

# Shiver Suppression Using Focal Hand Warming in Unanesthetized Normal Subjects

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**Background:** A decrease of 1 or 2°C in core temperature may provide protection against cerebral ischemia. However, during corporeal cooling of unanesthetized patients, the initiation of involuntary motor activity (shiver) prevents the reduction of core temperature. The authors' laboratory previously showed that focal facial warming suppressed whole-body shiver. The aim of the current study was to determine whether the use of hand warming alone could suppress shiver in unanesthetized subjects and hence potentiate core cooling.

**Methods:** Subjects (n = 8; healthy men) were positioned supine on a circulating water mattress (8–15°C) with a convective-air coverlet (14°C) extending from their necks to their feet. A dynamic protocol was used in which focal hand warming was used to suppress involuntary motor activity, enabling noninvasive cooling to decrease core temperatures. The following parameters were monitored: (1) heart rate; (2) blood pressure; (3) core temperature (rectal, tympanic); (4) cutaneous temperature and heat flux; (5) subjective shiver level (SSL scale 0–10) and thermal comfort index (scale 0–10); (6) metabolic data (n = 6); and (7) electromyograms.

**Results:** During cooling without hand warming, involuntary motor activity increased until it was widespread. After subjects reported whole-body shiver (SSL ≥ 7), applied hand warming, in all cases, reduced shiver levels (SSL ≤ 3), decreased electromyographic root mean square amplitudes, and allowed core temperature to decrease from 37.0 ± 0.2 to 35.9 ± 0.5°C (measured rectally).

**Conclusions:** Focal hand warming seems to be valuable in minimizing or eliminating the need to suppress involuntary motor activity pharmacologically when it is desired to induce or maintain mild hypothermia; it may be used in conjunction with facial warming or in cases in which facial warming is contraindicated.

It has been observed that the level of intracerebral brain temperature markedly influences the consequences of cerebral ischemia and that a mild reduction of core temperature by 1 or 2°C may confer significant cerebral protection.<sup>1,2</sup> Furthermore, it was reported in a study relating body temperature to stroke severity that infarct size and mortality were lower, and thus, outcomes were better, in patients who were mildly hypothermic at the time of admission to the emergency center.<sup>3</sup> Consistent with these findings, others reported the potential benefits of postischemic hypothermia in global ischemia. Specifically, Zimmerman *et al.*<sup>4</sup> showed that after an episode of

ischemia, 57% of hypothermic dogs survived *versus* only 25% of normothermic dogs; furthermore, the hypothermic dogs tended to have a better functional outcome. Clinically, it has also been shown that in patients with acute stroke, the occurrence of fever during the first 7 days was associated with a higher risk of death in the first 10 days, and it was concluded that patients with higher temperatures had worse stroke outcomes.<sup>5</sup> Mild hypothermia has also been shown to prevent intracranial pressure increases within patients in whom these pressures remain higher than 20 mmHg but less than 40 mmHg.<sup>6</sup>

During active cooling in unanesthetized subjects, involuntary motor activity (muscle tensing and shiver) is initiated as a normal thermoregulatory response that prevents induction of hypothermia. *Shivering* has been specifically defined as involuntary rhythmic muscular contractions used to maintain normal core temperature (homeostasis).<sup>7</sup> Studies have shown that shivering can be induced through various types of afferent stimuli. For example, a reduction of skin temperature from 33°C to 30°C, despite a brain temperature of 38°C, has been shown to initiate shiver.<sup>8</sup> In another study, it was observed that humans placed in a 10°C environmental chamber for a period of 15–40 min experienced intense shiver despite the fact that their core temperatures stayed the same or even slightly increased.<sup>9,10</sup>

Recently, surface cooling has been used to induce mild hypothermia in patients admitted to an emergency setting within several hours of stroke onset.<sup>11</sup> However, for this therapy to be effective, meperidine was administered to treat shivering.<sup>11</sup> Previous studies have shown that radiant thermal stimulation to the facial area helps to inhibit shiver during cold-air exposure.<sup>12,13</sup> In a recent study reported by this laboratory, it was shown that the application of warm, humid air to the lower facial area (and thus airways) increased the shivering threshold of unanesthetized patients.<sup>12</sup> However, in certain situations, application of warm air to the face is not desirable (*e.g.*, facial lacerations, patients with severe facial trauma), requiring other nonpharmacologic means of suppressing involuntary motor activity. It was the aim of the current study to further investigate such a focal warming effect on the control of thermoregulation and specifically to test the hypothesis that hand warming could be used to suppress shiver in unanesthetized subjects.

