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ORIGINAL ARTICLE

Enhancing Thermal Exchange in Humans and Practical Applications

H. Craig Heller and Dennis A. Grahn

Abstract

Normal human core body temperature is regulated within a narrow range. Deviations from this range can have serious consequences in both health and disease. However, it is difficult to efficiently manipulate body heat content because of the high heat capacity of the body and the low thermal conductance of the body surface. Mammals have evolved vascular adaptations of the nonhairy skin to enable enhanced heat loss. These include arteriovenous anastomoses that bypass the nutritive capillary beds to shunt the blood into retia venosa which serve as radiators. We have quantified the area-specific heat loss from glabrous skin (palms and face) and nonglabrous skin (upper arm, back, thigh, and abdomen). Results show that the heat loss from the nonglabrous skin does not change appreciably over the course of exercise in the heat, whereas the heat loss from the glabrous skin rises to values more than five times that of the nonglabrous skin. The application of a mild vacuum increases the heat loss from the glabrous skin by an additional 33%. The effect of cooling of these different skin areas on the heart-rate response to a fixed exercise load was significantly greater for the glabrous than the nonglabrous skin. The intermittent application of vacuum cooling to the palms of individuals exercising in a hot environment had the effects of lowering the rate of rise of core temperature and enhancing performance. The vacuum-enhanced heat exchange via the glabrous skin is a disruptive technology for several reasons. It forces re-formulation of the models of human thermoregulation that are used to design thermal protective gear. It offers an effective means of treating heat and cold stress. It provides an insight into controversies about the effects of temperature on human athletic performance, and offers a means of enhancing strength and work volume training responses that are more effective than performance-enhancing supplements such as anabolic steroids. There are many potential applications of vacuum-enhanced cooling of the glabrous skin in medicine, occupational health and safety, and sport.

Key words: glabrous skin; mammalian temperature regulation; performance enhancement; regional heat transfer

Introduction

HUMAN CORE BODY temperature is usually regulated within a narrow range. Deviations from this range (hypothermia and hyperthermia) have impacts on health, cognition, and performance, but such deviations are commonly experienced and frequently unavoidable. For example, the capacity of the large dynamic muscles of the body to produce heat exceeds the ability of the body to dissipate that heat and, therefore, physical activity can cause hyperthermia. The induction of hyperthermia is more likely in a hot environment. When environmental temperature approaches and exceeds core body temperature, hyperthermia can ensue even if the metabolic rate remains at low resting levels. Conversely, humans exist and work in cold environments where heat loss from the body can exceed the capacity of the body to produce metabolic heat, resulting in hypothermia. Hypothermia can develop even in slightly cool environments when metabolic heat production is compromised such as during anesthesia or during sleep in the aged. Countermeasures for hyper- and hypothermia require the ability to facilitate the movement of heat between the body and the environment. Such countermeasures are limited by the thermal conductivity of the body surface.

The thermal conductivity of the body surface of most mammals is reduced by fur, which is highly adaptive in cold environments. However, the insulation of fur poses a problem for mammals in hot environments or during intense exercise. The evolutionary solution to this problem has been special vascular anatomy of the nonhairy or glabrous skin. In most mammals, these surface areas are the pads of the feet, the tongue, and, in some species, the ears, tails, and

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Department of Biology, Stanford University, Stanford, California.

parts of the face. The unique vascular structures underlying these glabrous skin areas are arterio-venous anastomoses (AVAs) that can bypass the nutritive capillary beds and shunt the arterial blood into networks of veins called retia venosa. The potential for very high blood flow through the retia venosa makes the overlying glabrous skin a radiator of heat carried to those surfaces from the body core in arteries, and since the AVAs are gated by smooth muscle, these radiators can be controlled to minimize heat loss in a cold environment and to maximize heat loss in a hot environment.

Even though humans are not heavily furred, they still possess the vascular anatomy seen in the glabrous skin of other mammals. In this article, we will demonstrate the importance of the controlled radiator function of the glabrous skin of humans, a technology that is used for amplifying heat exchange through these surfaces, and some of the benefits of being able to manipulate core body heat content by this technology.

Materials and Methods

General

The basic methods of these protocols have been previously described in detail.[1,2] Only a brief summary of the general methods and a detailed description of the unique specifics of these studies are presented here. The protocols for these studies were approved by a Stanford University Institutional Review Board (IRB). The inclusion criteria were as follows: (1) No known medical problems, (2) not under treatment for a medical problem, (3) not on medication, and (4) engaged in 30 or more minutes of physical exercise for a minimum of three times a week for the previous 6 months.

Custom-built palm cooling devices consisted of a rigid acrylic cylindrical chamber (20 cm diameter. × 21 cm length) into which a hand was inserted through an closed cell foam sleeve that formed an airtight seal around the forearm. Inside the chamber, the palm rested on a water-perfused stainless steel heat exchanger. Cool water (15°C–16°C) was circulated through the heat exchanger from a circulating refrigerated water bath (Neslabs Model RTE 17; Thermo Scientific, Waltham, MA). The chamber was connected to an adjustable pressure relief valve, a pressure gauge, and an in-house vacuum system that created a pressure differential within the chamber (−40 mm Hg).

The laboratory-based experimental trials were conducted in a 2.4 × 3.3 × 2.4 m (width, length, height) temperature-controlled environmental chamber. The ambient conditions inside the environmental chamber were 35.5°C ± 0.5°C, at a relative humidity of 20%–35%. The environmental chamber housed two treadmills (model SC7000; SciFit, Tulsa, OK). V_{O2max} tests were conducted in a 23°C room on a treadmill using a respiratory gases/metabolic analysis system (Parvomedics, Salt Lake City, UT).

