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No Evidence of Heat-Induced Vasoconstriction in Human Skin Using Ultrasound Doppler after Passive Whole-Body Heat Stress

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Abstract

Aim: Heat-induced vasoconstriction (HIVC) plays a part in temperature regulation in some animal species by reducing heat gain in hot climates. In humans, conflicting results have been reported from studies on the skin of the finger. Using venous occlusion plethysmography, vasoconstrictions interpreted as HIVC have been observed in thermoneutral and hyperthermic humans. Similar studies using the ultrasound Doppler technique have not found any sign of HIVC in thermoneutral subjects. HIVC has not previously been investigated with ultrasound Doppler in hyperthermic subjects, which was the aim of the present study.

Methods: Eleven subjects were studied in a climatic chamber during continuous passive heat stress. The fingers of one hand were submersed in a water bath, and blood flow velocity was measured with ultrasound Doppler in the radial third finger artery. Control measurements were made in the radial artery of the contralateral hand. After the subjects became hyperthermic, the water temperature was raised gradually from 35 to 43°C over a 10-minute period.

Results: The main finding was that the heated hand showed no vasoconstriction, transient or permanent, in any of the subjects. On the contrary, there was a significant increase in finger skin blood flow following the increase in local temperature.

Conclusion: Blood velocity measurements on finger arteries by ultrasound Doppler methodology showed no evidence of HIVC in hyperthermic human subjects.

Keywords: arteriovenous anastomoses; hyperthermia; skin blood flow; ultrasound Doppler.

Introduction

Heat-induced vasoconstriction (HIVC) is a physiological mechanism that is important in temperature regulation in some animal species. When the skin is heated locally to above body core temperature, skin vessels constrict and limit heat influx. The phenomenon has been observed by direct microscopy in the jackrabbit [1]. In humans, conflicting results have been reported from studies on the finger. Using the venous occlusion plethysmography method (VOP), vasoconstrictions interpreted as HIVC have been observed in thermoneutral [2] and hyperthermic humans [3]. The conditions used corresponded to warm and hot environments, a hot environment is one that leads to an elevated body core temperature (> 37.5°C). Similar studies using the ultrasound Doppler technique [4] have not found any sign of HIVC in thermoneutral subjects. The aim of our study was to investigate whether HIVC is present in hyperthermic subjects, using the ultrasound Doppler method. This has not previously been done. We also discuss why the two methods of blood flow measurement can produce conflicting results.

Materials and Methods

The study was carried out in a laboratory designed for cardiovascular and thermoregulatory research, and approved by the regional ethics committee. Written informed consent was obtained from all participants.

Twelve healthy non-smoking volunteers, 8 females, and 4 male participated. The measurements from one female subject were excluded because of problems with ECG recordings, and results from 11 participants were therefore used (Table 1).

Experimental protocol

The subjects were resting on a bench in a semi-supine position wearing a T-shirt and shorts. The fingers on the right hand were submersed in a temperature-controlled water bath. The left hand was resting in the air. Heat stress was established by high ambient temperature (Ta) and humidity.

The main measurements were blood velocity measured by ultrasound Doppler from the radial third finger artery of the right hand (BVF), and control measurements were made from the radial artery at the wrist on the left hand (BVC). The subjects were considered to be hyperthermic when simultaneously core temperature (Tc) was above 37.5 °C, laser Doppler flowmetry on the forearm showed skin vasodilatation, and the onset of sweating was observed visually. The water bath temperature (Tw) was then raised gradually from 35 to 43°C over a 10-minute period. Blood velocities in the finger artery were measured continuously before, during and after the change in water temperature. In addition mean arterial pressure (MAP) and heart rate (HR) was measured.

The rationale behind the protocol

Ultrasound Doppler measurements of blood velocity have a high resolution and are measured as average velocity over a cardiac cycle, compared to every 30 seconds using VOP. Almost any abrupt change in sensory stimuli (visual, auditory, or tactile) will induce episodes of vasoconstriction of 5-10 seconds duration [5, 6, 7] and these can easily be detected using ultrasound Doppler on a peripheral artery. To avoid such stimuli all measurements were made by instruments localized outside the climatic chamber. In addition, to exclude any finger vasoconstrictions other than those caused by water temperature alone, Tw was increased gradually (almost linearly) and not stepwise. A priori, this would also reveal a possible HIVC temperature threshold for HIVC.