## Methods

### Subjects

These studies were approved by the Committee on the Use of Human Subjects in Research at the University of

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**Table 1. Morphometric Data of Eight Healthy Men**

Subject	Age	Height (cm)	Weight (kg)	Somatotype
1	24	175	75	Ecto/Meso
2	24	175	75	Ecto/Meso
3	27	188	78	Mesomorph
4	30	170	70	Mesomorph
5	25	186	91	Ecto/Meso
6	24	173	72	Ecto/Meso
7	43	188	83	Ecto/Meso
8	25	164	50	Ectomorph
Mean	27.8	177.4	74.3	—
SD	6.5	9.0	11.9	—

Body type categorized as ectomorph, mesomorph, or endomorph.

Minnesota (Minneapolis, MN). All subjects signed a consent form before participating in these studies. Eight experimental trials (cooling sessions) were performed using a subject pool of eight healthy male volunteers, aged 24–43 yr, without any known medical conditions. Particularly, they had no history or signs suggestive of a thyroid disorder and were not taking medications or drugs (table 1). All subjects were asked to refrain from eating or ingesting caffeine for 7 or 8 h and from exercising for 24 h before the experimental session. Basic morphometric measurements were recorded for each volunteer, including height, weight, age, and relative body type. The body type of each volunteer was categorized according to its appearance as endomorph (fat body type), ectomorph (lean body type), or mesomorph (muscular body type), which are classifications of the human body according to the Sheldon somatotype<sup>14</sup> (table 1).

### Monitoring

Cutaneous T-type heat flow sensors (Concept Engineering, Old Saybrook, CT) were used to measure skin surface temperatures and heat fluxes at the right cheek, right chest, right abdomen, right thigh, right forearm, and right index finger. A weighted average of the skin temperatures was used to calculate the mean skin temperature (MST) using the following equation<sup>15</sup>:

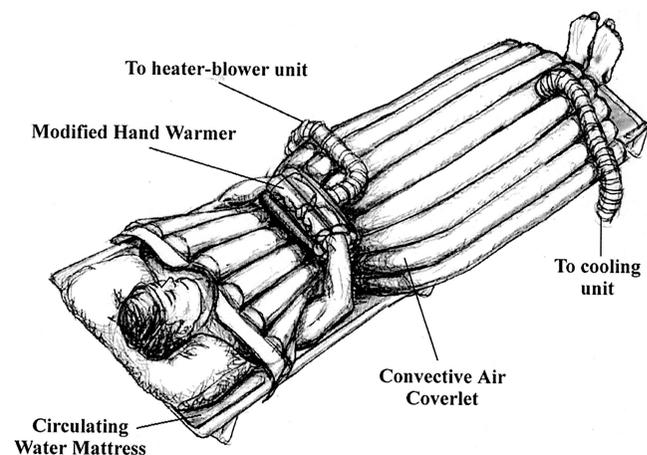
$$\begin{aligned} \text{MST} = & 0.14 \text{ cheek temp} + 0.19 \text{ chest temp} \\ & + 0.19 \text{ abdomen temp} + 0.32 \text{ thigh temp} \\ & + 0.11 \text{ lower arm temp} + 0.15 \text{ finger temp} \end{aligned}$$

Thermocouples at rectal and tympanic sites were used to assess changes in core temperature. The rectal temperature probe (Mon-a-therm<sup>®</sup> General Purpose Critical Care Temperature Probe; Mallinckrodt Medical, Inc., St. Louis, MO) was inserted 12–15 cm into the rectum. A tympanic-type thermocouple (Mon-a-therm<sup>®</sup> Tympanic, Mallinckrodt Medical, Inc.) was positioned adjacent to the tympanic membrane. All temperatures were continuously and automatically acquired every 10 s using a

Fluke Hydra<sup>®</sup> data acquisition unit (model 2620A; John Fluke Manufacturing Co. Inc., Everett, WA) with an accuracy of 0.1°C. Subsequently, the temperature data were sorted and processed with a Macintosh Quadra 650 computer, using a program written in Labview<sup>®</sup> 2.2.1 (National Instruments, Austin, TX).