Heart rates that were measured using portable heart rate monitors/data loggers (model S810; Polar Electro Oy, Kempele, Finland). Core temperatures (T_{core})—either esophageal or tympanic membrane temperatures (T_{es} and T_{ty})—were measured in some subjects. T_{es} was measured using a commercially available general-purpose thermocouple probe (Mon-a-Therm # 503-0028; Mallinckrodt Medical, Inc., St. Louis, MO) self-inserted through the nose or mouth to a depth of 38–39 cm and held in place by a loop of surgical tape. T_{ty} was measured using a commercially available tympanic thermocouple probe (Mon-a-Therm # 503-0013) self-inserted into an external auditory meatus to the point of subjective discomfort and taped in place. The thermocouple probes were connected to a laptop-based thermocouple transducer/data collection system (GEC instruments, Gainesville, FL) that recorded temperature data at 1-sec intervals. At the conclusion of each trial, heart rate and temperature data were downloaded to a central spreadsheet (Microsoft Office Excel for Windows2003; Microsoft, Inc., Redmond, WA) for subsequent off-line analysis.

All experimental trials on individual subjects were conducted at the same time of day and separated by a minimum of 48 h.

Determining regional heat transfer

Heat transfer across the nonglabrous skin regions was measured at five sites (the upper back, lower back, abdomen, thigh, and upper arm) and across the glabrous skin at two sites (the face and the palm of the hand). Urethane-coated nylon water perfusion pads (Plas-tech, Corona, CA) were used as the skin surface interface; a 35.6 × 21.6 cm rectangular pad for the nonglabrous skin regions, a 12.7 × 25.4 cm rectangular pad for the palmar surface of the hand, and a form-fitting mask for the face. The larger water-perfusion pads and face mask were backed on one side with matching pieces of 1.3 cm-thick closed-cell neoprene foam. Mounting harnesses—fashioned from lengths of neoprene, elastic strapping, and Velcro fasteners—securely abutted the water-perfusion pads to the targeted skin surfaces. For the palm of the hand, the subjects lightly grasped the smaller water perfusion pad wrapped around an 8 cm-diameter × 13 cm-long neoprene foam cylinder. Cool water (15°C–16°C) was circulated through the water-perfusion pads from a circulating refrigerated water bath.

Heat transfer calculations were based on the water temperature differential between the inlet to and the outlet from the water-perfusion pads and the flow rate of the water stream. Water temperatures were measured using thermocouples mounted in the inlet and outlet tubing lines immediately adjacent to the water perfusion pads. The thermocouple junctions were threaded through the male pipe thread (MPT) openings of barbed hose T-fittings (1/4 barbed × 1/4 barbed × 1/8 mpt) so that the tip of the thermocouple was at the center of the throughpath. The thermocouples placement in the T-fitting was secured by filling the MPT port with epoxy. The barbed T-fittings were inserted into the flexible plastic tubing lines directly adjacent to the water perfusion pads. These thermocouples were connected to the thermocouple transducer/data collection system, and data were recorded at 1-sec intervals. Flow rates were measured using an in-line turbine flow meter with analog output (model FLR 1005; Omega Engineering, Stamford, CT) at a 1 Hz sampling rate. Flow rate data were stored along with the temperature data. The heat transferred was calculated using the formula,

$$q = m(\Delta T)Cp,$$

where q = heat transfer (cal/sec), m = mass flow (g H_2O/sec), ΔT = the change in temperature (inlet—outlet water temperature [°C]), and Cp = the specific heat of water (1 cal/ g × °C). Heat transfer was converted from calories/sec to Watts (joules/sec) using the conversion factor 4.184 J = 1 cal. Baseline heat loss through the perfusion pads (parasitic heat loss) was determined for each trial by measuring the heat transfer of the pads alone (without contact with a skin surface) for a minimum of 10 min immediately before and immediately after each experimental trial. The heat transferred across the skin surface was determined by subtracting the mean parasitic heat transfer from each experimental heat transfer data point. The data collection method was validated by directly measuring the temperature differential between the inlet and outlet water streams using a two-junction type-T thermocouple circuit inserted into the inlet and outlet lines adjacent to the single thermocouples. The voltage of the contact potential between the two thermocouple junctions was amplified 10,000× (Instrumentation amplifier, model EI-1040; Electronics Innovations Corp., Lakewood, CO) and fed into a desktop computer, where the data were collected at a 1 Hz sampling rate. The heat transfer was calculated as described.

The skin surface areas of the palms of the hands were determined by tracing the outline of the hand on a sheet of paper of a known weight. The outline of the hand was cut out and weighed. The surface area was determined by the ratio of the weight of the cutout to the weight of the sheet of paper. Face surface area was determined in a similar manner: The face of the subject was covered with a thin coating of mineral oil, and a paper cutout of the water-perfused face mask was placed on the face. The paper cutout was removed from the face, flattened out, and the outlines of the oil marks were transferred to a clean sheet of paper. The transferred oil mark outlines were then cut out and weighed. The treatment surface areas of the nonglabrous skin were 35.6×21.6 cm.

Six male and seven female volunteers (19–22 years of age) participated in this study. Before the experimental trials, each subject participated in order: a V_{O2max} test in a thermoneutral environment, three hot environment baseline treadmill assessment trials (walking at 5.63 km/h with the slope increased by 2% increments at 3 min intervals), and three training trials. During the training trials, the treadmill slopes were adjusted so that the subjects would reach the temperature (39°C), heart rate (95% of maximum heart rate during the V_{O2max} test), or subjective fatigue stop criteria within 30–40 min of treadmill exercise. Treadmill speed and slopes remained constant for each subject throughout the experimental trials.

