of the brain (2, 18). Nevertheless the somewhat controversial notion of selective brain cooling (SBC) has also been proposed. This predicts that venous blood leaving the cooled tissues of the face and scalp finds a more direct venous pathway into the cranial cavity, so that it can, to some extent, cool the brain directly (5, 6, 17). The question of whether SBC in hyperthermia does influence human brain temperature is still open and is not likely to be resolved without direct measurement of intracranial temperature.

The hypothesis of SBC includes a respiratory heat loss component (19), but to date the influence of heat loss from the nasal cavity on brain temperatures has received little attention (22, 23). This is despite the fact that the distance between the roof of the nose and the floor of the anterior cranial fossa is usually only a fraction of a millimeter. This might be a site where respiratory evaporative heat loss does influence adjacent brain temperatures, especially because most of the warming of inhaled air occurs in the uppermost segment of the airways (15).

The main apparent limitation in the research on brain cooling is that all such studies have been based on tympanic temperature (Tty), which is taken as an indirect estimate of brain temperature (5, 6, 22, 23); however, the value of Tty as an index of brain temperature has been seriously questioned (2, 12). Intracranial temperatures are being measured more often after neurosurgery (14, 16) because it has been shown that the ischemic brain is very sensitive to relatively small increases in temperature (4, 7), and this provides the conditions for the study of brain temperatures. To explore how respiratory heat loss might contribute to brain temperature changes, we undertook a study for the monitoring of intracranial temperature. After aneurysm surgery, temperature measurements were made in the subdural space both on the superior aspect (Tsd) and at the base of the frontal lobes close to the cribiform plate (Tcr) in four conscious patients who were intubated and thus had an upper respiratory bypass.

MATERIALS AND METHODS

To study brain temperature during intracranial operative procedures and in the immediate postoperative period, direct measurement of intracranial temperature was carried out in 85 neurosurgical patients during the years 1992–1998 (14). Among these patients, only four subjects provided the opportunity for carrying out this investigation. They were selected from the 85 patients monitored and suffering from a spectrum of intracranial pathologies. Only the four patients mentioned above met the criteria for being closest to a normal physiological state. The pathology in these four cases was a small aneurysm, which did not cause any increase in intracranial pressure; they experienced only a minor subarachnoid hemorrhage (SAH), and, for nonmedical reasons, their operation was delayed by 7–14 days after onset of SAH. All were fully conscious and neurologically intact before and after the procedure.

The ethical approval for this program of brain temperature monitoring was given by the local Ethical Committee of Bialystok University Medical School. Patients were provided with information about the purposes and details of the
investigation and gave their informed consent. No complications occurred in any of the patients examined. The postoperative course of the four was uneventful, and recovery was full.

Equipment. Commercially available copper-constantan thermocouples (Physitemp) were used for the temperature measurements. Flexible, Teflon-coated thermocouples, 0.6 mm in diameter, were used for the measurement of Tsd. Esophageal temperature (Tes) was measured from a thermocouple introduced 0.42–0.46 m below the nares and the rectal (Tre) from a probe placed 50 mm into the rectum. Tty was measured in three subjects with a 0.2-mm thermocouple placed by a laryngologist on the anterior lower quarter of the tympanic membrane (3). The ear canal was filled with cotton. Tty was higher than Tes in all subjects at the beginning of the recording, thus fulfilling the criteria for the correct measurement of Tty (3). The temperatures were calibrated and read with a BAT-10 thermometer (Physitemp) with a precision of 0.1°C and resolution of 0.01°C. All temperature sampling was carried out with a data-acquisition system and computer.

Patients and procedure. Two women and two men, aged between 38 and 55 yr, participated in the study. All experienced a minor SAH due to rupture of a cerebral aneurysm and underwent surgery in our department within 1–2 wk after the SAH incident. Before surgery they were fully conscious and asymptomatic. After general anesthesia had been introduced, thermocouples were applied to measure Tre, Tes, and Tty. The operative procedure consisted of a standard small craniotomy in the frontotemporal region and elevation of the frontal lobe off the skull base. This brought the anterior part of the circle of Willis into view and enabled handling of the aneurysm. At this moment, two sterilized 0.6-mm thermocouples were positioned intracranially. The first thermocouple was positioned on the midline between the cribriform plate and frontal lobes (Tcr) and the second was placed in the subdural space on the vault of the cranium (Tsd). Both probes were secured to the skin with a surgical suture and left in place for 4–16 h postoperatively. In the postoperative recovery room, with the endotracheal tube in place, the patients were covered and passively warmed with a small (0.36 × 0.46-m) heating pad. This was intended to drive them out of typical intraoperative hypothermia into mild hyperthermia, indicated by the first signs of sweating. Intracranial temperatures (Tcr and Tsd), along with the Tre, Tes, and Tty, were recorded before, during, and after removal of the endotracheal tube. In this way the effect of the upper respiratory bypass on intracranial temperatures could be recorded in a conscious subject. After another 50–60 min, while fully conscious and cooperative, the patients were asked to breathe intensively for 3 min at a rate of 18–20 breaths/min with inhalation through the nose and exhalation through the mouth. The temperature of the inhaled air was 22°C.

