Inhalation of warm and cold air does not influence brain stem or core temperature in normothermic humans

IGOR B. MEKJAVIC,1,2 KLEMEM ROGELJ,3 MAJA RADOBULJAC,3 AND OLA EIKEN4

1Institute of Biomedical and Biomolecular Sciences, University of Portsmouth, Portsmouth, Hampshire PO1 2UP, United Kingdom; 2Institute Jozef Stefan and 3Faculty of Medicine, University of Ljubljana, SI-1000 Ljubljana, Slovenia; and 4Department of Aviation Medicine, Swedish Defence Research Agency, Karolinska Institutet, SE-171 77 Stockholm, Sweden

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Mekjavic, Igor B., Klemen Rogelj, Maja Radobuljac, and Ola Eiken. Inhalation of warm and cold air does not influence brain stem or core temperature in normothermic humans. J Appl Physiol 93: 65–69, 2002. First published March 22, 2002; 10.1152/japplphysiol.00873.2001.—The present study tested the hypothesis that inhalation rewarming provides a thermal increment to central neural structures adjacent to the nasopharyngeal region. Auditory-evoked brain stem responses of 14 subjects (7 men and 7 women) were monitored for 25 min while they inspired room air (24°C) followed by hot air (41°C) saturated with water vapor and cold dry air (−1°C). The latencies of peaks I, III, and V and the interpeak latencies (IPLs) I–III, III–V, and I–V were compared among the three conditions with a repeated-measures ANOVA. Changes in IPLs are sensitive markers of changes in brain stem temperature. Tympanic temperature (T\text{ty}) was measured with an infrared tympanic thermometer. There were no significant differences in T\text{ty}, peak latencies I, III, and V, and IPLs I–III, III–V, and I–V. The results indicate that inhalation of hot and cold air does not influence T\text{ty}, nor does it influence the temperature of the brain stem. We conclude that inhalation rewarming is not capable of warming the vital central neural structures adjacent to the nasopharynx.

INHALATION OF WARM SATURATED air was initially proposed by Lloyd and co-workers (14, 15) as a prehospital method for rewarming hypothermic subjects, which could be deployed successfully in the field. Their estimates of heat exchange suggested that the principal benefit of the method was in abolishing respiratory heat loss, rather than donating heat. Despite the initial theoretical (14, 15) and experimental evidence (2) that the method is not capable of donating heat to the core region of hypothermic subjects sufficient to enhance the rate of rewarming, a plethora of studies conducted subsequently have reported that, in hypothermic human subjects, inhalation rewarming increases the rate of rewarming of core temperature and decreases the magnitude of the postexposure drop in core temperature, commonly referred to as the “afterdrop” (5, 10, 11, 23–25). The reported efficacy of inhalation rewarming has been questioned by studies performed in laboratory (2, 17) and in simulated field conditions with ambient air temperature maintained at −1°C (27) and −20°C (22). Both Sterba (27) and Mekjavic and Eiken (22) concluded that inhalation rewarming provided no physiological benefit to hypothermic individuals, but we (22) limited our conclusions to shivering hypothermic subjects. In addition, we suggested that inhalation rewarming might provide local heating of vital structures in the central nervous system.

The recent study of Mariak et al. (18), in which brain temperature was monitored postoperatively in neurosurgical patients, demonstrated that enhanced heat loss in the upper respiratory tract can influence brain temperature as measured subdurally between the frontal lobes and cribriform plate. We postulated, therefore, that not only enhanced heat loss, but also heat gain in the upper respiratory pathways may influence brain temperature. Conceivably, inhalation rewarming, although not capable of providing a significant increment to all core regions of a hypothermic individual, may stabilize brain temperature, or parts thereof, at normothermic levels. The evaluation of this hypothesis was the principal aim of the present study. To achieve an index of brain stem temperature, we adopted the method of Jessen and Kuhnen (12), who monitored the peak and interpeak latencies (IPLs) of auditory-evoked brain stem responses (AEBRs) as a measure of brain stem temperature. Changes in brain stem temperature have been demonstrated to change the latencies and IPLs of AEBRs, such that a 1°C change in nasopharyngeal temperature can cause up to a 200-μs change in IPLs I–V (19). The sensitivity of this method as an index of brain stem temperature has been estimated as 0.4°C (12).

METHODS

In pilot experiments, we attempted to compare the AEBRs in hypothermic individuals rewarmed spontaneously and with inhalation rewarming. Because of the large artifacts

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Address for reprint requests and other correspondence: I. B. Mekjavic, Dept. of Automation, Bioengineering and Robotics, Institute Jozef Stefan, Jamova 39, SI-1000 Ljubljana, Slovenia (E-mail: igor.mekjavic@ijs.si).

