ORIGINAL RESEARCH

Impairment of Cardiovascular and Vasomotor Responses During Tilt Table Simulation of "Push-Pull" Maneuvers

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GOODMAN LS, LESAGE S. *Impairment of cardiovascular and vasomotor responses during tilt table simulation of "push-pull" maneuvers.* Aviat Space Environ Med 2002; 73:971–9.

Background: Numerous studies have shown that tolerance to positive acceleration (+Gz) is impaired subsequent to an exposure of less than +1 Gz. ***Hypothesis:*** Vasodilation induced by antecedent negative Gz (−Gz) exposure delays sympathetic vasoconstriction during subsequent +Gz, further reducing G-tolerance. ***Methods:*** There were 20 subjects tested on an electronic tilt table, and exposed to the following randomized head-up tilt (HUT) and head-down tilt (HDT) conditions +75° HUT for 60 s, followed by transition to either 0° (supine) HDT, or −25° HDT, or −45° HDT for 7 or 15 s at tilt rate of 45° · s^{-1}. This was followed by HUT, divided into three periods: HUT1 (~3–10 s), HUT2 (~15–22 s), and HUT3 (~27–35 s) Systolic blood pressure (SBP) was normalized to heart and head-levels Stroke volume (SV) was estimated using impedance cardiography; forearm blood flow (FBF) estimated by venous occlusion plethysmography and forearm vascular resistance (FVR) was calculated from FBF and SBP Total peripheral resistance (TPR) was estimated by MAP/(SV*HR) ***Results:*** Heart-level SBP decreased significantly during HDT for both HDT durations ($p < 0.01$) SBP increased significantly at head-level during HDT ($p < 0.001$) During HUT1 heart and head-level SBP decreased for all conditions ($p < 0.001$), recovering to baseline levels by HUT2 TPR decreased significantly for all HDT conditions ($p < 0.001$), with this decrease related to the degree of HDT angle ($p < 0.05$) During HUT1, TPR remained depressed below baseline At HUT2, TPR remained decreased for the −45°/7-s condition only ($p < 0.01$) FBF decreased significantly during HDT ($p < 0.02$), with the magnitude related to the HDT angle FBF remained elevated during HUT1 ($p < 0.01$) FVR decreased as a function of HDT angle during HDT ($p < 0.001$), with the decrease persisting into the HUT1 phase ($p < 0.01$) By the HUT2 and HUT3 periods, FVR were above baseline levels for the −45° HDT condition ($p < 0.01$) ***Conclusion:*** These results confirm in humans the delayed recovery of peripheral vascular resistance observed in animal studies when −Gz precedes +Gz Since SV recovered to baseline levels during the "pull" phase (HUT1–3), with TPR and forearm vascular resistance remaining depressed, baroreflex-mediated peripheral vascular control is delayed This delay at higher subsequent +Gz levels is dangerous for the military pilot, since symptoms of G-intolerance due to delay in head-level BP recovery will ensue at lower absolute +Gz levels during push-pull type maneuvers.

Keywords: push-pull maneuver, cardiovascular reflexes, acceleration

THE REDUCTION in headward acceleration (+Gz) tolerance when preceded by < +1Gz (relative −Gz) has been studied during in-flight research, rotating platform simulations, and more recently, using multi-gimballed centrifuges. This phenomenon, termed the "Push-Pull" effect, has assumed a greater role in acceleration protection research due to recent U.S. Air Force, U.S. