Neither Arm nor Face Warming Reduces the Shivering Threshold in Unanesthetized Humans

Anthony G. Doufas, MD, PhD; Anupama Wadhwa, MD; Chun-Ming Lin, MD; Yunus M. Shah, MD; Keith Hanni, BS; Daniel I. Sessler, MD

Background and Purpose—Hand warming and face warming, combined with inhalation of heated air, are reported to suppress shivering. However, hand or face temperature contributes only a few percent to control of shivering. Thus, it seems unlikely that manipulating hand or facial skin temperature alone would be sufficient to permit induction of therapeutic hypothermia. We tested the hypothesis that focal arm (forearm and hand) warming or lower facial warming, combined with inhalation of heated and humidified gas, only minimally reduces the shivering threshold (triggering core temperature).

Methods—We studied 8 healthy male volunteers (18 to 40 years of age) on 3 days: (1) control (no warming), (2) arm warming with forced air at $43^\circ$C, and (3) face warming with 21 L/min of air at $42^\circ$C at a relative humidity of 100%. Fluid at $4^\circ$C was infused via a central venous catheter to decrease tympanic membrane temperature 1°C/h to 2°C/h; mean skin temperature was maintained at $31^\circ$C. A sustained increase in oxygen consumption quantified the shivering threshold.

Results—Shivering thresholds did not differ significantly between the control ($36.7 \pm 0.1^\circ$C), arm-warming ($36.5 \pm 0.3^\circ$C), or face-warming ($36.5 \pm 0.3^\circ$C; analysis of variance, $P=0.34$) day. The study was powered to have a 95% probability of detecting a difference of $0.5 \pm 0.5^\circ$C (mean $\pm$SD) between control and either of the 2 treatments at $\alpha=0.05$.

Conclusions—Focal arm or face warming did not substantially reduce the shivering threshold in unanesthetized volunteers. It thus seems unlikely that these nonpharmacological modalities will substantially facilitate induction of therapeutic hypothermia. (Stroke. 2003;34:1736-1740.)

Key Words: body temperature regulation ■ shivering

Overwhelming evidence in animals indicates that even mild hypothermia provides substantial protection against cerebral and myocardial ischemia. Mild hypothermia has been shown to improve outcome after cardiac arrest in humans, and major randomized outcome trials are in progress to evaluate the potential benefits of mild hypothermia during aneurysm clipping and after stroke or acute myocardial infarction. Many of these studies target core temperatures between $33^\circ$C and $34^\circ$C.

Induction of hypothermia during surgery is relatively easy because anesthetics profoundly impair thermoregulatory responses. However, use of therapeutic hypothermia in stroke patients may be compromised because tiny reductions in core temperature trigger aggressive thermoregulatory defenses, even in stroke victims. Shivering is the most powerful autonomic cold defense in humans. This has led to a search for treatments that impair shivering without causing excessive toxicity. Many drugs inhibit shivering, but most are general anesthetics or major sedatives. For example, the combination of buspirone and meperidine significantly reduces the shivering threshold (triggering core temperature); however, meperidine doses sufficient to reduce core temperature to $33^\circ$C may be associated with respiratory toxicity.

An alternative to pharmacological treatment of shivering is surface warming. For example, Sweney et al recently reported that focal hand warming suppresses shivering in mildly hypothermic volunteers. The same group also reported that shivering can be suppressed by warming of the lower face, combined with inhalation of heated and humidified air. Others have also reported that facial warming reduces shivering, as does radiant heating of the face and upper chest.

The difficulty with these observations is that treatments reducing the shivering threshold only a couple tenths of a degree centigrade may be sufficient to attenuate shivering. Treatments that only slightly reduce the shivering threshold may appear to be effective in volunteers or postoperative patients but may be completely inadequate for...
induction of therapeutic hypothermia. Skin temperature contributes ≈20% to autonomic control of shivering, with the remainder being derived from core temperature. However, the arms and face are a small portion of the total skin surface. It thus seems unlikely that manipulating hand or facial skin temperature alone would impair thermoregulatory responses sufficiently to permit induction of therapeutic hypothermia. Therefore, we tested the hypothesis that focal arm warming or lower facial warming, combined with inhalation of heated and humidified gas, only minimally reduces the shivering threshold.