Blood pressure and heart rate were measured noninvasively at 5-min intervals using a cuff and monitoring system (Datascope Accutone2A<sup>®</sup>; Datascope Corp., Paramus, NJ). The hand-warming apparatus consisted of an air-warming unit (BairHugger<sup>®</sup>; Augustine Medical, Inc., Eden Prairie, MN) set to  $43 \pm 5^\circ\text{C}$  and attached to a body-warming coverlet (Augustine Medical, Inc.) to form a forced-air hand muff (fig. 1). Throughout the experimental session, an index of shiver and comfort level was obtained. Volunteers provided periodic subjective evaluations of both shiver magnitude and comfort level, respectively. The shiver scale ranged from 0 to 10; a score of 0 indicated no involuntary motor activity, 10 indicated maximal shiver, and 7 indicated uncontrollable whole-body shiver. The comfort scale also ranged from 0 to 10; level 0 indicated extreme cold discomfort, level 10 indicated extreme heat discomfort, and level 5 indicated a neutral comfort. These scales rely on the previous experiences of each individual, much in the same way as analog scales for pain assessment, and were identical to those used in the previous facial-warming study.<sup>12</sup>

Surface electromyograms were recorded from four muscle groups from each subject, which included cheek (masseter), chest (pectoralis major), abdomen (rectus abdominis), and thigh (rectus femoris). All signals were amplified using a Grass amplifier (Grass Medical Instruments, Quincy, MA) and were recorded on a VCR-based digital recorder (Vetter model 4000A pulse code modulation unit; AR Vetter, Rebersberg, PA). Subsequent determination of the root mean square (RMS) amplitudes of individual electromyographic signals was accomplished by using Labview<sup>®</sup> 2.2.1 software. In addition, compos-



**Fig. 1. Rendering of hand-warming apparatus used during trial.**

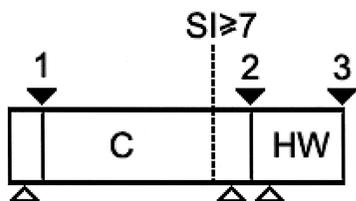


Fig. 2. Schematic diagram representing experimental protocol. C = convective/conductive cooling period;  $SI \geq 7$  = onset of uncontrolled whole-body shiver; HW = hand warming period; 1 = onset of active cooling ( $t = 0$ ); 2 = application of hand warming; 3 = removal of heating and cooling apparatus.

ite RMS values were derived by averaging together those from the chest, abdomen, and thigh.

Oxygen consumption ( $\dot{V}O_2$ ) and carbon dioxide production ( $\dot{V}CO_2$ ) were measured using a metabolic unit (KB1-C; AeroSport, Ann Arbor, MI), based on a galvanic fuel cell ( $\dot{V}O_2$ ) and on nondispersive infrared analysis ( $\dot{V}CO_2$ ) technologies.

#### Experimental Protocol

After initial physical assessments, volunteers were placed supine between a circulating-water-cooled mattress (Cincinnati Subzero Products, Inc., Cincinnati, OH) maintained at 8–15°C and a prototype convective-air cooling coverlet (PolarAir; Augustine Medical Inc.). Air was supplied to the coverlet by a refrigeration-cooled, air heat exchanger unit which was set to provide an air flow rate of 1,400 l/min and an air temperature of 14°C. Each experiment was based on a dynamic protocol similar to that used by Iazzo *et al.*<sup>12</sup> in which whole-body cooling was applied from time = 0 (fig. 2 and table 2). Thereafter, cooling continued until the subject indicated that a subjective shiver level of 7 had been reached.<sup>12</sup> After reaching this level, the modified hand warmer was applied, allowing warm air to be blown on the entirety of both hands up to the wrist. Metabolic data was obtained ( $\dot{V}O_2$ ,  $\dot{V}CO_2$ ; see previous paragraph) for 5- to 6-min intervals at three time points throughout six of the eight trials. The time points were as follows: (1) before cooling; (2) during uncontrolled whole-body shiver; and (3) during hand warming (fig. 2). Results for each were normalized to assess general trends in metabolic rate