Control measurements on the left hand were made at the radial artery because it is technically easier than the finger artery and because blood velocities here directly represent finger vasomotion in the same hand [4]. The fingers were not immersed in water because this could induce compensatory vasodilatation [2], but rather let the skin of the hand be exposed to Ta like the rest of the skin.

Details from the experimental protocol

On the day of the experiment, the subjects were instructed not to exercise, drink caffeinated beverages or eat prior to the experiment. Continuous blood velocity was measured using a pulsed ultrasound Doppler system (SD 100 and SD 50, Vingmed Sound, Horten, Norway) operating at 10 MHz. The circular transducer had a fixed angle of 45° between the sound beam and the underlying skin surface and was fastened with adhesive tape. Instantaneous cross-sectional mean velocities were calculated by the instrument and fed online to a computer for beat-by-beat time averaging, gated by ECG R waves.

Laser Doppler Flux (LDF) in the forearm was recorded by a laser Doppler instrument (DRT4, Moor Instruments, Devon, UK). The measuring point was on the right lower arm, halfway between the lateral epicondyle and the lateral styloid process. The probe was fastened using double-sided tape, and care was taken not to place the probe over a visible subcutaneous vein. The noise-limiting filter of the instrument was set at its highest level, 21 kHz, and the emitted wavelength was 820 nm. The flux output signal was filtered with a time constant of 0.1 s and sent to the computer for both beat-by-beat averaging and sampling at

20 Hz. Instantaneous arterial blood pressure (BP) was obtained from the left third finger using a photoplethysmographic device (Ohmeda 2300 Finapres, Madison, WI). The blood pressure data were fed to the computer, and MAP was calculated by numerical integration for each R-R interval. Tc was measured continuously using a tympanic probe [8] (Exacon, model 8940, Denmark) and sampled at 1 Hz. Initially, during instrument setup before data recording started, Ta was 28-30°C. After 30 minutes, data recording started, and Ta was raised gradually to 43°C. The air humidity was fixed at 45%. All instruments and temperature adjustments were made from outside the chamber, leaving the subjects undisturbed throughout the experimental period.

Data analysis and statistics

Blood velocity and blood pressure variables were sampled beat-by-beat, LDF at 20 Hz and all temperatures at 1 Hz. For comparison between subjects, all variables were converted to 1 Hz by interpolation. HR was calculated from ECG R waves. For each subject (n=11), average blood velocity was calculated for the 1-minute periods before and after the change in Tw from 35 to 43°C (Table 1). The values were compared using the paired Wilcoxon signed-rank test, two-sided test, significance level p=0.05.

To compare the changes in blood velocity in the finger artery and the radial artery, the 2 and 98% percentiles and average blood velocity for all 11 subjects were normalized and plotted in a ±45-sec sliding window average in the same panel. In two subjects, recordings of blood velocity in the control arm were not obtained because the probe was displaced during the experiment. Statistical analyses were performed using the statistical program Minitab.

Results

Figure 1 (A-F) shows simultaneous recordings of MAP, HR, LDF, Tc , blood velocity in the radial artery of the control hand (BVC), blood velocity in the finger artery (BVF) and Tw from one subject.

Mean arterial, systolic and diastolic blood pressure did not change with heat stress or local warming in any subject. HR and Tc increased steadily throughout the experiment. At the end of the experiment, HR was on average 101.4 (1.6) beats min-1 and Tc was 38.4 (0.2) °C. All subjects sweated heavily during the experiment.