RESULTS

Continuous data collection could not be started earlier than 15 min after the end of surgery, i.e., after patients arrived in the recovery room and the thermocouples were connected and calibrated. Nevertheless, passive warming was initiated immediately and was maintained throughout the procedure. All patients were mildly hypothermic at the end of general anesthesia, with Tre ranging from 35.8 to 36.6°C. The warming resulted in a steady increase in all core temperatures up to the first signs of sweating, unless a patient showed any signs of intolerance to the endotracheal tube. Before removal of the endotracheal tube, the intracranial temperatures in three of the patients were the highest core body temperatures. The offset between intracranial temperatures and Tes tended to increase from 0.17 ± 0.09°C at the beginning of data collection to 0.27 ± 0.07°C at extubation. At the beginning of data collection, Tcr was within 0.1°C of Tsd, and, up to the

Fig. 1. Time courses of core temperatures before and after removal of endotracheal tube (vertical arrow) in 4 patients (A–D). Restoration of airflow through upper airways causes intracranial temperature at basal aspect of frontal lobes (Tcr) to decrease below that of core trunk temperature, measured in esophagus (Tes), Tre, Tty, and Tsd; rectal, tympanic, and brain convexity temperatures, respectively.
moment of endotracheal tube removal, both temperatures were in line with each other, accompanied by $T_{ty}$ (Fig.1).

Removal of the endotracheal tube deflected the upward course of all core temperatures in all patients with a 10- to 20-min lag, despite maintenance of external warming (Fig. 1). The most striking reaction to extubation, however, was that of $T_{cr}$. This temperature dropped immediately in all cases, reaching its lowest point within a time period ranging from 5.3 to 18 min [mean 9.6 ± 5.7 (SD) min]. The amplitude of this temperature drop ranged from 0.40 to 0.85°C (mean 0.55 ± 0.21°C). The local cooling rate, calculated from these data, ranged from 0.03 to 0.11°C/min (mean 0.07 ± 0.04°C/min). In three of the four patients examined, the drop in $T_{cr}$ was great enough to exceed that of $T_{es}$. In these cases $T_{cr}$ established itself as the lowest core body temperature and remained in this position to the end of the recording time. The one exception was a patient whose temperature record is shown in Fig. 1C, in whom an abrupt fall in $T_{cr}$ was accompanied by a diminution in $T_{es}$ of a similar range. Unlike $T_{cr}$, another intracranial temperature, $T_{sd}$, ran a course parallel to the trunk temperatures, in particular to $T_{es}$ after extubation. As can be seen in Fig. 1, $T_{ty}$ still closely paralleled $T_{sd}$ after extubation.

After stabilization of the temperatures was achieved, the patients were asked to breathe intensively through the nose for 3 min (Fig.2). This intense breathing was immediately followed by decreases in $T_{cr}$, whereas $T_{sd}$ remained relatively constant. $T_{cr}$ reached its minimum value within 3-4.3 min from the start of intense breathing, and the fall in this temperature ranged from 0.20 to 0.30°C, with a mean of 0.26 ± 0.04 (SD)°C. The cooling rate for $T_{cr}$, calculated from these values, ranged from 0.05 to 0.10°C/min, with a mean of 0.07 ± 0.03°C/min. Interestingly, these values closely resemble the cooling rates found after elimination of the upper respiratory bypass.

**DISCUSSION**

These studies demonstrate that removal of the upper respiratory bypass had the potential to break the ascent of the thoracic and intracranial core temperatures during the course of mild passive hyperthermia. Furthermore, the restitution of airflow through the upper respiratory pathways affected the local temperature of basal aspects of the brain, at a rate and amplitude much higher than those exerted on general body temperature.

After removal of the upper respiratory bypass, $T_{cr}$ decreased immediately and in three subjects this temperature fell below $T_{es}$, which, in turn, was generally not affected to the same extent by extubation. In one case, $T_{es}$ and $T_{cr}$ dropped to the same extent after reinstitution of airflow in the upper respiratory tract. Nevertheless, in this patient $T_{cr}$ actually fell below the initial level of $T_{es}$, which was recorded before bypass removal (Fig. 1C). This suggests that, during normal breathing in an ambient temperature of 22°C, the increased heat loss from the nasal mucosa influences the temperature of basal aspects of the brain. Moreover, in mild hyperthermia this influence may be sufficient to cool local parts of the brain, adjacent to the roof of the nose, to below the trunk temperature, as indicated by $T_{es}$. This finding seems to constitute an argument in favor of SBC. To date, the main arguments supporting SBC in humans have concentrated on demonstrating $T_{ty}$ falling below $T_{es}$ in hyperthermic subjects, in whom heat loss from the outer surface of the head was promoted by facial fanning (5, 6). These studies have been contested by those questioning the validity of $T_{ty}$ as a measure of brain temperature (2, 12).

The controversy surrounding SBC in humans is still unresolved (2, 5). This study demonstrates directly for the first time that, under conditions of mild passive hyperthermia, the temperature of the frontobasal brain surface does fall below $T_{es}$, if airflow through the upper respiratory tract is restituted. This finding fulfills the ultimate criterion for demonstrating local SBC. From our data we cannot predict how deep into the brain tissue the effect of cooling may reach. Generally, it may be supposed that warmer arterial blood perfusing the brain will tend to affect this cooling effect within the brain parenchyma.

The possibility that a selective cooling mechanism may affect only some regions of the brain is an option that immanently cannot be discussed on the basis of $T_{ty}$ alone (12). Indeed, it has been suggested that $T_{ty}$ is rather an index of global brain temperature, because it is the venous blood, flowing in the jugular vein from the brain, which is thought to make the thermal link between the brain and the tympanic membrane (3, 6, 17). Our present results demonstrate that such local selective cooling of basal aspects of the frontal lobes can easily be produced by heat loss from the upper respiratory tract in mild hyperthermia. It is worth noting that $T_{ty}$, in the three subjects in whom it was measured, did not reflect this prominent, but apparently local, phenom-
T is also worthy of note that the time course of T
made a good approximation with intracranial temperature at the convexity of the brain, an observation that may add support to arguments favoring the notion of the validity of T
as an index of brain temperature (3, 5, 17, 20).

These results also demonstrate that the human brain may contain substantial temperature gradients, as the difference between the temperature of its convexity and that of the basal aspect of the frontal lobes (T
after extubation reached a value between 0.4 and 0.9°C. This may refer to another point in the controversy surrounding human SBC, in which its contestants targeted one of their arguments at the supposed homogeneous distribution of temperature within the brain (2). Our present finding confirms our previous suggestions, on the basis of indirect estimation of brain temperature, that such gradients do exist in the human brain not affected by intracranial pathology (13).

When a patient breathed intensively for 3 min (Fig. 2), a noticeable decrease in T
ranged from 0.20 to 0.30°C, and corresponding to a local cooling rate of 0.05–0.1°C/min, was easily produced. That the response was localized to regions of the brain adjacent to the cribiform plate was suggested by the demonstration of the relative stability of T
as measured on the vault of the brain. The rate of local brain cooling with intense breathing was similar to the rates found after extubation. Because both of these values are concordant, they may reflect the efficiency of heat exchange between the upper respiratory tract and the intracranial cavity. Such avenues of heat exchange have been suggested by several other studies on the basis of indirect data. It has been shown that the nose alone is the site of the highest resistance met by the stream of inspired air (9), and nasal mucosa has been demonstrated to vasodilate in passive hyperthermia (22).

Hirata et al. (11) showed that oral-only respiration gives a higher T
than does nasal-only respiration. Ventilation has been demonstrated to increase at a greater rate than might be expected to meet the metabolic needs after a threshold of 70–80% of an individual’s maximal work rate has been reached (8). This excess in ventilation was hypothesized to serve thermoregulatory purposes (10) and, even more preciously, SBC (23). Local evaporative cooling of the nasal mucosa is therefore suggested to be the source of the T
change, due to extubation and intensive breathing. Figures 1 and 2 illustrate that, in all instances, the drop in T
was immediate. This supports the possibility that convective rather than conductive heat transfer was responsible for the decrease in T
, especially in view of the fact that numerous venous anastomoses are known to exist between the nasal mucosa and the interior of the skull (21). If the change in temperature was due to conduction of heat, a slower change in T
might be expected.

Brains in a number of mammalian species are selectively cooled during hyperthermia relative to trunk temperatures (1), mainly through respiratory heat loss mechanisms. Until the present study, the influence of respiratory cooling on brain temperature in humans had not been directly demonstrated. To our knowledge, this is also the first time that a decrease in any brain temperature to below that of the trunk (which is the unequivocal criterion for demonstrating SBC) has been demonstrated to occur in unanesthetized humans. These results give direct evidence to support previous suggestions (22, 23) that the human brain can be cooled, at its outer frontobasal aspects, by heat loss to the upper airways.

Conclusions. Unanesthetized, mildly hyperthermic patients, after extubation from upper respiratory bypass procedures and during intensive breathing, demonstrated responses consistent with the hypothesis that heat loss from the airways can directly affect intracranial temperatures in humans.

The outer frontobasal aspects of the human brain in mild hyperthermia can be cooled locally to below the trunk temperature by a mechanism of SBC.

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