The daily procedure for the experimental trials was as follows: (1) attach the monitoring equipment and rest quietly for 5 min in a thermoneutral room (T_a = 22°C–24°C); (2) rest for 10 min in the hot environment; (3) don the heat transfer equipment and commence the treadmill exercise; (4) walk on the treadmill to a stop criterion; (5) rest for 10 min in the hot environment; and (6) remove the heat transfer equipment and monitoring equipment.

Heat transfer, heart rate, and T_{core} data for each trial were plotted against time. The heat transfer data were compiled on a central spread sheet and sorted by skin surface area and subject. Mean and maximum heat transfer, maximum heart rate, and core temperatures (at 5 min intervals) were calculated for each trial and sorted by subject and treatment area.

Temperature and performance during repeated high-intensity exercises: a field trial

We coordinated with the coaching staff of the Stanford University Football Program to test the effects of palm cooling on performance during a training exercise: "Getting yards"—a repeated high-intensity sprint drill. The six subjects were varsity athletes selected by the coaching staff. The exercises consisted of a series of 2-min sprints (back and forth across a 91.44 m-long practice field) separated by 3-min rest intervals. The getting yards drills were managed by members of the coaching staff. A stopwatch was used to time the exercise starts and stops. The exercise start and stop times were communicated to the subjects by the coach's whistle. The final 10 sec of each exercise bout was counted down by the coach wielding the stopwatch, and time intervals during the rest periods were also periodically announced (e.g., "2 min," "1 min," 30 sec," "10 sec"). During the rest intervals, the subjects walked back to the starting line area, received treatment, and prepared for the next sprint. Treatment entailed placing one hand in a palm-cooling device or rest only. The subjects participated in four trials: paired palm cooling and rest-only trials at two ambient temperatures (35°C and 22°C, 30% relative humidity).

The distance traveled during each sprint was recorded manually, and the data were subsequently transferred to a spread sheet. The sprint distances were tabulated for each trial. The data were sorted by subject and trial conditions (ambient temperature and treatment).

Temperature and repeated sprint exercises in the laboratory

Twelve subjects (6 men and 6 women, 18–21 years of age) participated in these trials. The basic protocol was as just described in the regional heat transfer section with the following variations: (1) the exercises were six repeated 5-min exercise/rest cycles of 110% V_{O2max} work loads on a treadmill housed in the 35°C environmental chamber; (2) treatment (palm cooling or no palm cooling) was applied during the rest phases of the exercise/rest cycles; (3) the subjects were clad in track warm-up suits; and (4) the stop criterion for exercise was subjective fatigue (i.e., the subjects hit the treadmill stop button to end the exercise). Each subject participated in two sets of paired trials: In one set of trials, the subjects rested in a 35°C environment and in the other set of trials, the subjects rested in a 22°C environment.

Total sprint durations and mean sprint durations were calculated for each trial. The rate of change of core temperature (ΔT_{core}) was determined by subjecting individual T_{ty} and, if available, T_{es} versus time plots (from initial exercise onset to final exercise offset) to a regression analysis (Microsoft Office Excel for Windows 2003 data analysis tools). Performance and core temperature data were grouped by subject, treatment, and ambient conditions. To determine the effects of treatment on ΔT_{core} and performance, the value of the dependent variable in the palm-cooling trial was divided by the value of the same variable in the paired control (rest only) trial. The 24 data sets (12 subjects, 2 paired trials each) were sorted based on the influence of the palm cooling on the rates of the rise of core temperature and divided them into two equal groups based on the rank order of the treatment effect.

Statistical analysis

Descriptive statistics were calculated for the data sets, and the data sets were subjected to analysis of variance (ANOVA) and appropriate *post-hoc* tests (Microsoft Office Excel for

Windows2003 data analysis tools). The specifics of each statistical analysis are presented in the results section and the figure captions.

Results

Heat loss through the glabrous skin is more variable and can reach higher values than heat loss through the nonglabrous skin

Figure 1 shows the data from one subject on the area-specific heat loss from different body surfaces, glabrous and nonglabrous, during treadmill exercise in a hot environment. The subject rested in the 42°C room for 15 min before the onset of exercise, so he was in a state of thermal vasodilation when exercise commenced. During the 35 min of exercise, his core body temperature (esophageal) increased linearly by about 2°C. At the onset of exercise, the heat loss (W/cm^2) from the glabrous skin of the face and palm was two to three times higher than the heat loss from the various nonglabrous skin areas. The rates of heat loss from the nonglabrous skin did not increase significantly during the exercise and onset of hyperthermia, whereas heat loss from the glabrous skin increased steadily so that by the end of exercise, the area-specific heat loss from the glabrous skin areas was approximately five times higher than the area-specific heat loss from the nonglabrous skin areas. Figure 2a (left panel) shows the heat loss data from 13 subjects undergoing the same experimental procedures. The open bars indicate heat loss values at the beginning of exercise, and the shaded bars are the values at the end of exercise. The initial values for the glabrous skin areas are more than twice those for the nonglabrous skin areas. Most nonglabrous skin areas show no significant increase in heat loss over the exercise bout, but the glabrous skin areas show a more than doubling of heat loss during the exercise. The two nonglabrous areas that show some increase during exercise are the upper back and the thigh. Notably, these areas overlie muscles that are actively engaged in the exercise effort.

