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MEASUREMENT AND PREDICTION OF MAXIMAL SHIVERING CAPACITY IN HUMANS

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Measurement and Prediction of Maximal Shivering Capacity in Humans

Report to

Defence and Civil Institute of Environmental Medicine,
Department of National Defence, Canada

by

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Abstract

Prediction formulae of shivering metabolism (M_{shiv}) are critical to the development of models of thermoregulation for cold exposure. Most formulae use a combination of body composition measures, with skin and core temperatures to predict ongoing shivering metabolism. Although maximum shivering capacity itself has not been predicted, a maximum shivering oxygen consumption (M_{shiv}max) of 1.4 l $O_2 \cdot min^{-1}$ (or 5 times resting metabolic rate) has been reported. We completed studies on 16 subjects (4 females) (mean ± SD: age = 24.9 ± 6 yrs; height = 176 ± 9 cm; weight = 76 ± 19 kg; body fat = 21.3 ± 5 %: and VO_{2max} = 51.8 ± 10 $ml \cdot kg^{-1} \cdot min^{-1}$). In this protocol, subjects were immersed in 8°C water until metabolic rate increased and plateaued. Water temperature was then gradually increased at 0.8°C min^{-1} to a value of 20°C. This was expected to further increase shivering heat production as peripheral cold receptors fire maximally at ≈ 20°C. This in combination with the relatively low core temperature was hypothesized to stimulate maximal shivering heat production. During 8°C water immersion M_{shiv} plateaued at 1.04 ± 0.3 l $O_2 \cdot min^{-1}$ at core temperatures of ≈ 35°C. After water temperature rose to 20°C, M_{shiv} reached peak values of 1.68±0.3 l $O_2 \cdot min^{-1}$. Data from one male subject were not included in the prediction equations because his BMI was 3 SD's above the group mean and his VO_{2max} was 2 SD's below the group mean. Although % fat was significantly correlated to absolute M_{shiv}max, the following best fit formulae for predictions included VO_{2max} and BMI values: Relative $Shiv_{max}$(ml $O_2 \cdot kg^{-1} \cdot min^{-1}$) = 0.339(Relative VO_{2max}) - 0.951(BMI) + 26.2, (adjusted R^2 = 0.726, SEE = 2.195, p = 0.0003); and Absolute $Shiv_{max}$(l $O_2 \cdot min^{-1}$) = 0.331(Absolute VO_{2max}) - 0.056(BMI) + 1.6, (adjusted R^2 = 0.727, SEE = 0.156, p = 0.0004).

Introduction

Shivering is a well-recognized mechanism in the maintenance of core body temperature (T_{co}) in response to cold exposure (6, 11). Cold water immersion studies in our laboratory have demonstrated that pharmacologic inhibition of shivering causes an increase in the rate of core cooling, an increased T_{co} afterdrop, and attenuation of the rate of rewarming (2, 4). It may be reasonable to assume that the duration which shivering can be maintained (before an individual is unable to continue due to fatigue) would be an important determinant of survival time during cold water immersion. However, in the assessment of shivering endurance, it would be useful to first quantify the maximal shivering response attainable, and to determine predictive variables for this response.

In a single subject, Benzinger (1) demonstrated an inverse hyperbolic relationship between shivering intensity and T_{co} within the range of 37.2°C and 36.2°C, and a parabolic relationship between shivering intensity and skin temperature (T_{sk}), with a maximal response at a T_{sk} of about 20°C. This is consistent with the average temperature that elicits maximal firing rates of peripheral cold receptors.

The intensity of maximal shivering has been the issue of much discussion since the work of Iampietro et al. (5) who assessed metabolic work due to shivering by measuring O_2 consumption (VO_2) in sixteen humans exposed to cold air. They observed an increase in shivering intensity as the air temperature was decreased and/or wind velocity was increased. In this study, the highest metabolic rate of 1.67 $l\ O_2\ min^{-1}$ was observed in 2 subjects who were cooled for a longer period of time than the others. The authors concluded that this response, which averaged about five times the resting metabolic rate, and approximately 50% of maximal VO_2, was the maximal shivering response attainable in humans. These values are currently being used in mathematical models of shivering metabolism (8, 9), however, they have limitations in their applicability to maximal shivering responses. First, Iampetro et al.'s experiments were only 30 min long, which may not be sufficient time for a maximal shivering response to be achieved. Second, the coldest air temperature was -7°C, whereas humans may be subjected to much greater cold stress and heat loss; eg., during cold water immersion. Additionally, no measurements of T_{sk} or T_{co} were obtained in this study. These limitations indicate that the highest observed shivering intensity observed in these trials might not truly represent the maximal shivering intensity obtainable.

We therefore developed a strategy to elicit the maximal shivering intensity in humans, and to determine which factors may be used to consistently predict the shivering response to a given set of variables.

Subjects were immersed in 8°C water for 60 - 70 min before the water temperature was gradually increased to 20°C over 15 min. We hypothesized that the combination of low T_{co} (~ 35°C) and a T_{sk} of 20°C would elicit the maximal shivering response based, in part, on the work of Benzinger (1).

Methods

Subjects

Seventeen young, fit and healthy males (n = 12) and females (n = 5) were studied. The protocol was approved by the Faculty's Human Ethics Committee, and informed consent was obtained from the subjects prior to the study. A medical history and physical examination were performed on each subject by a physician, and a physician was present throughout each experiment. The subjects' anthropometric characteristics are listed in Table 1.

Table 1. Subject characteristics.

Subject	Gender	Age (y)	Wt (kg)	Ht (cm)	BMI ($kg \cdot m^{-2}$)	BSA (m^2)	Siri (% fat)
1	m	22	79.0	181	24.1	1.99	18.6
2	f	26	52.2	161	20.1	1.54	20.1
3	m	34	70.0	180	21.6	1.89	24.2
4	f	22	58.0	159	22.9	1.59	n/a
5	m	25	102.0	193	27.4	2.33	23.6
6	m	40	83.3	183	24.9	2.05	21.5
7	f	20	61.0	167	21.9	1.68	25.1
8	f	19	70.5	172	23.8	1.83	27.1
9	m	20	74.5	182	22.5	1.95	22.7
10	m	24	61.0	166	22.1	1.68	11.8
11	m	20	65.0	173	21.7	1.78	11.2
12	m	28	133.5	185	39.0	2.53	31.3
13	m	26	79.5	184	23.5	2.02	19.4
14	m	23	63.0	165	23.1	1.69	16.3
15	m	21	78.5	172	26.5	1.92	27.6
16	m	26	68.5	177	21.9	1.85	14.3
17	f	24	73.5	177	23.5	1.90	26.3
Mean		24.7	74.9	175.1	24.2	1.9	21.3
± SD		5.4	19.0	9.4	4.2	0.3	5.8

Instrumentation

Esophageal temperature (T_{es}) was measured with an esophageal thermocouple positioned at the level of the heart. Rectal temperature (T_{re}) was measured with a rectal thermocouple inserted to a depth of 15 cm. Auditory canal temperature (T_{ac}) was measured with a cotton covered thermocouple positioned next to the tympanic membrane and the ear was then insulated. Skin temperature and heat flux measurements were obtained by 12 thermal flux transducers attached to the forehead, chest, abdomen, and extremities according to previous protocols (3). Serial data from the thermocouples and thermal flux transducers were acquired using an electrically isolated desktop computer. At 30-s intervals the results were averaged for the preceding 30-s period, displayed graphically on the computer screen, and recorded in spreadsheet format on a hard disk. The process was controlled by a "virtual instrument" written using Lab View II graphic signal processing software (National Instruments, Austin, TX). A single channel electrocardiogram (Hewlett-Packard 43100A monitor-defibrillator) was used to obtain continuous readings of heart rate and rhythm. At regular intervals blood pressure was measured automatically by a cuff applied to the left upper arm (Dinamap 845XT).

Oxygen consumption was measured via an open circuit method from measured expired minute ventilation and gas concentrations (inspired and expired) sampled from a 1L fluted mixing box (Sensor Medics Vmax Series 229). These data were averaged every 30 s, collected and displayed by computer and recorded on a hard disk in the same manner as the thermal measurements.

Experimental Protocol

Subjects were studied on 2 separate days. On one day maximal exercise capacity (VO_{2max}) was determined by measuring heart rate (via ECG) and VO_2 while on a treadmill, using a modified Bruce protocol.

On the cold water immersion day, subjects were dressed in a swimsuit and instrumented in a room with an ambient temperature of ~22°C. Baseline measurements were collected for 10 min while the subjects sat quietly. They were then immersed to the level of the sternal notch in 20°C stirred water. Water temperature (T_w) was subsequently lowered to 8°C over 15 min by the addition of ice.