throughout the trial. The experiment was continued until either shiver returned despite warming ( $n = 2$ ) or the subject asked to stop because of bladder discomfort (cold-induced diuresis;  $n = 6$ ). After completion of an experiment, the cooling was stopped, and the subject was rewarmed using a heater-blower unit (BairHugger® model 250).

#### Statistical Analysis

Statistical analysis of the data was based on Student *t* tests, linear regression for paired data, Wilcoxon matched-pairs signed-rank test, and the Friedman test (repeated-measurements analysis of variance with the Dunn multiple comparison posttest) for nonparametric data (normalized data, shiver scales, comfort levels). Statistical significance was inferred if  $P \leq 0.05$ . All reported values are given as mean  $\pm$  SD.

#### Results

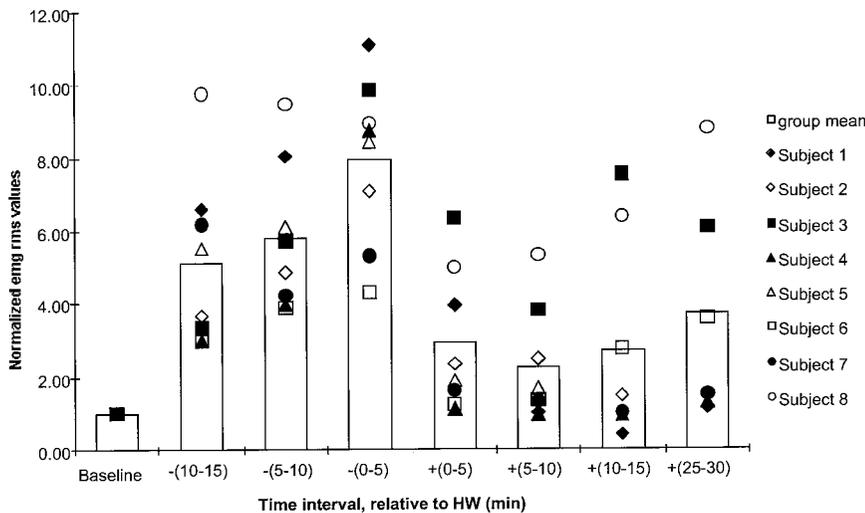
Subjects' physical measurements are provided in table 1. The somatotypes of subjects were categorized according to their appearance as ectomorph, endomorph, or mesomorph. In general, the subjects were quite fit with a well-defined muscle mass and thus could effectively produce heat *via* involuntary motor activity.

In all cases, there was a significant difference between average composite electromyographic RMS values 5 min before and after hand warming ( $n = 8$ ;  $P < 0.01$ ). Pooled data indicated a 63% reduction in normalized electromyographic RMS values after hand warming was initiated (HW + 5) compared with the values obtained 5 min before hand warming (HW - 5), with levels of  $8.1 \pm 2.4$  and  $3.0 \pm 2.1$ , respectively (fig. 3). Also in each trial, subjective shiver index decreased from  $6.3 \pm 0.5$  (5 min before hand warming) to  $1.6 \pm 1.9$  ( $n = 8$ ;  $P < 0.01$ , Wilcoxon test), and subjective comfort level increased from  $1.8 \pm 0.7$  to  $3 \pm 0.5$  ( $n = 8$ ;  $P < 0.05$ , Wilcoxon test) 15 min after the application of hand warming.