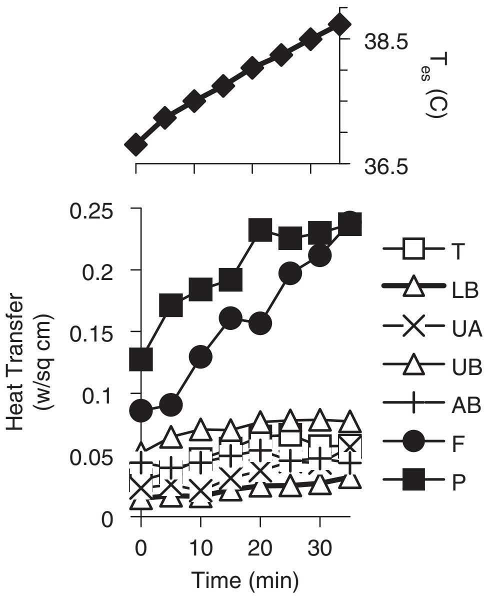


FIG. 1. Local heat loss across various regions of the body surface during fixed-load treadmill exercise in a 42°C environment: Individual subject data. Top panel: T_{es} versus time. Lower panel: heat transfer/unit surface area versus time. Closed symbols: glabrous skin regions. Open symbols: nonglabrous skin regions. T, thigh; LB, lower back; UA, upper arm; AB, abdomen; UB, upper back; F, face; P, palm.

Heat exchange across the glabrous skin can be amplified by the application of mild negative pressure

Figure 2b (right panel) shows that the rate of heat loss across the glabrous skin of the palm can be significantly increased (33%) by the application of negative pressure. The values shown are the mean rates of area-specific heat loss across the 35 min bouts of treadmill exercise for the 13 subjects.

End-of-exercise heart rates reflect greater efficiency of heat extraction from glabrous skin

Figure 3 shows the mean heart rates at the end of the 35 min exercise bouts for the 13 subjects when cooling is applied to different body surfaces. Cooling of the nonglabrous skin areas was administered with cooling pads that were $722\,cm^2$, whereas the cooling pads applied to the face averaged only $288\,cm^2$, and the cooling pads applied to the palm averaged about $152\,cm^2$. Exercise intensity and duration for each subject were the same in all trials. Treatment (skin surface regions cooled: thigh, lower back, upper arm, abdomen, upper back, face, palm, and palm with vacuum) had a significant effect on maximum heart rate (two-factor ANOVA without replication (subject [13] × treatment [8] $p < 0.05$). There were no significant differences in the end-of-exercise heart rates between the runs in which the different regions of nonglabrous skin were treated (two-factor ANOVA without replication (subject [13] × treatment [5] $p = 0.20$), and there were no significant differences between the runs in which the different regions of the glabrous skin were treated (two-factor ANOVA without replication (subject [13] × treatment [3] $p < 0.26$). However, end-of-exercise heart rates trended lower for trials in which the glabrous skin of the face or palm was treated in spite of the fact that the cooling was applied over a smaller surface area (multiple paired *t*-tests. p range 0.06–0.2). This trend was significant when comparing the palm cooling with vacuum trials to the cooling trials of the thigh ($p < 0.01$), lower back ($p < 0.02$), upper arm ($p < 0.04$), or abdomen ($p < 0.03$). The fact that the palm-cooling area was only about 1/5 the cooling area on the nonglabrous skin makes these data more impressive.

Vacuum-enhanced heat extraction from the glabrous skin reduces rate of core temperature rise during heat exposure and exercise and improves performance

An experiment to address whether heat extraction in a situation of repeated bouts of maximal metabolic effort could improve performance was carried out on the Stanford football team engaged in a practice routine called "getting yards." In this routine, the subjects started at a goal line and did repeated 2 min sprints up and down the field. Between the sprints, there was a 3 min interval during which the subjects returned to the goal line and rested. We inserted episodes of palm cooling that averaged no more

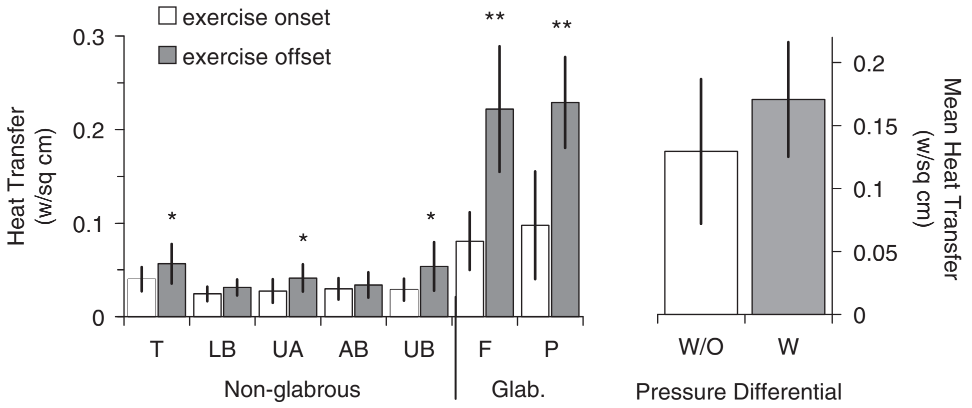


FIG. 2. Local heat transfer across various regions of the body surface at the onset and offset of 35 min of fixed load exercise in a 42°C environment: Group data (mean ± s. d., $n = 14$). Left panel: heat transfer/unit surface area. A two-way ANOVA with treatment (skin regions) and time (exercise onset and offset) as the variables and time as the repeated measure determined significant treatment and time effects ($p < 0.0001$). *F and P onset values significantly different from other regions ($p < 0.01$, paired *t*-tests) and offset values different from onset values ($p < 0.0001$). **UB, T, and UA exercise offset values different from exercise onset values ($p < 0.01$, paired *t*-tests). Abbreviations are as in Figure 1. Right panel: the effect of applying a −40 mm Hg pressure differential to the hand on heat transfer ($n = 24$, $p < 0.02$, paired *t*-test). ANOVA, analysis of variance; s. d., standard deviation; W, with; W/O, without.