					Blood velocity-finger			Blood velocity-control		
Subject	Sex	Age	BMI	Tc	before BV	after BV	Δ BV	before BV	after BV	Δ BV
1	m	27	20,2	38,4	0,044	0,061	0,018	0,155	0,165	0,010
2	f	19	20,1	38,4	0,067	0,055	0,012	0,070	0,060	0,010
3	f	20	30,5	38,2	0,077	0,079	0,003	0,051	0,061	0,011
4	f	20	21,6	38,2	0,066	0,071	0,005	*	*	*
5	m	19	19,6	38,2	0,053	0,059	0,006	0,036	0,037	0,000
6	m	36	26,3	38,4	0,026	0,037	0,011	*	*	*
7	m	29	26,6	38,5	0,042	0,047	0,005	0,051	0,062	0,011
8	f	31	24,8	38,0	0,065	0,071	0,007	0,080	0,094	0,014
9	f	23	20,5	38,5	0,060	0,079	0,019	0,084	0,097	0,014
10	f	20	19,5	38,4	0,047	0,062	0,015	0,067	0,093	0,026
11	f	37	20,2	38,6	0,053	0,069	0,016	0,059	0,081	0,021
Median		23,0	20,5	38,4	0,053	0,062	0,007	0,067	0,081	0,011
Mean		25,5	22,7	38,4						
SD		6,8	3,7	0,2						

Table 1. The table displays sex (male/female), age (yrs), Body Mass Index (kg/m2) and core temperature at the end of the heating period (Tc °C) for each subject. Average blood velocity (m/s) from a 1 min period before and after a change in water bath temperature (ΔTw= 8 °C) from the radial third finger artery (blood velocity-finger) and control measurements from the radial artery on the left hand (blood velocity-control). The change in blood velocity is displayed as ΔBV

Blood velocities were compared using the Sign test, a two- sided test, with a level of significance P=0.05. There was a significant increase in blood velocities in both the finger artery (p=0.001) and in the control artery (p=0.004)

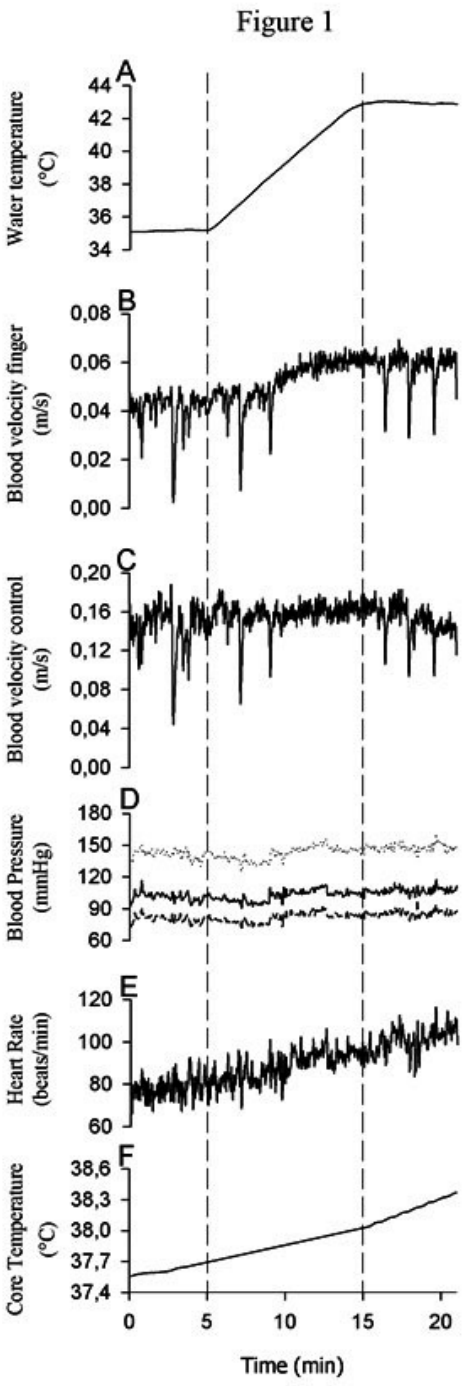

Figure 1. A-F shows simultaneous recordings from one female subject. From top: water bath temperature (°C), blood velocity in finger artery (m/s), blood velocity in radial artery of the control hand (m/s), blood pressure (systolic, mean arterial, and diastolic pressure in mmHg), heart rate (beats/min) and core temperature (°C). Change in water bath temperature between two broken lines (at 5-15 min).