Rectal temperature data were considered to provide the most accurate indication of core temperature, with mean baseline ( $t = 0$ ) temperature at  $37.0 \pm 0.2^\circ\text{C}$  and

Table 2. Duration of Warm Air Application and Time until Shiver Initiation and until Warm Air Application

Subject	Time until Shiver Initiation (min)	Time until Warm-air Application (min)	Duration of Warm-air Application (min)	Notes
1	40	113	37	Metabolic information recorded
2	105	162	28	Metabolic information recorded
3	1	128	31	—
4	5	122	43	Metabolic information recorded
5	15	131	20	Metabolic information recorded
6	5	100	65	Metabolic information recorded
7	5	56	61	—
8	1	34	137	Metabolic information recorded
Mean	21.89	104.5	52.75	—
SD	36.05	41.25	37.44	—



**Fig. 3.** Normalized composite electromyographic (emg) root mean square (rms) values averaged over 5-min increments (HW - 15 to HW + 15), in addition to HW + (25-30). Composite electromyographic values were determined by averaging chest, abdomen, and thigh locations. Composite values were then normalized with baseline readings to yield a percent value. The application of focal hand warming significantly decreased involuntary muscle activity for the subsequent 15-min interval.

significantly lower mean final temperature at  $35.9 \pm 0.5^\circ\text{C}$  ( $n = 8$ ;  $P < 0.01$ ). Tympanic temperatures were slightly more erratic, possibly because of patient movement and environmental effects (although in all cases, the probes were well-insulated within the ear),<sup>16</sup> and yielded a significant decrease from a mean  $t = 0$  temperature of  $36.8 \pm 0.5^\circ\text{C}$  to a mean final temperature of  $35.8 \pm 0.6^\circ\text{C}$  ( $n = 8$ ;  $P < 0.01$ ). The identified cooling rates were nearly the same for the rectal and tympanic temperature measurements. MST showed a progressive and significant decrease throughout the course of the experiment, with a pooled mean baseline temperature of  $35.1 \pm 0.9^\circ\text{C}$  and a mean final temperature of  $28.6 \pm 1.9^\circ\text{C}$  ( $n = 8$ ;  $P < 0.01$ ).

Rectal cooling rates were determined for each experimental block for the 15 min before and after hand warming. Analysis showed that there were no significant differences in cooling rates. Heart rates and blood pressures did not differ significantly throughout the experimental protocols.

Because of the subject-to-subject variance in whole-body-cooling times and hand-warming durations, the normalized time periods for analyses were selected as 15 min before hand warming (HW - 15) and the 15 min after hand warming (HW + 15; table 2). These intervals were selected to isolate the immediate physiologic impact of the focal hand warming, as well as for experimental uniformity, because several trials did not extend past HW + 30. Composite electromyographic RMS data were normalized with a 10- to 15-min baseline period after the onset of cooling and were averaged over six 5-min intervals within the pre- to post-hand-warming block, as well as for HW + (25-30) (fig. 3). Mean shiver levels for each time interval had a strong correlation with electromyographic RMS values ( $r^2 = 0.86$ ).

Oxygen consumption and  $\dot{V}_{\text{CO}_2}$  were measured and normalized to assess relative metabolic activity (full data sets were obtained for six of the group of eight subjects because of technical difficulties) (figs. 4A and B). In all

subjects, normalized  $\dot{V}_{\text{O}_2}$  and  $\dot{V}_{\text{CO}_2}$  increased during maximum shiver from precooling rates, both of which were significant ( $\dot{V}_{\text{O}_2}$ :  $n = 6$ ;  $P < 0.01$ ;  $\dot{V}_{\text{CO}_2}$ :  $n = 6$ ;  $P < 0.01$ ). In five of six cases, normalized  $\dot{V}_{\text{O}_2}$  decreased; in all but two cases, normalized  $\dot{V}_{\text{CO}_2}$  decreased during focal hand warming, although overall differences were not significant.