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caused by the shivering muscles, particularly the sternocleidomastoideus and masseter muscles, it was not possible to obtain peak latencies I, III, and V, nor the IPLs I–III, III–V, and I–V. We reasoned that, should inhalation rewarming provide a significant thermal increment to the tissue in the nasopharyngeal region, then this should also be observed in normothermic subjects. Assuming that the temperature of the inspired air (T\text{in}) is maintained at 41°C, then the thermal gradient in normothermic subjects (core temperature = 37°C) would be 4°C, and in mildly hypothermic subjects (i.e., core temperature = 35°C), it would be 6°C. Any significant warming effect in the nasopharyngeal region that might be noted in hypothermic subjects should also be observed in normothermic subjects.

Fourteen healthy subjects (7 women and 7 men) volunteered their participation in the present study. Their mean ± SD age was 25.5 ± 5.8 yr. The protocol of the study was approved by the National Ethics Committee (Republic of Slovenia).

Subjects rested semirecumbent on a bed and breathed through an oronasal mask. Air at three different temperatures was delivered to the oronasal mask via corrugated respiratory tubing. All subjects commenced the experiment by breathing air at room temperature (24°C) and relative humidity (RH) (45%) for 25 min. Thereafter, they breathed successively cold dry air (−1°C) and hot air (41°C) saturated with water vapor. Each condition lasted 25 min. The order in which subjects breathed the cold and hot air, after the room air session, was counterbalanced.

Cold inspired air was generated by connecting the inlet side of the oronasal mask to a parallel network of seven 0.7-m-long copper tubes (outer diameter = 6 mm; inner diameter = 4 mm). The tubes were immersed in liquid nitrogen and connected to a compressed air cylinder. The airflow through the tubes was regulated with a Dwyer Instruments (Michigan City, IA) air flowmeter. Once cooled in the copper tube network, the air was directed to a 3-liter insulated polyvinyl bag, and subjects inspired the cooled air from the bag. In this manner, the inspiratory resistance was minimized.

In the condition in which hot air saturated with water vapor was inspired, the inspiratory side of the oronasal mask was connected to a commercially available inhalation rewarming device intended for deployment in field conditions (model HT-200, Electric Heat Treat System, C.F. Electronics, Comack, NY). On inspiration, air passed through an electric steam generator, which maintained the T\text{in} between 41 and 43°C and ensured that it was saturated with water vapor. At the outlet of the steam generator, the air passed through a temperature control valve and water trap. Thereafter, the air was directed via a corrugated hose to a one-way valve connected to the oronasal mask. In the event that the air temperature exceeded 43°C, the temperature control valve was opened sufficiently to maintain the temperature of the air arriving at the oronasal mask at 43°C. In the present study, the air temperature was maintained at 41°C.

In each condition, once 15 min of quiet breathing had elapsed, three successive measurements of tympanic temperature (T\text{ty}) were made with an infrared tympanic thermometer (model 6005, ThermoScan, Braun, Germany) in the left ear. In each of the three conditions, immediately after the measurement of T\text{ty}, AEBRs were recorded during the final 10 min. In both conditions, a thermometer (Tel-Tru, Rochester, NY) mounted on the mask continuously monitored the temperature of the air inside the mask.

An electroencephalogram was recorded from silver-silver chloride scalp electrodes placed on the vertex, left earlobe, and forehead (ground). Electrode impedance was maintained ≤5 kΩ. AEBRs were recorded with a MP100WS data-acquisition system (Biopac Systems, Goleta, CA) comprising an evoked-response amplifier module (model ERS 100A), a single-channel stimulator amplifier (model STM 100), and a Universal Interface module (model UIM 100). The acoustical stimuli were 0.1-msec rarefaction monaural clicks at a rate of 15 Hz and intensity of 70 dB, generated by the single-channel stimulator amplifier and presented to a tube earphone (model TubePhone-ER3A) placed in the right ear. The electroencephalogram was amplified, band-pass filtered (100–3,000 Hz), and recorded at a rate of 50 kHz for 10 ms after the onset of the acoustical stimulus (“click”). Each AEBR represented the average of 2,000 stimuli. For all subjects during each condition, three AEBRs were obtained to evaluate the repeatability of the measurement.

In each condition, the latencies of peaks I, III, and V and interpeak intervals (IPLs) I–III, III–V, and I–V were determined by using the AcqKnowledge Software for the Macintosh computer (Apple Computer, Cupertino, CA).

Group mean values for T\text{ty}, peak latencies for peaks I, III, and V, and interpeak intervals (IPLs) I–III, III–V, and I–V were compared with an ANOVA for repeated measures by using the AcqKnowledge Software for the Macintosh Powerbook G3 computer. The level of significance for the comparisons was chosen as 0.05.