This was visually confirmed in all subjects, and LDF readings increased to values in excess of 50 arbitrary units (a.u), indicating considerable vasodilatation in non glabrous skin. High mean blood velocity was observed in both the radial third finger artery and the radial artery of the control hand throughout the experiments, only interrupted by occasional minor, transient vasoconstrictions. Such vasoconstrictions were observed simultaneously in the control artery as well (Figure.1), and were not related to changes in temperature.

Figure 2 displays average Tc (A) and average blood velocity and 98 and 2% percentiles in the finger artery (C) and control hand (B) for all 11 subjects. Average blood velocity for the 1-minute periods before and after the change in Tw from 35 to 43°C was calculated for each subject (Table 1). There was a significant increase in blood velocity both in the finger ($p=0.001$) and in the control artery ($p=0.004$). In the figure, relative average blood velocity and percentiles from the recordings in the finger and the control hand are plotted together for comparison (D). There is a striking similarity between the two plots.

Discussion

Brief description of general responses to passive heat stress.

General responses to passive heat stress are increased blood flow and sweat gland activity in the skin. The initial response is the dilatation of skin arterioles due to the cessation of nerve impulses in the sympathetic vasoconstrictor system in both glabrous and non glabrous skin. If Tc continues to increase, arterioles of the active vasodilator system in non glabrous skin dilate, presumably in response to increased activity in cholinergic sympathetic fibers [9]. This coincides with the onset of sweating [10]. Arteriovenous anastomoses (AVAs) in the glabrous skin of the palm and nailbeds of the hand, the sole of the foot and the skin of the nose, also dilate, allowing blood to pass directly into the superficial veins of the arms and legs [11]. AVAs are under strict central nervous control, and their vasomotion is probably independent of the arterioles [12]. AVAs in different skin beds open and close synchronously [13, 14] and will shift from cycles of opening and closing 2-3 times per minute in a thermoneutral environment to remaining predominantly open if the body is subjected to heat stress [7]. Passive heating can increase cardiac output to more than 8 litres min-1 [15]. These general responses were also observed in all subjects in our study. Blood velocity in the finger artery and control artery rose to high values and AVA constrictions became rare, indicating a predominately di-