than 1.5 min during those rests. These experiments were carried out on hot days (T_a averaged 35°C) and on cooler days (T_a averaged 22°C). The dependent variable was the total distance gained during the sprints (Fig. 4). The total yards gained for each successive sprint decreased under all conditions. On the warm days, the distance gained in the first sprints were lower than they were on the cool days, and in the runs without palm cooling, the rate of drop off of distance in the successive sprints was greater than in the cool days or on the hot days with palm cooling. There was no effect of palm cooling on the cool days. The effect of palm cooing on the hot days was to decrease the drop off in the distance gained so that the performance was similar to the performance on the cool days. As a result of the effect of palm cooling on the hot days, the distance gained in the last three sprints and in the overall distance gained was significantly greater with palm cooling than without it. Thus, the experiment showed that the applications of palm cooling in situations where heat stress is an issue can lead to improved performance. However, these field experiments did not make the connection between the treatment, core temperature, and performance. We, therefore, designed a laboratory experiment to replicate the conditions of the "getting yards" routine.

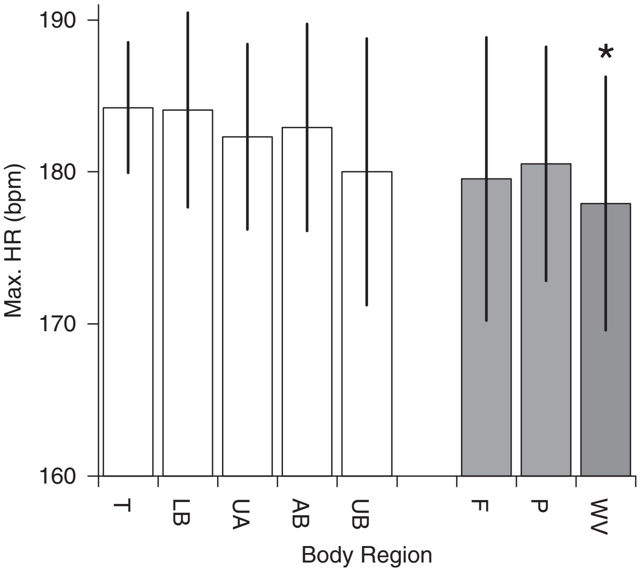


FIG. 3. The effect of regional cooling on maximum heart rate during fixed-load exercise in a 42°C environment. Open bars: cooling of nonglabrous skin regions. Closed bars: cooling of glabrous skin regions. Abbreviations as in Figure 1 and WV, Palm w/vac (−40 mmHg pressure differential applied to the hand along with cooling). A one-way ANOVA determined a significant treatment (skin region) effect ($p < 0.01$).*Different from T, LB, UA, and AB ($p < 0.05$, paired *t*-tests).

In this laboratory experiment on the effects of palm cooling on the rate of rise of core temperature (T_{ty} and/or T_{es}) and performance, 12 subjects engaged in six sprints to subjective fatigue at 5 min intervals on a treadmill set to a speed that required an effort of 110% VO_{2max}. The inter-sprint rest conditions in these experiments were a cool ambient (22°C) and a warm ambient (35°C) with and without palm cooling. Figure 5 shows the effects of palm cooling on the rates of the rise of esophageal and tympanic temperatures from a single subject performing the sprint routine in the hot environment. Clearly, the palm cooling had an effect. The effects of treatment on the two-core temperature measures (T_{es} and T_{ty}) were indistinguishable. Figure 6a (left panel) shows the core temperature (T_{ty}) data from all 12 subjects in all 4 rest conditions and also shows the performance measures. The left four bars show the effects of the thermal environment and palm cooling on performance (summed sprint durations). The first bar is the optimal situation of a cool environment with palm cooling, whereas the fourth bar is the worse

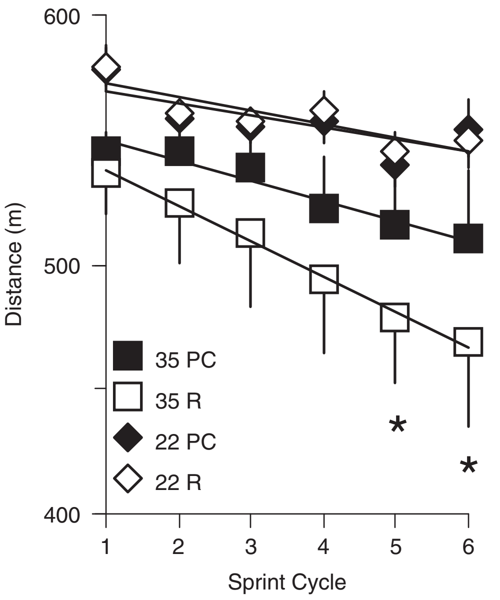


FIG. 4. Field trial: Getting Yards drill (repeated 2 min sprints with a 3 min rest between exercises) under 2 ambient conditions and with and without palm cooling. Distance traveled in a 2 min sprint versus sprint number (mean ± s. d., $n = 6$). Conditions: 22 PC–$T_a = 22°C$ with palm cooling, 22 R–$T_a = 22°C$ with rest only, 35 PC–$T_a = 35°C$ with palm cooling, and 35 R–$T_a = 35°C$ with rest only. A two-way ANOVA with repeated measures for treatments (4 combinations of palm cooling and ambient temperature) and sprint cycles (six) determined a significant treatment and sprint cycle effect ($p < 0.0001$). *35 R different from other conditions ($p < 0.05$, paired t-tests). T_a, ambient temperature; PC, palm cooling; R, rest only.