After 60 - 70 min of immersion, or when T_{es} decreased to a minimum of 33.5°C, T_w was then raised to 20°C over 15 min by the addition of warm water. T_w was maintained at this temperature until shivering metabolism consistently decreased and T_{es} increased. Afterwards, subjects were then transferred to a tank of 40°C water for rewarming and the trial was terminated when T_{es} reached 37.0°C.

Data Analysis

Baseline VO_2 was averaged over the 10 min period immediately prior to immersion. Pre-warming VO_2 was averaged over a 10 min period either immediately prior to increasing T_w from 8°C to 20°C, or during the most consistent plateau phase (depending on the subject's response). Maximal VO_2

was determined as the highest value after increasing T_w to 20°C. Results are reported as mean ± SD.

The maximal shivering response was determined as Absolute $Shiv_{max}$ ($l\ O_2 \cdot min^{-1}$) and Relative $Shiv_{max}$($ml\ O_2 \cdot kg^{-1} \cdot min^{-1}$). A correlation matrix (StatView SE+Graphics) was then created to determine which factors (i.e., anthropometrics, age, gender or fitness variables) were most strongly correlated with Absolute $Shiv_{max}$ and Relative $Shiv_{max}$. Based on these results a stepwise regression was then performed, using height, weight, % body fat, body mass index (BMI), Absolute VO_2max and Relative VO_2max as predictors for Absolute $Shiv_{max}$ and Relative $Shiv_{max}$. Best fit equations were then regressed for predicting maximal shivering responses.

Results

Subjects were closely monitored throughout each trial. No adverse effects were noted in any of the subjects and 16 completed the trial. One subject (# 4) requested to have the trial terminated at an early stage and was therefore not included in any further analysis.

Core Temperature Responses

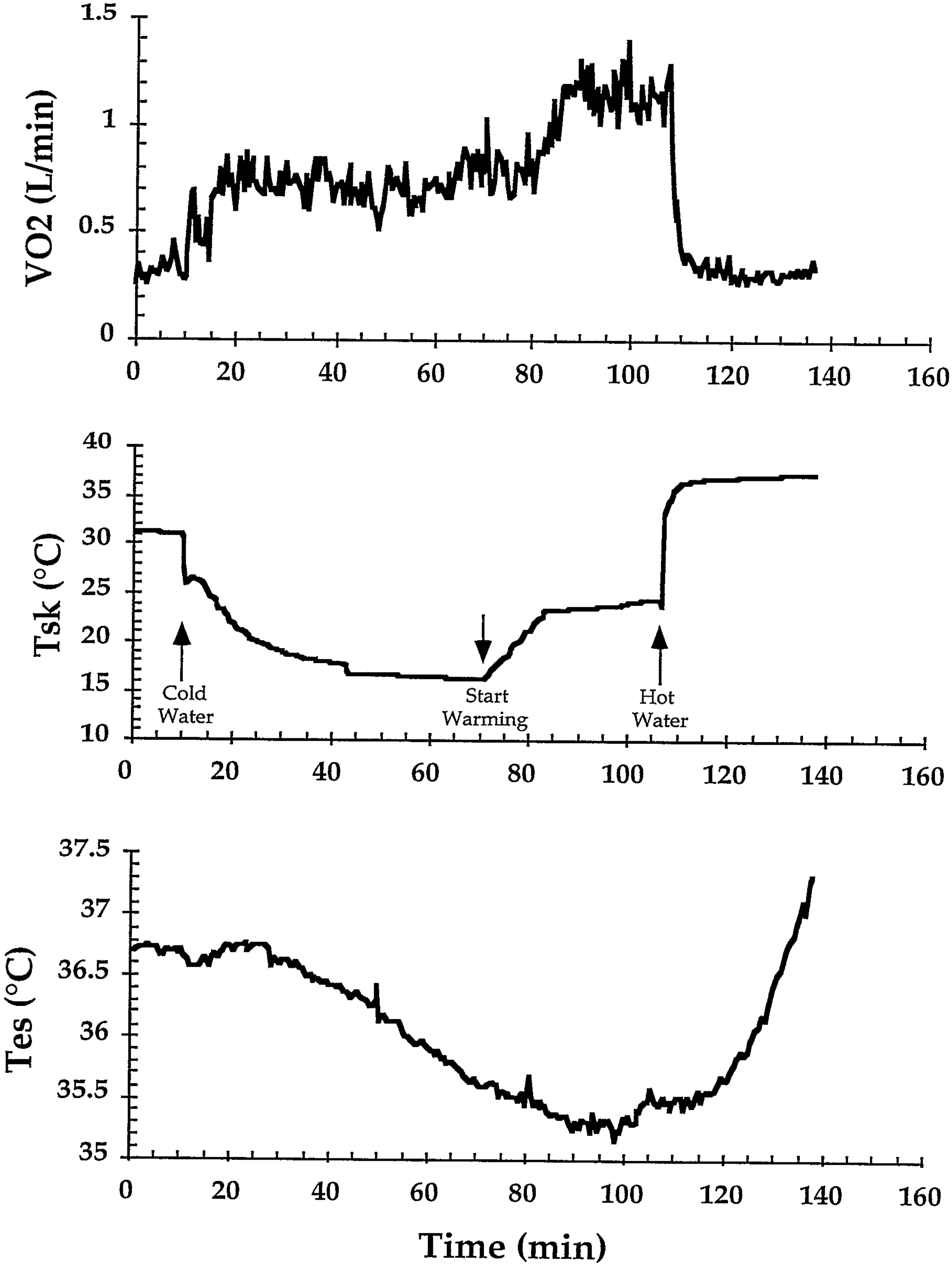
During immersion, T_{es} decreased while T_w was maintained at 8.0°C, reaching a nadir of 35.0 ± 1.0°C. T_{es} started to increase 0 - 12 min prior to the period of maximal shivering (see below), and returned to normal during rewarming in 40°C water.