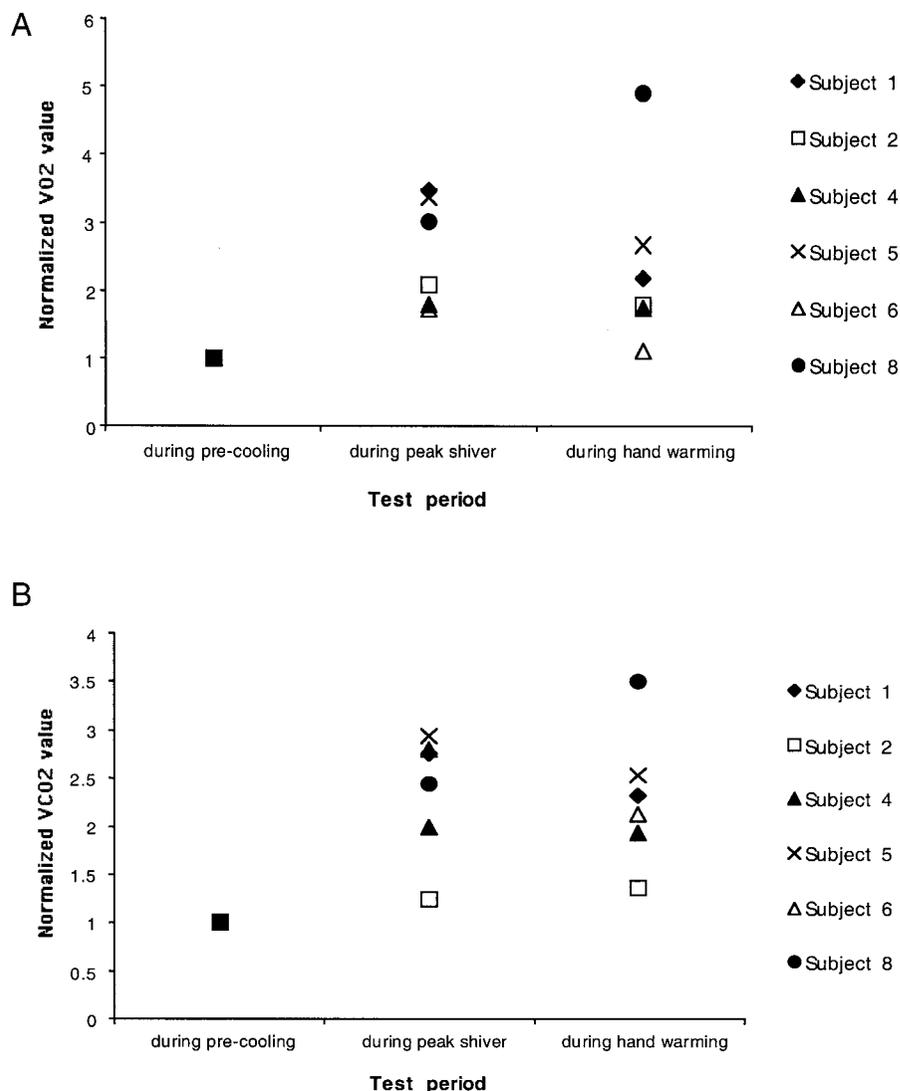
Individual heat fluxes (excluding right finger) were analyzed to determine any patterns in cooling. Based on pooled data, the primary sources of heat flux during cooling were the thigh ( $106.8 \pm 8.0 \text{ W/m}^2$ ), abdomen ( $96.1 \pm 26.1 \text{ W/m}^2$ ), and chest ( $76.3 \pm 15.1 \text{ W/m}^2$ ). Individual heat flux readings varied throughout the course of the experiment, primarily after hand-warming application. The shift in position due to the movement of arms from underneath the cooling blanket resulted in generally lower postwarming heat flux values in most locations (fig. 5). Because of substantial subject-to-subject variability in heat flux values, only differences in pre- and post-hand-warming values for the right finger ( $n = 8$ ;  $P < 0.01$ ), the forearm ( $n = 8$ ;  $P < 0.01$ ), and the abdomen ( $n = 8$ ;  $P < 0.01$ ) were significant.

## Discussion

In previous studies, the effects of blowing warm, humidified air over the face and airways has been shown to suppress shiver and facilitate the induction of hypothermia.<sup>12</sup> In the current study, our goal was to continue on this premise and evaluate the potential of focal hand warming in providing a similar result. This is the first study to provide quantitative evidence that focal hand warming is effective in reducing involuntary motor activity in subjects exposed to cold stress.