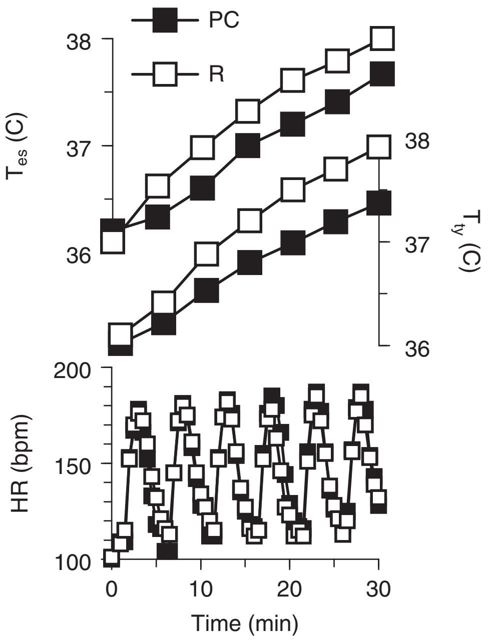


FIG. 5. Core temperatures (T_{es} and T_{ty}) and heart rate during repeated 5 min high-intensity work/rest cycles in a 35°C environment: Individual subject. Open symbols: rest only between exercises. Closed symbols: palm cooling during rest. HR, heart rate.

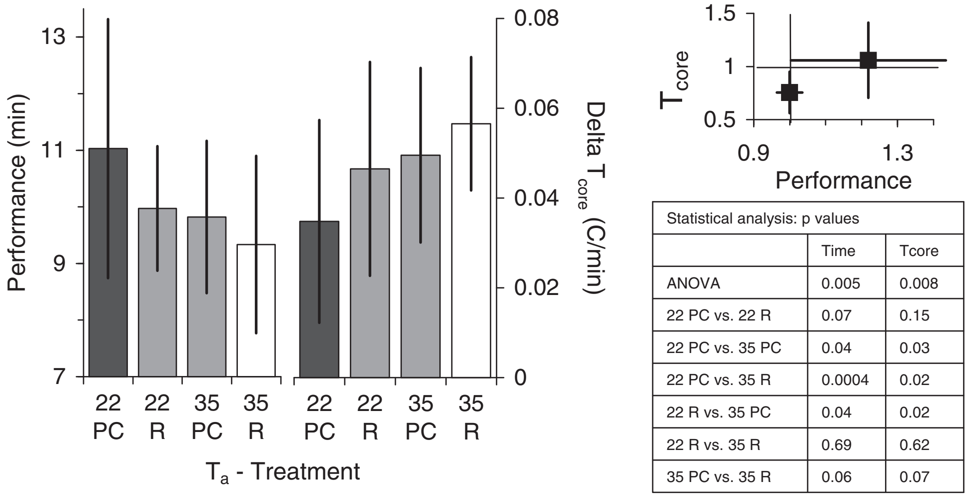
situation of a hot environment with no palm heat extraction. In spite of a great deal of variability in the responses of the subjects, these two sets of data are significantly different ($p = 0.0004$, paired t-test). The two center bars (not significantly different) represent trials in which there was either an environmental cooling factor or a palm cooling factor. The performances in these two groups of trials were intermediate between the two sets of runs at extreme conditions.

The four bars at the right of Figure 6a represent the effects of the environment and treatment on core body temperature. Under conditions of cool ambient and palm cooling, the rate of the rise of core temperature was the least, and under conditions of a warm environment without palm cooling, the rate of core temperature rise was the greatest ($p = 0.02$). Intermediate values were seen in the cool environment without palm cooling and in the warm environment with palm cooling. Thus, in terms of effects on the performance and effects on the rate of rise of core temperature, the application of palm cooling was the equivalent of a 13°C drop in the ambient temperature.

The high variance in these data sets led us to look at how different subjects were responding to the palm-cooling treatments. We sorted the 24-paired data sets (12 subjects, 2 paired trials each) based on the influence of the palm cooling on the rates of the rise of core temperature and divided them into two equal groups based on the rank order of the treatment effect (12 highest vs. 12 lowest). If there was no effect of palm cooling, then the ratio of the rates of the rise of core temperature for cooling and control runs was 1, and if there was an effect of palm cooling, then this ratio was less than 1. For the two groups, we then plotted the ratios of the core temperature effects against the ratios for the performance differences (Fig. 6 right panel). The plot clearly shows that the subjects with the greatest effects of palm cooling on the rate of the rise of core temperature showed no performance benefits. However, the subjects with no apparent effect of palm cooling on the rate of the rise of core temperature showed large performance improvements. Our conclusion is that the two groups represented pacers and pushers. The pacers maintained the same performance level, but suffered a lesser rate of rise in core temperature. The pushers converted the cooling effect into a performance gain and, therefore, showed the same rate of core temperature rise in the experimental and control conditions.

Discussion

The realization of the importance of the vascular structures underlying the glabrous skin for the dissipation of excess heat from the body explains why various models of human heat exchange have been more successful in modeling thermoregulation in a cold environment than in a hot environment.[3,4] Most models have not included the hands and feet, and, therefore, failed to take into account the capacity of the glabrous skin for enhancing heat loss. This omission would be less serious for modeling responses to cold environments, as under those conditions, the AVAs would be closed, and the heat loss from the hands and feet would be minimal. The rationale for not including hands and feet in human heat exchange models was that these appendages were difficult to describe geometrically and they comprised only a small surface area. In fact, some experiments that tested



Statistical analysis: p values		
	Time	Tcore
ANOVA	0.005	0.008
22 PC vs. 22 R	0.07	0.15
22 PC vs. 35 PC	0.04	0.03
22 PC vs. 35 R	0.0004	0.02
22 R vs. 35 PC	0.04	0.02
22 R vs. 35 R	0.69	0.62
35 PC vs. 35 R	0.06	0.07

FIG. 6. The effects of the rest environment and palm cooling during rest between sets of high-intensity sprint exercises ($T_a = 35°C$) (mean ± s. d., $n = 12$). Rest conditions: 22 PC—$T_a = 22°C$ with palm cooling, 22 R—$T_a = 22°C$ with rest only, 35 PC—$T_a = 35°C$ with palm cooling, and 35 R—$T_a = 35°C$ with rest only. Left panel: performance (summed sprint times) and rates of change of T_{ty} versus rest conditions. Upper right; effects of palm cooling on core temperature versus effects on performance: value during cooling trial/value during control trial. Lower right: Statistical analysis for data graphed in left panels (A one-way ANOVA and paired *t*-tests).

skin blood flow placed tourniquets on the wrists and ankles to eliminate a potential source of error,[5] but in reality, they eliminated a highly significant thermoregulatory effector mechanism. Understanding the thermoregulatory role played by the glabrous skin will make it possible to improve human thermoregulatory models and their use in the design of thermally protective gear.

Exploiting the thermoregulatory functions of the glabrous skin makes it possible to advance the understanding of the effects of core body temperature on various aspects of human health and performance and to intervene in those effects. For example, we have shown how vacuum-enhanced heat extraction from only one hand can decrease the rate of rise of core body temperature during aerobic exercise and thereby extend endurance by a large amount.[1] Similarly, the same treatment can be used in heat-stressed subjects to dramatically speed recovery.[6] Every year, young athletes suffer from heat illness and even occasional deaths due to exercise-induced hyperthermia during summer and fall practices and competition. Such tragedies have also occurred in professional athletics. The fact that heat stroke is one of the leading causes of sudden death in sport stimulated the founding of the Korey Stringer Institute at the University of Connecticut dedicated to reducing the occurrences and consequences of heat illness in athletes. Even though whole-body immersion in cold water is still the gold standard for treatment of hyperthermia, that treatment option is not always immediately available. When a cold water bath is not available or until it is available, vacuum-enhanced heat extraction from a palm is a safe and efficient alternative or an additional means of avoiding morbidity and mortality due to hyperthermia.

Two studies have claimed no effect of palm cooling on performance.[7,8] In both cases, the experimental protocol precluded positive results, but for opposite reasons. The Amorim et al. study involved a level of thermal stress that far exceeded the heat loss capacity of a single palmar surface.[7] The subjects walked on a treadmill (5.4–6.7 $Km \cdot h^{-1}$, 0% to 4% grade) in a 42°C environment wearing military battledress uniforms, body armor, and a weighted backpack. The workload was designed to be at 50% of the subjects VO_{2max}. and averaged 537 W. Given the level of heat production and the insulation of the uniform plus body armor, the authors conclude that the maximal possible heat extraction from a single palmar surface was insufficient to have a substantial effect on the rate of the rise of core body temperature. A similar finding was reported by Grahn et al.[1] in a comparison of the effectiveness of palmar cooling at different workloads. That study demonstrated that the effect of cooling a single palm on exercise endurance was exponentially related to workload. Endurance at a workload that produced fatigue in controls at only 15 to 20 min. was minimally improved by palmar cooling, but endurance at a workload that produced fatigue in 60 min. in controls was doubled by palmar cooling. Both these studies applied the cooling device to only one palmar surface. It should be kept in mind that the effects of cooling multiple glabrous skin areas is additive.[6]

The Walker et al. study[8] purported to test whether palmar cooling "… during active rest periods of multiple set training is an effective means to increase performance." The protocol was for the subjects to do 8, 30 s, self-paced treadmill sprints interspersed with 1.5 min walk/jog rests. During the rests, they used the palm-cooling device, rested a hand on a gel pack at the same temperature, or rested the hand on a shelf. The data showed no significant drop off of the distances covered in the sprints under any of the test conditions. The only claim made for acute use of palmar cooling is that it mitigates heat-related impairment of performance. Therefore, since there was no impairment of performance, it was impossible to show a mitigation of impairment with palmar cooling.

Vacuum-enhanced heat exchange across the palm has also been used in reverse to insert heat into the core of hypothermic individuals recovering from anesthesia.[9] The standard methods of body surface warming used in the recovery room to raise the core temperatures of patients to the normal range and stop tremors took hours. In fact, one study of a method of forced warming that is still a standard of care showed that it had no significant effect compared with blankets on speeding the rise of core temperature.[10] In contrast, the use of a vacuum-enhanced palm-heating device reduced the time for core temperature rewarming and tremor cessation to 10 min or less. The ability to insert significant amounts of heat into the body core through the glabrous skin opens up the possibility of designing devices that would improve the functionality and survival of humans working in extremely cold environments.

Experiments on palm heat extraction from subjects engaged in high levels of large dynamic muscle exercise led to the very interesting observation that muscle fatigue may be largely due to the rise in the temperature of the muscle.[2] The work capacity of muscles was greatly enhanced by palm cooling, and when this benefit was applied to strength-conditioning regimes, the rates of gain were dramatic, exceeding what has been observed through the use of anabolic steroids.[2,11] Given the facts that steroid use is prohibited by most collegiate and professional sports associations, and that steroid use carries very significant health risks, the option of a safe alternative for those who wish to improve their strength and work capacity could greatly decrease the use of performance-enhancing drugs and supplements.

