Simulated Microgravity Increases Cutaneous Blood Flow in the Head and Leg of Humans

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Background: The cutaneous microcirculation vasodilates during acute 6° head-down tilt (HDT, simulated microgravity) relative to upright conditions, more in the lower body than in the upper body. Hypothesis: We expected that relative magnitudes of and differences between upper and lower body cutaneous blood flow elevation would be sustained during initial acclimation to simulated microgravity. Methods: We measured cutaneous microvascular blood flow with laser-Doppler flowmetry at the leg (over the distal tibia) and cheek (over the zygomatic arch) of eight healthy men before, during, and after 24 h of HDT. Results were calculated as a percentage of baseline value (100% measured during pre-tilt upright sitting). Results: Cutaneous blood flow in the cheek increased significantly to 165 ± 37% (mean ± SE, p<0.05) at 9–12 h HDT, then returned to near baseline values by 24 h HDT (114 ± 29%, NSD), despite increased local arterial pressure. Microvascular flow in the leg remained significantly elevated above baseline throughout 24 h HDT (427 ± 85% at 3 h HDT and 215 ± 142% at 24 h HDT, p<0.05). During the 6-h upright sitting recovery period, cheek and leg blood flow levels returned to near pre-tilt baseline values. Conclusions: Because hydrostatic effects of HDT increase local arterial pressure at the carotid sinus, baroreflex-mediated withdrawal of sympathetic tone probably contributed to increased microvascular flows at the head and leg during HDT. In the leg, baroreflex effects combined with minimal stimulation of local veno-arteriolar and myogenic autoregulatory vasconstriction to elicit relatively larger and more sustained increases in cutaneous flow during HDT. In the cheek, delayed myogenic vasoconstriction and/or humoral effects apparently compensated for flow elevation by 24 h of HDT. Therefore, localized vascular adaptations to gravity probably explain differences in acclimation of lower and upper body blood flow to HDT and actual microgravity.

Materials and Methods

In order to examine the effects of simulated microgravity on regional cutaneous blood flow, eight healthy male subjects were tilted 6° head-down for 24 h at the NASA-Ames Research Center Human Research Facility. Female subjects were not used in order to minimize gender-related variability in our data. Subjects in this study were...
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36 ± 7 years old (mean ± SD), they weighed 77.0 ± 11.7 kg, and they were 175.7 ± 8.0 cm tall. Subjects were deemed normal and healthy on the basis of a routine physical examination, medical history, hematology, and urinalysis. During the study, subjects were taking no medications, and caffeine and alcohol were not consumed 24 h prior to or during the study. The protocol was approved by the NASA Ames Research Center Human Research Experiments Review Board. Informed written consent was obtained.

Regional cutaneous microvascular blood flow was measured with two laser Doppler flowmeters equipped with right-angle probes (Vasamedics, St. Paul, MN). Flowmeter output was zeroed while placing the probe face against a white surface. One probe was placed on the right cheek over the zygomatic arch; the other was placed over the distal anterior tibia 7 cm proximal from the malleolus. The probes were secured (but not compressed) with tape for the 33-h protocol (3 h setup and pre-tilt control, 24 h HDT, and 6 h recovery). After baseline values were obtained in the upright sitting position at 8:30 a.m., the subjects were instructed to lie in the horizontal supine position for 5 min. They subsequently assumed the 6° head-down position for 24 h. During HDT, cutaneous blood flow was measured at 30 min, every 3 h until 10 p.m. and at the end of 24 h. Following the 24-h HDT protocol, subjects returned to the horizontal supine position for 5 min, then assumed upright postures for 6 h. During the 6-h recovery, flow was assessed hourly in the seated position after a 1-min stabilization period. Subjects were allowed to ambulate when not being studied during recovery. Because of the sensitivity of the cutaneous microcirculation to thermal stimuli, room temperature was monitored and maintained at 23.4 ± 0.8°C (mean ± SD). Subjects wore shorts and a shirt and covered themselves with a sheet and blanket as necessary for comfort.

Arterial blood pressure at heart level (manual arm auscultatory sphygmomanometry) and room temperature (Hg thermometry) were measured at the same time points that blood flow was measured. Cutaneous blood flow data were collected on a strip chart recorder (Astromed, West Warwick, RI). Flowmeter output was determined by averaging values recorded during the final 30 s of a 3-min data observation period at each data collection time point. Raw flowmeter outputs were analyzed with repeated measures ANOVA and post-hoc paired t-tests (p < 0.05). For presentation, raw flowmeter outputs (mV) at each site were normalized to the average baseline value (measured during pre-tilt upright sitting) calculated across subjects. Blood flows are reported as a percentage of the mean baseline value. Therefore, error bars in figures at all time points, including baseline, represent variability in raw data adjusted to the percentage scale. All data are reported as means ± SE.

RESULTS

Relative to seated baseline values, mean arterial pressure at heart level was increased significantly at 6 and 12 h of HDT, and at the post-HDT supine measurement (Fig. 1, part A). Recovery blood pressures were no different than pre-tilt values. Seated baseline raw cutaneous microcirculatory blood flowmeter output means equaled 112 ± 26 mV in the cheek and 55 ± 39 mV in the leg. Although microcirculatory responses of our eight subjects were highly variable, cheek and lower leg cutaneous blood flow were significantly increased by HDT. Acute pre-tilt horizontal recumbency significantly increased leg skin flow, and tended to increase flow in the cheek. During HDT, neither site exhibited consistently increased flow until 3 h. Cheek cutaneous microvascular blood flow increased to 111 ± 18% of control by 3 h of HDT, and increased further to 165 ± 37% at 9–12 h HDT (Fig. 1, part B). By 24 h HDT, cheek blood flow had returned to near-baseline (114 ± 29%). Microvascular flow in the leg increased and remained significantly elevated above baseline after 3 h HDT (to 427 ± 85% of baseline at 3 h HDT, and 215 ± 142% at 24 h HDT; Fig. 1, part C). During pre-tilt supine and HDT periods, percentage increases in leg cutaneous blood flow were
at least twice those seen in the cheek. Subjectively, most subjects experienced some degree of facial edema, headache and nasal congestion during the 24 h HDT.

During upright seated recovery, cheek flow was significantly depressed at 4 h post-tilt relative to pre-tilt baseline, and tended to be reduced at other recovery time points (Fig. 1, part B). Leg cutaneous blood flow exhibited marked variability during recovery, and was not significantly different from pre-tilt baseline values (Fig. 1, part C). Room temperature increased significantly from 22.3 ± 0.2°C at 8:30 a.m. to 23.8 ± 0.2°C at 6:00 p.m. (Δ = 1.5°C) on day 1 of the study, and from 22.4 ± 0.2°C at 9:00 a.m. to 24.1 ± 0.2°C at 2:00 p.m. (Δ = 1.7°C) on day 2 (recovery).

**DISCUSSION**

In accordance with literature reports (1,3), we found that acute recumbency and HDT increase lower body cutaneous microvascular blood flow, while upper body flow increases to a lesser extent, indicating that skin blood flow does not simply follow site-specific changes in cutaneous arterial pressure. Our results further demonstrate that both upper and lower body cutaneous blood flow remain substantially elevated during early HDT. Relative increases in leg skin blood flow, where local perfusion pressure was reduced by HDT (12,13,21,27), were more than two times greater than concomitant cheek flow increases, where local perfusion pressure is known to increase during HDT (13,24). Moreover, leg microcirculatory blood flow exhibited sustained elevation during HDT, while cheek flow returned to baseline levels within 24 h HDT.

Head-down tilt increases blood pressures at atrial and carotid baroreceptors relative to pressures seen in upright posture (6,7). Increased baroreceptor loading results in a general relaxation of sympathetic arteriolar tone, and is probably partially responsible for augmentation of cutaneous blood flow at both leg and cheek sites. However, the delayed vasodilatory response at the cheek suggests baroreflex involvement is less likely there. It is possible that baroreflex effects are more strongly expressed in the lower body than in the upper body. Because magnitude of cutaneous microvascular blood flow response to 24 h HDT exhibits site-specificity (i.e., leg cutaneous blood flow elevation exceeds that seen at the cheek during HDT), other factors which influence regional cutaneous blood flow also help explain our findings. These other factors include myogenic autoregulation, local neuronal regulation, and humoral effects.