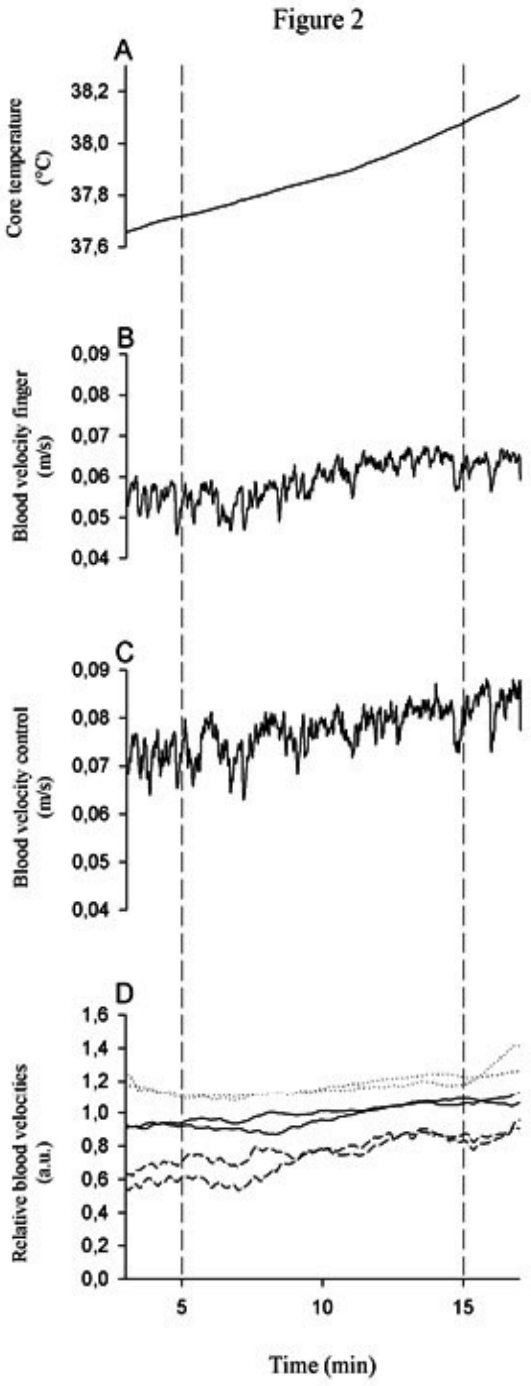

Figure 2. From top, the plot A-D displays average core temperature (°C) for all 11 subjects, average blood velocities (m/s) in finger artery and control artery for 9 subjects. At the bottom the 2 and 98% percentiles and average blood velocity from both arteries (9 subjects) were normalized and plotted in a ±45-seconds sliding window and plotted together in the same panel for comparison. The raise in water bath temperature occurs between dotted lines (at 5-15 minutes).

lated vascular bed in the fingers and palm of the hand. The same level of increase was observed in non glabrous skin, and all the subjects sweated heavily. In addition, there was a steady increase in HR (figure 2). Mean arterial blood pressure was unchanged so that given the substantial fall in total peripheral resistance caused by dilatation of the vessels, the increase in heart rate represents a large increase in cardiac output. At the end of the experiment, the average Tc was well above 38 °C, and we conclude that the subjects were heat-stressed and hyperthermic.

The effects of local warming on finger blood flow

In thermoneutral subjects, blood flow through a hand that is heated above 35-37°C is higher than through a hand in a thermoneutral environment [16]. Different mechanisms mediate the effects of local temperature on skin blood flow in glabrous and non glabrous skin. The local effect disappears when high Tc suppresses vasoconstrictor tone in the skin vessels, and skin blood flow is near its maximum [17, 15]. Figure 2 (C) shows that there was no sign of HIVC in our subjects. In fact, blood velocity increased in both the finger artery and the radial artery of the control hand. The increase probably occurs because the heat loss control mechanism has been pushed to its limits. A comparison of blood flow velocities in the finger and control arteries indicates that the local application of warm water has no local effect on finger circulation. This is displayed in figure 2 (D). Blood velocities recorded from the distal part of the radial artery reflect vasomotion in a finger artery [4]. Plots of normalized values of synchronously recorded blood velocities from the two sites should be similar in shape if locally applied warm water has no local effect on finger circulation in heat-stressed humans. Figure 2 (D) shows the relative average blood velocities and fractiles as recorded from the finger and the control hand plotted together, and the two plots are very similar.

Continuous measurements of skin blood flow during heat stress

The main finding in this study was that HIVC could not be observed in the skin of the finger during passive heat stress. Figure 1, E and F, shows continuous hand and finger blood velocity measurements. The high velocities indicate persistent dilatation of the AVAs. There are short transient episodes of vasoconstriction in both hands simultaneously, independently of Tw. These represent simultaneous activity in the AVAs, a phenomenon previously described in subjects exposed to a hot environment [7]. The vasoconstriction is short-lived, and occurs every 3 to 7 minutes, resulting in a 40-50% reduction in average mean blood velocity. The physiology behind this is not known. Such

episodes were also observed by Burton in 1939, and are probably not related to HIVC.

Observations using venous occlusion plethysmography (VOP)

Nagasaka and co-workers observed reduced blood flow in both thermoneutral [18] and heat-stressed [3] subjects using VOP methodology. Blood flow in the finger was recorded every 30 seconds, and Tw was raised stepwise, 2 °C at a time, from 35 to 43 °C. Otherwise, the VOP studies were similar to our ultrasound doppler studies. Briefly, Nagasaka and co-workers observed vasoconstrictions in the finger at Tw of 39 and 41°C only, not at 37 and 43°C. The vasoconstrictions were brief, appearing during the period when Tw was being increased. In addition, vasoconstriction was accompanied by an increase in local thermal sensation in the heated hand, as reported by the subjects. A gradual decrease in local thermal sensation was matched with the gradual return of finger blood flow to previous values. In another experiment, the local thermal sensation was not perceived during the simultaneous mental calculation, and when Tw was raised, no reduction in finger blood flow was observed [19].