Knowledge of the thermoregulatory functions of the AVAs and retia venosa has helped resolve some physiological quandries. In the 1960s, experiments were conducted on humans at rest in a hot environment for the purpose of understanding the effects of heat on cardiovascular performance.[12] The cardiac output was seen to increase by more than a factor of 2, from 6 to 14 L/min. Where did this blood go? The researchers found that blood flow to the internal organs and skeletal muscles actually decreased. The only large rise in blood flow, they observed, was in the forearm. They concluded that the increased cardiac output had to be accommodated by a large increase in cutaneous blood flow due to thermoregulatory vasodilation. However, increases in blood flow through nonglabrous skin have since been demonstrated to be only modest.[13] It did not occur to the investigators that the great increase in forearm blood flow and in cardiac output was due to the opening of the AVAs and the subsequent increased flow through the retia venosa in the glabrous skin.

The fact that heat extraction can mitigate muscle fatigue in both endurance events and anaerobic metabolism events indicates that heat *per se* is a cause of muscle fatigue.[2] What could be the mechanism for this dramatic effect of temperature on muscle function? *In vitro* studies of rabbit skeletal muscle have shown that pyruvate kinase, a critical enzyme for the flow of substrate into oxidative phosphorylation, is highly temperature sensitive.[14–16] Its activity is greatest around 35°C–38°C and drops off rapidly as the temperature rises due to conformational changes. If the rise in muscle temperature during exercise compromises the activity of pyruvate kinase, then the flow of the substrate into the Krebs cycle and, therefore, the rate of production of ATP will be reduced. Continued glycolysis, however, will result in a build up of lactate. These considerations of the possible role of the temperature sensitivity of pyruvate kinase in muscle fatigue cast a new light on the role of lactate in fatigue. Lactate accumulation may be a consequence of muscle fatigue rather than a cause.

There are many medical conditions that could potentially be influenced by a technology that rapidly and efficiently influences the heat balance of the human body. One that we have already demonstrated is the mitigation of heat exacerbation of symptoms in multiple sclerosis. The vast majority of MS patients are highly temperature sensitive such that a small increase in ambient temperature or body temperature can incapacitate them. Being able to efficiently counter an exercise or an environmentally induced rise in core temperature can prevent the exacerbation of symptoms and preserve functionality.[17] Examples of other conditions that are targets for investigation of the effects of this heat exchange technology are as follows: induction of hyperthermia to augment chemo- or radiation therapy for cancer, maintenance of core body temperature perioperatively, peripheral neuropathy, and quality of life issues such as menopausal hot flashes and insomnia. This simple new tool can have far-reaching impacts.

Disruptive Science and Technology

The temperature of the body core is a crucial factor in health and disease. However, it is difficult to manipulate body core temperature efficiently due to the large heat capacity of the body and the thermal conductance of the body surface. Our work has revealed the thermoregulatory significance of a general mammalian vascular feature of the nonhairy skin—AVAs and retia venosa—that has previously been ignored in models of human thermal exchange. Incorporating these thermoregulatory effectors into such models will improve their accuracy and usefulness in the design of protective thermal gear. We have developed a technology that amplifies the heat exchange capacity of these structures. Experiments using that technology have demonstrated its disruptive potential in several areas. In medicine, it challenges the current standard of care for perioperative temperature management. In sport and fitness, it challenges the dogma of the cause of fatigue and introduces a means of improving performance that far exceeds the effects of the use of anabolic steroids and other performance enhancers. In occupational health and safety, it can lead to the development of devices that can reduce the incidence of heat illness due to working in hot environments, in fire-fighting, or in chemical/biological protective gear. Many other applications in medicine and in emergency medicine are possible.

Barriers to Be Overcome

Human thermal exchanges have been studied and modeled for more than 50 years without consideration of the special adaptations of the glabrous skin for heat loss. Thus, there is an enormous amount of literature and practice that should be re-examined, so resistance to these new views is expected. Practical applications of technologies that enhance heat exchange across the glabrous skin have been demonstrated, but technological challenges exist for the design of devices for optimal effectiveness in different applications. For example, wearable (rather than episodic use) devices that have a minimal impact on mobility or manual dexterity are desirable for applications such as firefighting and construction or industrial work. Clinical trials will be necessary to show the effectiveness of the technology in potential medical applications such as cancer therapy, peripheral neuropathy, and perioperative temperature management. Large-scale epidemiological studies will be necessary to support the use of vacuum-cooling devices for the immediate treatment of heat illness in venues such as high-school sports programs. None of these barriers are insurmountable, but they will require considerable resources.

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Author Disclosure Statement

Patents have been issued for the vacuum-enhanced heat transfer technology discussed in this article (D. Grahn and H.C. Heller [Inventors]; Stanford University [Assignee]), and Stanford University has entered into a licensing agreement with AVAcore Technologies, Inc., for the commercialization of the technology. Included in the license is a royalty agreement that grants Stanford University a percentage of the net sales of the technology, which will be shared by the University and the inventors. D. Grahn and H.C. Heller are founders of AVAcore Technologies but receive no ongoing compensation from the company, and AVAcore Technologies provided no financial support for the research. No AVAcore equipment was used in this research. To assure that potential conflicts of interest did not influence the outcome of the research, Stanford University required that Grahn and Heller had no participation in the recruitment of subjects, the conduct of the experimental trials, or the initial analysis of the data in studies that employed the technology.

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Address correspondence to:
H. Craig Heller
Department of biology
Stanford University
371 Serra Mall
Stanford, CA 94305-5020

E-mail: hcheller@stanford.edu

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