Hormonal factors may have contributed to the progressive elevation of cheek cutaneous blood flow over the first 12 h of HDT, and its subsequent reduction by 24 h HDT. Slight HDT-induced reductions of vasopressin and plasma renin activity (vasoconstricting effectors) mirror the flow increase we observed in the cheek (23). Also, HDT-induced elevation of plasma atrial natriuretic peptide (ANP) could increase facial blood flow (10). Indeed, pharmacologic ANP administration is known to increase skin blood flow (4,33) and elicit facial flushing in humans (26). HDT measurements of cutaneous blood flow during blockade of specific hormones would test their importance in explaining our findings. Nevertheless, it appears that hyperemic influences (increased perfusion pressure, baroreflex vasodilation, and endocrine changes) overwhelmed flow-reducing influences (myogenic autoregulatory vasoconstriction, increased venous back-pressure, and local veno-arteriolar reflexes, if any) to increase cheek blood flow during the first 12 h of HDT.

Increased facial blood flow may be partially responsible for the facial edema associated with HDT and microgravity, because increased blood pressure and flow enhance capillary filtration. However, return of cheek cutaneous blood flow to near baseline within 24 h of HDT suggests that prolonged elevation of microvascular perfusion alone does not sustain the facial edema associated with HDT simulation of microgravity. Studies of cerebral blood flow velocity indicate that it too increases (15-20% relative to seated values) during the first hours of HDT, then returns towards upright baseline during the first 2 d of HDT (9,18). Therefore, in terms of blood flow, the circulation of the head largely acclimates to HDT-induced local blood pressure elevation within 24 h. Facial edema and other sequelae of headward fluid redistribution may be due more to increased microvascular pressure than to increased flow. Tendencies toward sub-baseline flows post-tilt were probably due to vasoconstriction to maintain blood pressure in the face of bed rest-induced hypovolemia (2,6,8,17,22,23).

In the leg cutaneous microcirculation, sustained reduction of all vasoconstricting influences probably explains the marked increase in flow seen throughout 24 h HDT. Hassan and Tooke (14) found that local neurogeno-veno-arteriolar reflexes, systemic baroreflexes, and local myogenic autoregulatory effects collectively mediate cutaneous vasoconstriction in the dependent leg. Increased carotid sinus and atrial pressures, and reduced leg arteriolar pressure and venous pooling during HDT would minimize vasoconstricting effects of all of these mechanisms. In apparent contrast to our 24 h HDT results, other more chronic studies report leg vasoconstriction after several days of actual (32) and HDT-simulated (2,8) microgravity. However, those studies employed supine baseline conditions. Whether vasoconstriction seen in those studies equals or exceeds that seen in upright baseline conditions (as used in the present study) relative to supine remains to be demonstrated. As in the head, it is possible that the leg vasodilation seen in the present study represents a transient prelude to subsequent vasoconstriction during HDT. Reduction of central venous pressure coincident with hypovolemia in both simulated (23) and actual (19,20) microgravity could explain eventual elevation of vascular resistance.

It is unlikely that circadian rhythms in skin blood flow or fluctuations in room temperature caused the responses seen in this study. During the day, finger cutaneous blood flow normally reaches a nadir (supine subjects; 16) and body core temperature a peak (upright subjects; 30) at the same time (late afternoon) that we observed relatively high leg and cheek cutaneous blood flows. Therefore, if cheek and leg circadian rhythms in cutaneous flow parallel those in the finger, they would oppose, and not contribute to, the trends we noted. Further, the small room temperature changes we measured do not significantly affect cutaneous blood flow (31,34).

Laser Doppler flowmetry is a generally accepted method...
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for measurement of changes in skin blood flow (5,11,29). Although it is a safe, convenient, reliable, and noninvasive technique, certain limitations exist in its application: 1) values obtained only indicate relative changes in cutaneous blood flow; 2) local variations in skin microvascular density and blood flow make this technique site-specific (25); and 3) ambient temperature and emotional factors influence cutaneous flow, and so must be controlled in any investigation of cutaneous hemodynamic regulation (28). Our study design acknowledged these limitations. Our measurements do not quantify the total amount of cutaneous blood flow to the face or leg, or absolute changes therein.

In summary, 24 h HDT produced marked and sustained elevation of leg cutaneous microvascular blood flow, along with a lesser, more transient increase of cheek flow. Although it is probable that these findings may be extrapolated to female subjects, further studies must confirm this. Contrary to the headward fluid volume redistribution known to occur during HDT and microgravity, cutaneous blood flow is preferentially increased in the lower body, at least for 24 h. It is well documented that the cutaneous circulation serves a principally thermoregulatory function, and is highly sensitive to variations in body core temperature. However, at rest in euthermic conditions, this system is subject to regulatory mechanisms similar to those found in other tissues such as skeletal muscle. The observed cutaneous responses in this study may, therefore, be representative of microvascular responses in deeper, less accessible tissues.

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