**RESULTS**

For all subjects, T\text{ty} remained stable during the three conditions. Despite a tendency for lower T\text{ty} in the control condition, there were no statistically significant differences in the mean ± SD T\text{ty} for the three conditions (Table 1).

For every subject in each condition, the observed peaks I, III, and V and IPLs I–III, III–V, and I–V were identical for the three successive AEBRs recorded. Only the third AEBR (recorded at minute 20) was used for subsequent analyses. The group-averaged AEBRs for the three conditions are presented in Fig. 1. As evident, there were no significant differences in the latencies of peaks I, III, and V among the three conditions (T\text{in} = 24, −1, and 41°C). Also, the latencies among peaks (IPLs) I–III, III–V, and I–V were similar for the three conditions, as shown in Table 1.

**DISCUSSION**

In euthermic subjects, inhalation of either hot moist air or cold dry air did not influence auditory-evoked brain stem potentials. On the basis of findings that a 0.4°C change in brain stem temperature would be detected as a change in IPL I–V (12, 19), the implication of the present results is that, in resting subjects, inhalation of either −1°C dry air or 41°C air saturated with water vapor is not capable of initiating sufficient heat exchange in the nasopharyngeal area to affect any significant local cooling and warming, respectively. Contrary to earlier observations (5, 10, 11, 23–25), core temperature was not affected by subjects breathing either warm or cold air via an oronasal mask.

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Auditory-evoked Brain Stem Potentials as an Indicator of Core Temperature

The hypothesis of the present study, that the $T_{in}$ affects brain stem temperature, was tested by comparing the latencies of the AEBRs while subjects inspired either hot or cold air. As such, the underlying assumption of the present study was that changes in brain stem temperature alter somatosensory-evoked potentials (20, 26). On the basis of observations that hyperthermia (3, 13) and hypothermia (19, 28) significantly change the IPLs of AEBRs, we postulated that any regional change in tissue temperature, as a consequence of hot and cold air inhalation, would be reflected in the AEBR. Our observation of no change in the IPLs of the observed AEBRs in the three conditions suggests that inhalation of cold or hot air does not influence brain stem temperature.

**Table 1. Individual interpeak latencies I–III, III–V, and I–V and tympanic temperatures as a function of inspired air temperature in the 3 experimental conditions**

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Control (24°C)</th>
<th>Cold Air (−1°C)</th>
<th>Hot Air (41°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPL, ms</td>
<td>IPL, ms</td>
<td>IPL, ms</td>
</tr>
<tr>
<td>1</td>
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</tr>
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<td>2.48</td>
<td>1.60</td>
<td>4.08</td>
</tr>
<tr>
<td>4</td>
<td>2.78</td>
<td>1.63</td>
<td>4.40</td>
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<td>1.70</td>
<td>3.93</td>
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<td>1.63</td>
<td>4.28</td>
</tr>
<tr>
<td>8</td>
<td>2.20</td>
<td>1.75</td>
<td>3.95</td>
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<tr>
<td>9</td>
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<td>1.70</td>
<td>4.35</td>
</tr>
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<td>4.30</td>
</tr>
<tr>
<td>11</td>
<td>2.20</td>
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</tr>
<tr>
<td>12</td>
<td>2.25</td>
<td>1.73</td>
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<td>2.40</td>
<td>1.93</td>
<td>4.33</td>
</tr>
<tr>
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<td>2.15</td>
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<td>3.98</td>
</tr>
<tr>
<td>Average</td>
<td>2.40</td>
<td>1.80</td>
<td>4.19</td>
</tr>
</tbody>
</table>

IPL, interpeak latencies; T<sub>Tty</sub>, tympanic temperature.

**Inhalation Rewarming of Hypothermic Individuals**

Inhalation rewarming was initially introduced by Lloyd and co-workers (14, 15) as a field method to aid in stabilizing hypothermic victims, principally by abolishing respiratory heat loss. They estimated that the total amount of heat donated by their inhalation rewarming device was 1.2 kcal·m<sup>−2</sup>·h<sup>−1</sup>. The main benefit of an inhalation rewarming device was its ability to minimize respiratory heat loss, which, according to their estimates, can range from 8 to 9 kcal·m<sup>−2</sup>·h<sup>−1</sup>. Animal experiments conducted by Lloyd et al. (16) and Auld et al. (2) confirmed the notion that inhalation rewarming does not improve the rate of rewarming of hypothermic animals. Auld et al. reported that it took, with or without inhalation rewarming, 12 h to return hypothermic animals that were given muscle relaxants to abolish shivering to normal temperature. In contrast, in the spontaneous rewarming condition, with shivering present, animals rewarmed within 2 h. Despite this elegant demonstration of the inability of inhalation rewarming to influence the rate of rewarming of hypothermic animals, numerous later studies conducted on human subjects reported significant benefits of inhalation rewarming therapy, either in minimizing the postexposure decrease in core temperature (commonly referred to as the afterdrop) or in enhancing the rate of rewarming (1, 5, 8–11, 23–25). These reported benefits of inhalation rewarming compared with spontaneous rewarming have been questioned by several studies, which have evaluated the method in thermoneutral laboratory conditions (17) and in simulated field conditions with ambient air at 1°C (27) and −20°C (22). Sterba (27) observed no physiological benefits of inhalation treatment and thus concluded that its use was unwarranted in the prehospital treatment of hypothermia. We (22) concurred with the find-