The results of the current study seem to associate well with the previous facial-warming study.<sup>12</sup> The strong correlation between shiver index and electromyographic RMS values regarding the application of hand

Fig. 4. Metabolic activity is represented *via* normalized oxygen consumption ( $\dot{V}O_2$ ; A) and carbon dioxide production ( $\dot{V}CO_2$ ; B) levels. With both  $\dot{V}O_2$  and  $\dot{V}CO_2$ , shiver and hand-warming levels were normalized with pre-cooling data, yielding a percent value. In all cases, there was a significant increase between precooling and maximum shiver readings. Five of six subjects showed a decrease from shiver to hand-warming  $\dot{V}O_2$  levels, whereas four of six subjects showed a decrease in corresponding  $\dot{V}CO_2$  levels.



warming indicate reduction in involuntary muscle activity. Also, both studies facilitated significant core temperature decreases as monitored *via* both the tympanic and rectal sensors. This is particularly encouraging for the population studied; healthy men with a fairly high percentage of muscle mass could be considered as a group that would be most efficient at maintaining core temperature *via* the initiation of involuntary motor activity (shiver).<sup>17</sup> For the subjects in this study, without the application of focal warming, there was minimal core cooling before the hand warming. At time = 0, the mean core temperature (rectal) was 36.8°C; after 30 min of cooling, it increased to 36.9°C; at 60 min, it was 36.7°C; and after 90 min, it only decreased to 36.5°C. To expand on this, we reanalyzed other subject data in cases in which we cooled subjects using a similar protocol (*i.e.*, active cooling *via* convection and conduction before shiver suppression). In this later population of 13 healthy male subjects, at time = 0, the mean core temperature (rectal) was 36.9°C. After 30 min of cooling, it increased to 37.0°C; at 60 min, it was 36.8°C; and after

90 min, it decreased to 36.5°C (unpublished data, P. A. I., 1998). Hence, in the current study and in the previously reported study by our laboratory in which we used focal facial warming, the warming resulted in dramatic changes in the induced rates of cooling.<sup>12</sup> Additionally, in both studies, the application of focal warming was noted by subjects to improve their tolerance to this rigorous but noninvasive cooling protocol. Hand warming should be considered as a potential alternative or adjunct to facial warming in cases in which suppression of involuntary motor activity is desired without the use of pharmacologic agents. For example, it may be the optimal clinical means to suppress shiver temporarily in a head trauma patient in which one desires to perform neurologic assessments.

The time needed for shiver induction was fairly variable with our described protocol, but it was considered that the observed variability encountered in this study was in part due to the normal range of physiologic responses. It should be noted that our subject population possessed a varied group of somatotypes. Specifi-