Conflicting results from ultrasound Doppler and VOP

Almost any abrupt change in sensory stimuli will induce episodes of vasoconstriction of 5-10 seconds duration [3, 6, 7] and the venous occlusion plethysmograph technique has an inherent tendency to impose such sensory stimulation. This together with local thermal sensation may explain the observations of Nagasaka and co-workers.

To conclude, neither the results of this study nor previous work from our laboratory [4] provide any support for the claim that HIVC in glabrous skin is part of human temperature regulation. Locally applied warm water has no local effect on finger circulation in heat-stressed humans.

References

1. Schmidt-Nielsen K, Dawson TJ, Hammel HT, Hinds D & Jackson DC (1965) The Jack Rabbit - a study in its desert survival. Hvalrådets Skrifter 48: 125-142.

2. Nagasaka T, Cabanac M, Hirata K & Nunomura T (1986) Heat-induced vasoconstriction in the fingers: a mechanism for reducing heat gain through the hand heated locally. Pflugers Archiv.European Journal of Physiology 407: 71-75.

3. Nagasaka T, Hirata K, Nunomura T & Cabanac M P (1987) The effect of local heating on blood flow in the finger and the forearm skin. Can.J.Physiol Pharmacol 65: 1329-1332.

4. Bergersen TK, Eriksen M & Walloe L (1995) Effect of local warming on hand and finger artery blood velocities. Am.J.Physiol 269: R325-R330.

5. Bini G, Hagbarth KE, Hynninen P & Wallin BG (1980) Thermoregulatory and rhythm-generating mechanisms governing the sudomotor and vasoconstrictor outflow in human cutaneous nerves. J.Physiol 306, 537-552.

6. Burton AC & Taylor RM (1939) The range and variability of the blood flow in the human finger and the vasomotor regulation of body temperature. Am.J.Physiol 127: 437-453.

7. Thoresen M & Walloe L (1980) Skin blood flow in humans as a function of environmental temperature measured by ultrasound. Acta Physiol Scand. 109: 333-341.

8. Sato KT, Kane NL, Soos G, Gisolfi CV, Kondo N, et al. (1996) Reexamination of tympanic membrane temperature as core temperature. J.Appl.Physiol 80: 1233-1239.

9. Grant RT & Holling H E (1938) Further observations on the vascular responses of the human limb to body warming; evidence of sympathetic vasodilator nerves in the normal subject. Clinical Science 3: 273-285.

10. Roddie IS & Shepherd JT (1957) The contribution of constrictor and dilator nerves to the skin vasodilation during body heating. J.Physiol 136: 489-497.

11. Vanggaard L (1975) Physiological reactions to wet-cold. Aviation Space and Environmental Medicine 46: 33-36.

12, Grant RT (1930) Observation of direct communication between arteries and veins in the rabbit's ear. Heart 15: 281-303.

13. Bergersen TK (1993) A search for arteriovenous anastomoses in human skin using ultrasound Doppler. Acta Physiol Scand 147: 195-201.

14. Walløe L (2015) Arterio-venous anastomoses in the human skin and their role in temperature regulation. Temperature. 3: 92-103.

15. Taylor WF, Johnson JM, O'Leary D & Park MK (1984) Effect of high local temperature on reflex cutaneous vasodilation.

J.Appl.Physiol 57: 191-196.

16. Spealman CR (1945) Effects of ambient temperature and hand temperature on blood flow in hands. Am.J.Physiol 145: 218-222.

17. Pergola PE, Kellogg DL, Jr. Johnson JM, Kosiba WA & Solomon DE (1993) Role of sympathetic nerves in the vascular effects of local temperature in human forearm skin. Am.J.Physiol 265: H785-H792.

18. Nagasaka T, Cabanac M, Hirata K & Nunomura T (1987) Control of local heat gain by vasomotor response of the hand. J.Appl. Physiol 63: 1335-1338.

19. Hirata K, Nagasaka T, Nunomura T & Cabanac M (1988) Local thermal sensation and finger vasoconstriction in the locally heated hand. Eur.J.Appl.Physiol 58: 92-96.