![Fig. 1. Average auditory-evoked brain stem response (AEBR) for the 3 experimental conditions. The latencies of peaks I–VII are indicated at the top of the graph.](image-url)
lings of Sterba (27) but limited our conclusions regarding the ineffectiveness of inhalation rewarming to the shivering hypothermic subject.

Several factors must be taken into consideration when evaluating inhalation rewarming.

**Heat donation.** The amount of heat donated to an individual at a given body temperature by inhalation rewarming will depend on the temperature and RH of the inspired air and minute ventilation. Optimally, the $T_{in}$ should be 43°C (higher temperatures are perceived as painful), and it should be saturated with water vapor. The efficiency of inhalation rewarming decreases with decreasing temperature and water vapor content of the inspired air, such that, at $T_{in} = 40^\circ$C and RH = 70%, there is no heat donation: only respiratory heat loss is eliminated (24). Under optimal conditions, the amount of heat donated to the core may be increased by increasing ventilation. This was demonstrated by Morrison et al. (24), who observed significantly higher levels of heat donation, also reflected in the rate of rewarming of hypothermic subjects, when their ventilation was maintained at 40 l/min by increasing the end-tidal $PCO_2$. However, it is questionable whether such hyperventilation is a plausible means of increasing heat transfer to a hypothermic individual in an “open-field scenario.”

**Inhibition of shivering.** Any calculation of the benefit of inhalation rewarming should account for the amount of heat production inhibited by inhalation rewarming. Namely, inhalation of hot moist air via an oronasal mask will provide a warm stimulus to the trigeminal region of the face and nasopharyngeal region, and application of warm stimuli to these regions has been demonstrated to inhibit shivering (21). Because the heat donated by inhalation rewarming is only a fraction of the endogenous heat generated by shivering thermogenesis, inhalation rewarming may inhibit a greater amount of heat production than it is able to donate (22).

**Warming of central neural structures.** It has been speculated that, other than increasing core temperature, the potential benefit of inhalation rewarming may be the warming of central neural structures, such as the brain stem, medulla, and hypothalamus (22). These regions contain neural foci responsible for temperature regulation and cardiovascular and respiratory function, and maintaining them at normal temperatures will most likely minimize any hypothermia-induced dysfunction of these physiological systems. However, the present results indicate that no such warming was evident during inhalation of hot moist air, suggesting that the method is not capable of donating significant amounts of heat to this region.

**Inhalation Cooling of Hyperthermic Individuals**

The impetus for the present study was primarily to evaluate whether inhalation rewarming is capable of donating heat to structures adjacent to the nasopharyngeal region, specifically the brain stem. However, increased heat loss from the upper respiratory tract has been reported to initiate direct cooling of the brain (18), evidenced by a drop in the temperature between the frontal lobes and cribiform plate and the vault of the skull and also reflected in decreased $T_{sk}$. In fact, inhalation of cold dry air has even been suggested as a method for improving physical performance in the heat by reducing the exercise-induced elevation in core temperature (7). Consequently, we also tested the hypothesis that increased respiratory heat loss may reduce body core and/or local brain stem temperature.

Our finding that $T_{sk}$ and AEBRs were similar in all three conditions suggests that, during quiet breathing, inhalation of cold air does not affect body core or brain temperature nor the temperature of local neural structures adjacent to the nasopharynx. These results are in agreement with the findings of Deklunder et al. (6) and Jessen and Kuhnen (12), who have found no evidence to support the theory that selective brain cooling may occur in humans as proposed by Cabanac and Caputa (4).

That the neural structures adjacent to the nasopharynx are relatively insensitive to a substantial drop in airway temperature may, to a large extent, be attributed to the high-specific heat of the water lining the upper respiratory tract compared with the specific heat of dry inspired air (29). Water lining the respiratory tract acts as a thermal reservoir, such that most of the heat exchange occurs between the inspired air and the water lining the mucosa. This minimizes the heat lost from the tissues surrounding the upper airways and hence prevents thermal damage to these structures.

The present study demonstrates that varying $T_{in}$ by 42°C does not influence brain stem temperature and that inhalation rewarming is not an efficient means of reviving brain stem and hypothalamic function in hypothermic individuals.

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