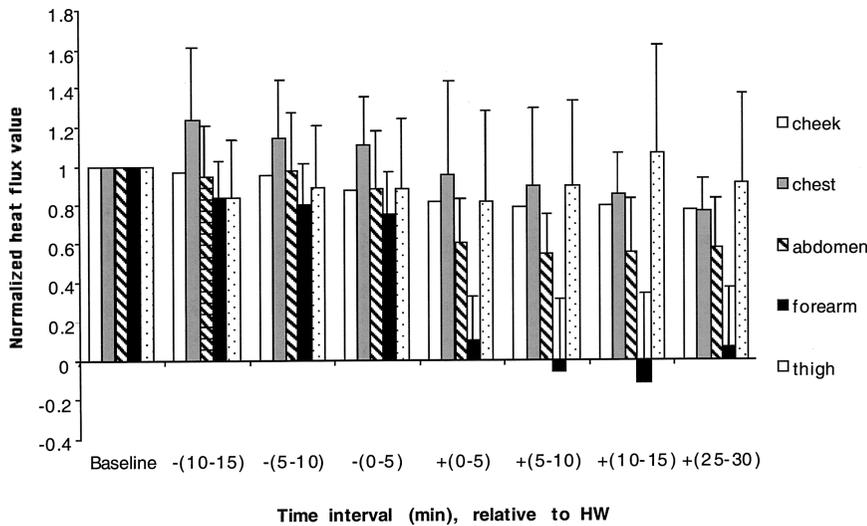


Fig. 5. Normalized mean heat fluxes of five body locations per 5-min time interval [HW - 15 to HW + 15, HW + (25-30)]. Heat fluxes were normalized with baseline data to provide a percent value. Using repeated-measurement analysis of variance for nonparametric data (Friedman test with Dunn posttest), heat fluxes were significantly different *versus* baseline at HW + (0-5) (abdomen, forearm:  $P < 0.05$ ), HW + (5-10) (cheek:  $P < 0.05$ ; abdomen, forearm:  $P < 0.01$ ), HW + (10-15) (cheek:  $P < 0.05$ ; abdomen, forearm:  $P < 0.01$ ). The last data point [HW + (25-30)] could not be included in the statistical data analysis because several subjects completed the study before (incomplete matrix).

cally, it was observed that subject 8 was physiologically atypical (an extreme ectomorph) when compared with the remaining subject pool. An example of this is shown in metabolic rate analysis, in which seven of eight subjects had a decrease in  $\dot{V}O_2$  readings from maximal shiver to hand-warming application. Although the lack of any statistically significant decrease in metabolic rate could be due in part to the presence of nonshiver thermogenesis, we believe that with larger subject pools, we would find a reduction in metabolic activity during hand warming. However, subject 8 showed a substantial increase in  $\dot{V}O_2$  and  $\dot{V}CO_2$  levels. Also, subject 8 reached uncontrolled whole-body shiver within 25 min of cooling onset, which was substantially faster than the remaining volunteers. The fact that the changes in metabolic rates were not as dramatic as those described in clinical situations is to be expected. Shiver-induced oxygen uptake increases of sevenfold do not occur in normal subjects in such a laboratory setting. An expected clinical situation in which one may expect dramatic effects would be in cases in which recorded oxygen uptake is compared between patients in a deeply anesthetized state and in a recovery room setting.<sup>17</sup>

Another variable of interest involved with our protocol was the testing environment. The warm climate of the test room ( $24 \pm 2^\circ\text{C}$ ), in conjunction with the lack of facial coverage, could have increased the time necessary to reach uncontrolled whole-body shiver, based on the conclusions of the previous study.<sup>12</sup> However, this slightly warm environmental temperature could be considered as a worst case scenario for such a protocol.

A point of interest for further study could be to determine the relative degree of shiver suppression in comparing hand and facial warming. For example, the intensity with which involuntary muscle activity is suppressed might be more of a short-term effect with hand warming relative to facial warming. This may be indicated by the subjects in whom shiver returned to

near-maximal levels despite the application of hand warming. This shorter duration of the effectiveness of hand warming may limit its use for prolonged suppression of involuntary motor activity. However, it should be noted that in all but two subjects, shiver remained below maximal levels for the duration of the experiment. Furthermore, in all subjects, core temperatures continued to decrease even with the return of motor activity. It should be noted that the cooling protocol used was not without a fair degree of subjective discomfort, but the application of hand warming improved individual tolerances to this thermal stress. However, in almost all the subjects, the cold-induced diuresis became severe toward the end of the study. In six of eight subjects, this was the reason for termination of the experiment. Such a suppression method may have larger benefits in cases in which anesthetics have been used, such that thermoregulatory mechanisms are affected.<sup>17</sup> Nevertheless, a larger subject pool is necessary to assess the full clinical potential and detailed effects of physiologic response to hand warming accurately.

In summary, the primary purpose of our study was to physiologically assess the potential for focal hand warming to suppress whole-body shiver. Based on our preliminary findings, we consider that such a method can readily suppress shiver and allow for core body cooling. Yet, it is clear that further investigations are needed to clarify the clinical utility of this approach and to understand better the underlying physiologic mechanisms evoked during this pilot study. Hand warming may be used as an alternative or adjunct to facial warming in cases in which suppression of involuntary motor activity is desired without the use of pharmacologic agents.

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