Methods
With approval of the Human Studies Committee at the University of Louisville and informed consent, we studied 8 healthy male volunteers. None was obese, was taking medication, or had a history of thyroid disease, dysautonomia, or Raynaud’s syndrome.

Protocol
The volunteers fasted 8 hours before each study day. They were minimally clothed and rested supine on a standard operating room table. Ambient temperature was maintained at ≈22°C. Each volunteer was studied on 3 days: (1) control (no warming), (2) lower-arm warming (forearm and hand), and (3) face warming. Each study day was separated by at least 48 hours.

The arm warming apparatus consisted of 2 forced-air warming units (Bair Hugger, Augustine Medical, Inc) set to high (≈43°C), each attached to an upper-body coverlet that was wrapped into a muff surrounding each forearm and hand. Face warming was achieved by injection of 21 L/min air at ≈42°C at a relative humidity of 100% into a continuous positive airway pressure mask, which was tightly fitted around the volunteer’s face (Respironics). Air was warmed and humidified with a Vapotherm (Vapotherm, Inc).

A central catheter was introduced into the superior vena cava via an antecubital vein and used for cold-fluid infusion. Throughout the study period, mean skin temperature was maintained at 31°C, excluding the warming sites, by adjusting the temperature of circulating-water (Cincinnati Sub-Zero) and forced-air warmers. Furthermore, the back, upper body, and lower body were individually maintained at the designated skin temperature. On each day of the experiment, core cooling started 20 minutes after arteriovenous shunt vasocostriction was documented (defined below).

Lactated Ringer’s solution, cooled to ≈4°C, was infused at rates sufficient to decrease tympanic membrane temperature 1°C/hr to 2°C/hr because these rates are not associated with induction of dynamic thermoregulatory responses. Fluid was given until the shivering threshold was identified.

Measurements
Heart rate was measured continuously with an ECG; blood pressure was determined oscillometrically at 5-minute intervals from the left ankle. A pulse oximeter continuously determined arterial oxygen saturation.

All temperatures were recorded with Mon-a-therm thermocouples (Mallickrodt Anesthesiology Products, Inc). Core temperature was recorded from the tympanic membrane. Volunteers inserted the aural probe until they felt the thermocouple touch the tympanic membrane; appropriate placement was confirmed when volunteers easily detected gentle rubbing of the attached wire. The aural canal was occluded with cotton; the probe was securely taped in place; and a gauge bandage was positioned over the external ear.

Mean skin surface temperature was determined from 15 area-weighted sites. On the arm-warming day, lower-arm and hand temperatures were excluded from the calculation of mean skin temperature; similarly, facial temperature was excluded from the calculation of mean skin temperature on the face-warming day. Air temperature inside the mask was measured by a thermocouple hanging freely within the mask space, whereas facial skin temperature was measured by a thermocouple attached to the volunteer’s cheek.

Temperatures were recorded from thermocouples connected to calibrated Iso-Thermex 16-channel electronic thermometers having an accuracy of 0.1°C and a precision of 0.01°C (Columbus Instruments International, Corp). Individual and mean skin temperatures were computed by a data acquisition system, displayed at 1-second intervals, and recorded at 1-minute intervals.

Arteriovenous shunt vasomotor tone was evaluated with forearm-minus-fingertip and calf-minus-toe skin temperature gradients. There is excellent correlation between skin temperature gradients and volume plethysmography. Vasoconstriction was defined by a forearm-fingertip skin temperature gradient >0°C.

Shivering was quantified by oxygen consumption measured by a DeltaTrac (SensorMedics Corp) metabolic monitor; the system was used in canopy mode. Measurements were averaged over 1-minute intervals and recorded every minute. End-tidal PCO₂ was measured with an Ultima monitor (Datex), and exhaust gases from this monitor were returned to the oxygen consumption monitor.

Data Analysis
On each study day, hemodynamic, respiratory, ambient temperature, and relative humidity data were averaged for each volunteer across the cooling period; these values were then averaged for all volunteers. A sustained increase in oxygen consumption (V˙ O₂) of ≧30%, as determined by a blinded investigator, identified the shivering threshold. The baseline for this analysis was the steady-state value (±5% variation in V˙ O₂) before core cooling had started.