Metabolic Responses

Prior to immersion, baseline VO_2 was 4.6 ± 0.7 $ml\ O_2 \cdot kg^{-1} \cdot min^{-1}$. During immersion, three different types of responses were shown by different subjects. In 7 subjects, VO_2 increased rapidly upon water cooling prior to any decrease in T_{es} (Figs. 1 and 2). In these subjects a plateau in VO_2 was reached. In each case VO_2 increased once T_w reached 20°C with peak values occurring ~ 6 min after T_{es} reached a nadir and started to increase.

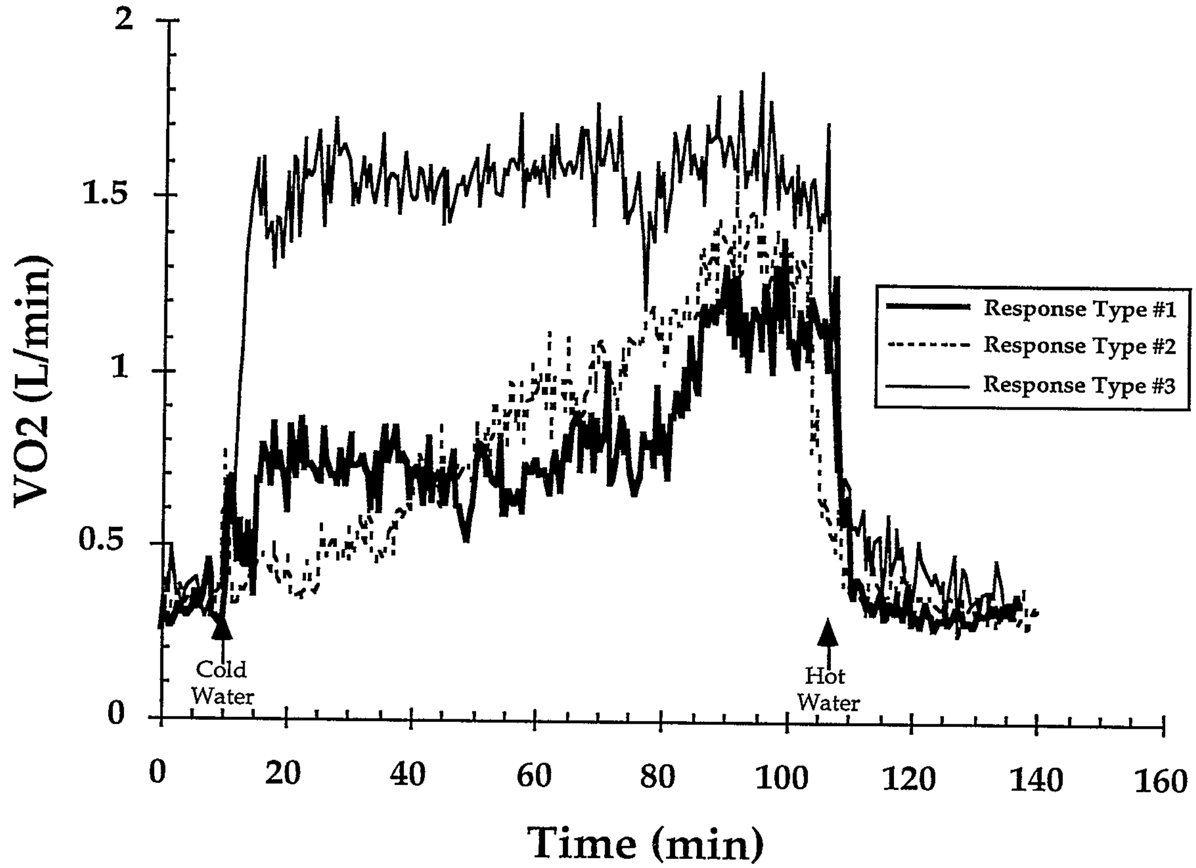
In the second type of response (n = 5), VO_2 increased steadily throughout the cooling period and increased further, as T_w increased to 20°C, peaking ~ 5 min later, until T_{es} started to increase (Fig. 2). A third response (n = 4) was a rapid rise in VO_2 upon immersion to a plateau with only a small further rise in VO_2 when T_w reached 20°C (Fig. 2). In this response, VO_2 started to decrease ~ 2 min after T_{es} started to increase.