Results on the 3 study days were compared by use of repeated-measures analysis of variance (ANOVA) and Dunnett’s posthoc tests. Results are expressed as mean±SD; differences were considered statistically significant at P<0.05.

Results
The volunteers were 28±3 years old, weighed 81±10 kg, and were 175±7 cm tall. One volunteer dropped out of the study after the control and arm-warming days.

Ambient temperature, relative humidity, mean arterial pressure, heart rate, respiratory rate, average end-tidal PCO₂, and SpO₂ were similar on each study day (Table 1). Mean skin temperature was maintained at ≈31°C. Per protocol, all volunteers were vasoconstricted before the cold-fluid infusion started. Air temperature inside the continuous positive airway pressure mask on the face-warming day averaged 38.6±1.4°C (Table 2).

Arm warming reduced the shivering threshold by 0.2±0.3°C, from 36.7±0.1°C to 36.5±0.3°C. Face warming reduced the shivering threshold by 0.1±0.3°C, from 36.7±0.1°C to 36.5±0.3°C (the Figure). The value for ANOVA across all 3 treatments was P=0.34, so posthoc comparisons were not undertaken. This study achieved a 95% power to detect a 0.5°C difference between the control threshold and either of the treatment thresholds at α=0.05.

Discussion
The extent to which induction of core hypothermia will prove therapeutic in stroke victims remains unknown. Results in animals, though, are overwhelmingly positive and indicate that 3°C to 4°C of hypothermia provides better protection than existing pharmacological treatments. Uncontrolled human studies are also encouraging.

Arm or face warming reduced shivering thresholds by only ≈0.2°C. Neither of these decreases was statistically significant (although we had 95% power to detect 0.5°C changes),
and neither decrease was clinically important. Our data thus fail to support the proposal of Iaizzo et al.15 that “this cooling paradigm holds promise as a means for the induction of mild hypothermia which may enhance cerebral protection in individuals at risk of brain injury.”

The theory behind using cutaneous warming to treat shivering is that both skin and core temperatures contribute to control of thermoregulatory responses. Warming the skin surface reduces the core temperature that triggers shivering. However, skin temperature contributes only 20% to steady-state control of shivering.24,25 Furthermore, the extremities are relatively insensitive to thermal manipulation.31,32 Hand temperature in the 2 studies was presumably similar. However, we warmed both the hands and forearms rather than the hands alone. The forearm and hands constitute 10% of the total skin surface area and were warmed 6°C. We would thus expect that hand warming would reduce the shivering threshold only ~0.1°C, which is entirely consistent with our results.

Thermal sensitivity of the upper chest and face is greater than that of the remaining skin surface.31,32 Furthermore, there are substantial regional differences within the face.33 We warmed the face and airway by injecting 21 L/min air at ~42°C at a relative humidity of 100% into a tightly fitted mask. This increased facial temperature by 2.6°C. In contrast, Iaizzo et al.15 used air at 32°C with 55% humidity and failed to report facial skin temperature. The difficulty with using facial warming to ablate shivering is that the surface area of the face is tiny, perhaps only 4.5% of the total skin area. It thus seems unlikely that facial warming alone would markedly reduce the shivering threshold. The extent to which oropharyngeal and airway thermal receptors contribute to control of shivering remains unknown. However, our results do not suggest that warming facial skin and airway receptors produces clinically important inhibition of shivering.

A critical difference between our study and previous similar ones14,15 is that we quantified the shivering threshold rather than simply observing a short-term reduction in shivering intensity. Thus, although Sweney et al.14 and Iaizzo et al.15 found that acute application of hand or face warming reduced shivering in nearly normothermic volunteers, we observed only trivial reductions in the steady-state shivering threshold. The most likely explanation is that unlike sustained warming, rapid increases in skin temperature provoke powerful dynamic responses.34 Thermoregulatory response thresholds35,36 and thermal sensation37–39 depend not only on static temperatures but also on the rate at which temperatures change. For example, rapid changes in skin temperature markedly augment cutaneous contribution to the sweating threshold35,36 and improve thermal sensation during hyperthermia.38 The magnitude of dynamic thermoregulatory response to facial warming remains unknown but may be even greater than for the skin surface as a whole.

Rapid increases in skin temperature ameliorate shivering.17–19 A brief reduction in shivering intensity might well facilitate performing a neurological examination, as proposed by Sweney et al.14 Nonetheless, therapeutic hypothermia must be maintained for hours or days and thus represents a thermal steady state. Therefore, the steady-state conditions of our study may best represent the typical clinical situation. Our results suggest that neither lower-arm nor face warming will prevent shivering over the period needed for therapeutic hypothermia.

### Table 1. Potential Confounding Factors

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Arm Warming</th>
<th>Face Warming</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient temperature, °C</td>
<td>22.0±1.4</td>
<td>23.2±1.5</td>
<td>23.4±1.9</td>
<td>0.085</td>
</tr>
<tr>
<td>Relative humidity, %</td>
<td>41±7</td>
<td>40±4</td>
<td>42±5</td>
<td>0.083</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>102±7</td>
<td>106±10</td>
<td>98±14</td>
<td>0.521</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68±12</td>
<td>64±11</td>
<td>69±13</td>
<td>0.079</td>
</tr>
<tr>
<td>SPO2, %</td>
<td>99±1</td>
<td>98±5</td>
<td>100±1</td>
<td>0.466</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>16±2</td>
<td>16±4</td>
<td>16±2</td>
<td>0.697</td>
</tr>
<tr>
<td>End-tidal Pco2, mm Hg</td>
<td>41±4</td>
<td>41±3</td>
<td>35±7</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Values were first averaged over the infusion period in individual volunteers and then averaged among the volunteers. Data are presented as mean ± SD.

### Table 2. Values at the Shivering Threshold

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Arm Warming</th>
<th>Face Warming</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lactated Ringer’s, L</td>
<td>1.2±0.9</td>
<td>1.4±1.2</td>
<td>1.3±0.6</td>
<td>0.581</td>
</tr>
<tr>
<td>Core cooling rate, °C/h</td>
<td>1.3±0.3</td>
<td>1.4±0.3</td>
<td>1.4±0.4</td>
<td>0.754</td>
</tr>
<tr>
<td>Facial skin temperature, °C</td>
<td>34.2±0.4</td>
<td>34.2±0.6</td>
<td>36.8±0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arm skin temperature, °C</td>
<td>28.8±1.9</td>
<td>35.1±0.9</td>
<td>28.9±2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean skin temperature, °C</td>
<td>30.9±0.1</td>
<td>31.0±0.1</td>
<td>31.0±0.1</td>
<td>0.731</td>
</tr>
<tr>
<td>Shivering threshold, °C</td>
<td>36.7±0.1</td>
<td>36.5±0.3</td>
<td>36.5±0.3</td>
<td>0.377</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.
Individual values (○) for shivering thresholds on the 3 experimental
tabular format. Mean ± SD (●) for each day is also indicated. Thresh-
olds did not differ significantly on the 3 treatment days.

Our volunteers were much younger and healthier than stroke victims, and temperature sensitivity is linearly depend-
on age,40 with older people having a reduced cutaneous
thermal sensitivity and a reduced thermal perception during
heating.

Because skin temperature contributes 20% to control of
vasoconstriction and shivering,24 each 1°C decrease in mean
skin temperature increases the shivering threshold ≈0.2°C. Mean
skin temperature was kept constant at a low value throughout
our study to increase the threshold, thereby
minimizing risk from infusion of large amounts of cold fluid.

A limitation of our study is the use of tympanic membrane
temperature as an indicator of core body temperature during
face warming. Previous work suggests that tympanic mem-
brane temperatures can be artifactually elevated during
head43,44 or facial 15,45,46 skin warming. However, the observed
differences between tympanic and esophageal temperatures
were tiny. Even small inaccuracies in our temperature mea-
surements would not obviate our major finding that physical
warming fails to induce useful amounts of thermoregulatory
tolerance.

In summary, we found that neither lower-arm nor facial
warming substantially reduces the shivering threshold in
unanesthetized volunteers. It thus seems unlikely that either
nonpharmacological intervention will contribute meaning-
fully to induction of therapeutic hypothermia.

Acknowledgments

Funding was received from the Outcomes Research Institute and
Departments of Anesthesiology and Pharmacology, University of
Louisville, Louisville, Ky; Department of Anesthesiology, Chang
Gung Memorial Hospital, Taipei, Taiwan; and the Ludwig Boltz-
mann Institute, University of Vienna, Vienna, Austria. This work
was supported by Augustine Medical, Inc (Eden Prairie, Minn), NIH
grant GM 58273 (Bethesda, Md), and the Commonwealth of
Kentucky Research Challenge Trust Fund (Louisville). Mon-a-therm
thermocouples were kindly provided by Tyco-Mallinckrodt Anes-
thesiology Products, Inc (St Louis, Mo). The facial and airway
heating system was generously donated by Vapotherm, Inc (Annap-
olis, Md). We thank Gilbert S. Haugh, MS, and Nancy L. Alsip, PhD,
for statistical and editorial assistance.

References

1. Popovic R, Linger R, Pickler PE. Anesthetics and mild hypothermia


3. Due MW, Gao DW, Sessler DI, Chair K, Stoltenhoff CA. Effect of endo-
vascular cooling on myocardial temperature, infarct size, and cardiac

4. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G,
Smith K. Treatment of comatose survivors of out-of-hospital cardiac

5. Group THACAS. Mild therapeutic hypothermia to improve the neuro-

1730–1737.

7. Lopez M, Sessler DI, Walter K, Emerick T, Ozaki M. Rate and gender
dependence of the sweating, vasoconstriction, and shivering thresholds in

8. Zweifler RM, Sessler DI, Zivan JA. Thermoregulatory vasoconstriction
and shivering impede therapeutic hypothermia in acute ischemic stroke

9. De Watte J, Sessler DI. Perioperative shivering: physiology and pharma-
cotherapy. Anesthesiology. 2002;96:467–484.

10. Annadata RS, Sessler DI, Tayefeh F, Kurz A, Dechert M. Desflurane
slightly increases the sweating threshold, but produces marked, non-linear
decreases in the vasoconstriction and shivering thresholds. Anesthe-

11. Matsukawa T, Sessler DI, Sessler AM, Schroeder M, Ozaki M, Kurz A,
Cheng C. Heat flow and distribution during induction of general anes-

Christensson R. Meperidine decreases the shivering threshold twice as
much as the vasoconstriction threshold. Anesthesiology. 1997;86:
1046–1054.

13. Mokhtarani M, Mahgob AN, Morioka N, Doufas AG, Sessler DI.
Buspirone and meperidine synergistically reduce the shivering threshold.

14. Sweny MT, Sigg DC, Tahvildari S, Iaizzo PA. Shiver suppression using
2001;150:1089–1095.

15. Iaizzo PA, Jeon YM, Sigg DC. Facial warming increases the threshold for

16. Mekjavic IB, Eiken O. Inhibition of shivering in man by thermal stimu-

17. Murphy MT, Lipton JM, Loughran P, Giesecke AH Jr. Postanesthetic
shivering in primates: inhibition by peripheral heating and by taurine.

18. Sharkey A, Lipton JM, Murphy MT, Giesecke AH. Inhibition of postan-

19. Sharkey A, Gulden RH, Lipton JM, Giesecke AH. Effect of radiant heat
on the metabolic cost of postoperative shivering. Br J Anaesth. 1993;70:
449–450.

comparably decreases the thermoregulatory thresholds for vasocon-

21. Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C.
Dexmedetomidine does not alter the sweating threshold, but comparably
and linearly reduces the vasoconstriction and shivering thresholds. Anes-
thesiology. 1997;87:835–841.

22. Delaunay L, Bonnet F, Duvaldestin P. Clonidine decreases postoperative
oxygen consumption in patients recovering from general anaesthesia. Br J

Esch J. Phystostigmine prevents postanesthetic shivering as does

Olofsson P. Increasing mean skin temperature linearly reduces the core-
temperature thresholds for vasoconstriction and shivering in humans.


Neither Arm nor Face Warming Reduces the Shivering Threshold in Unanesthetized Humans
Anthony G. Doufas, Anupama Wadhwa, Chun-Ming Lin, Yunus M. Shah, Keith Hanni and Daniel I. Sessler

Stroke. 2003;34:1736-1740; originally published online May 29, 2003;
doi: 10.1161/01.STR.0000077014.47422.DB
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/34/7/1736

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/