Figure 1. Response of One Subject



At rest, baseline VO_2 values were 4.6 ± 0.7 ml $O_2 \cdot kg^{-1} min^{-1}$. During cooling, the average VO_2 just prior to the initiation of increasing water temperature, reached a value of 14.4 ± 5.9 ml $O_2 \cdot kg^{-1} min^{-1}$. Relative $Shiv_{max}$ reached an average peak value of 21.5 ± 4.6 ml $O_2 \cdot kg^{-1} min^{-1}$. This value corresponded to 41.5% of VO_{2max} and 4.7 times resting baseline values (Table 2). At the time of maximal shivering mean T_{es} and T_{skavg} were 35.3 ± 1.1°C and 22.0 ± 2.1°C, respectively. In all subjects shivering was rapidly extinguished, with a return of VO_2 to baseline levels, upon transfer to 40°C water.

Figure 2. Three Types of Response



Prediction of Maximal Shivering Response

Anthropometric, age and fitness variables were examined for their degree of correlation with Absolute $Shiv_{max}$ and Relative $Shiv_{max}$. The results were skewed by data from one subject (# 12) who had a BMI 3 SD's above the group mean, a Relative VO_{2max} 2 SD's below the group mean and a T_{es} at maximal shivering more than 2 SD's above the group mean. Because these data did not fall within the normal distribution, results from this subject were not included in the prediction analysis for the group as a whole.

Table 2. Baseline and maximal exercise and shivering metabolism. Note that data for subject #4 are intentionally missing.

Subject	Absolute VO_{2max} ($l \cdot min^{-1}$)	Relative VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	Absolute Shivering Max ($l \cdot min^{-1}$)	Relative Shivering Max ($ml \cdot kg^{-1} \cdot min^{-1}$)
1	4.323	54.7	1.837	23.3
2	2.796	53.6	1.141	21.9
3	3.448	49.3	1.515	21.6
5	5.881	57.7	1.973	19.3
6	4.052	49.2	1.303	15.6
7	2.925	48.0	1.443	23.6
8	3.127	44.3	1.514	21.5
9	3.937	52.8	1.694	22.7
10	3.598	59.2	1.478	24.2
11	3.619	55.7	1.712	26.3
12	3.954	30.6	1.744	13.1
13	5.125	64.5	1.843	23.2
14	3.517	55.7	1.484	23.6
15	3.479	44.3	1.295	16.5
16	4.896	71.1	2.196	32.1
17	2.753	37.5	1.190	16.2
Mean	3.8	51.8	1.6	21.5
± SD	0.9	9.9	0.3	4.6

Separate step-wise regression analyses were conducted for Relative $Shiv_{max}$ and Absolute $Shiv_{max}$ with appropriate significantly correlated variables included in each analysis. The following predictive equations were derived:

$$\text{Relative } Shiv_{max}(ml\ O_2 \cdot kg^{-1} \cdot min^{-1}) = 0.339(\text{Relative } VO_{2max}) - 0.951(BMI) + 26.2$$

(adjusted $R^2 = 0.726$, SEE = 2.195, $p = 0.0002$)

and

$$\text{Absolute } Shiv_{max}(l\ O_2 \cdot min^{-1}) = 0.331(\text{Absolute } VO_{2max}) - 0.056(BMI) + 1.6$$

(adjusted $R^2 = 0.727$, SEE = 0.156, $p = 0.0002$)

Discussion

This study has demonstrated that peak shivering metabolism in mildly hypothermic human subjects reaches an average of 4.7 times the resting metabolic rate with maximal values of 21.5 ± 0.5 $ml \cdot kg \cdot min^{-1}$. The unique feature of this protocol is that the high shivering metabolism at a significantly decreased core temperature (35.2 ± 0.9°C) was increased further when skin temperature was increased to ~ 22°C. This is consistent with the original hypothesis that the combination of low T_{co} (~ 35°C) and a T_{sk} of ~ 20°C would elicit a higher shivering response.

This study characterizes the shivering reponse at significantly lower core temperatures than achieved in other studies of shivering heat production (1, 5). Both of these previous studies of shivering assessed subjects' response to a maintained or increasingly severe cold stress, whereas our study was the first to utilize cold stress followed by actual gradual skin warming to bring about maximal shivering.

The present results are consistent with other observations on shivering control (1, 10) which demonstrate contributions of both T_{co} and T_{sk} towards the shivering response. There was an inverse relationship between T_{co} and shivering metabolism as previously observed. Also the further increase in shivering metabolism in response to increasing T_w to 20°C is consistent with the parabolic relationship of T_{sk} to shivering with maximum values occurring at about 20°C (1).

The maximal shivering response observed in our study represents the first consistent demonstration of maximal shivering brought about in more than 2 subjects. Our results are consistent with those of Iampietro et al. (5) who found the highest shivering metabolic rate to be approximately 5 times the resting metabolic rate and 1/2 of VO_{2max}. They also indicate that $Shiv_{max}$/resting VO_2 = 4.7, and $Shiv_{max}$ / VO_{2max} ≐ 0.41.

The inclusion of BMI and VO_{2max} values in the prediction equations for both Absolute and Relative $Shiv_{max}$ values was not surprising. Maximal VO_2 provides an index of the aerobic capacity of muscles which may be ultimately involved in shivering heat production. Therefore, a higher VO_{2max} should result in greater shivering capacity at the maximal shivering output by the thermoregulatory control center. Although BMI is derived from the ratio of mass over height squared, it is related to other anthropometric characteristics such as body fat. The negative correlation between BMI and maximal shivering intensity is consistent with the inverse relationship between shivering intensity and body fatness at a given skin temperature shown by Leblanc (7).

Limitations of the Study

Although a peak shivering intensity was demonstrated when lower core temperatures were combined with increased skin temperatures to ~ 20°C, we cannot conclude that this invoked the absolute highest level of shivering possible in each subject. The maximal core temperature stimulus for shivering likely occurs between 35 and 32°C and decreases until shivering is extinguished at core temperatures below 30°C. Half of our subjects reached core temperatures in this maximal range (34.1 - 35°C). However, ethical limitations precluded decreasing core temperatures to lower values such as 32°C to determine if a greater shivering response could be attained. Likewise, the maximal skin temperature stimulus for shivering is about 20°C (1) although there is individual variability about this value (10). In the present study, peak shivering values were observed at a mean T_{skavg} of 22°C (range 21 - 24°C; these values were slightly higher than the water temperature of 20°C because the head and upper portions of the shoulders were out of the water). Our protocol involved increasing water temperature to 20°C and maintaining it at that level until shivering intensity decreased. It is possible that slight variations about this water temperature may have increased shivering intensity but each iteration would have required another complete trial.

One further limitation to the protocol is the different cooling rates of subjects with different anthropometric characteristics. Subjects with greater body mass and % fat consistently had higher core temperatures at the end of 70 min of cooling. As a result, fatter subjects had higher core temperatures and possibly a lower shivering stimulus when water temperature was raised to 20°C. This is a limitation of a protocol with a standard cooling time.

Conclusion

The maximal shivering response in 16 subjects characterized in this study are consistent with other reports on maximum shivering. BMI and VO_{2max} were found to be significant variables in the prediction of the maximal shivering response. These findings will be used to further the development of a reliable means of predicting survival times for those individuals accidentally subjected to prolonged cold-water immersion.

Acknowlegments

This work was supported by the Canadian Department of National Defense (through D.C.I.E.M. and the New SAR Initiatives program under contract no. 2668ND18BN04099 FL707) and the Natural Science and Engineering Research Council of Canada.

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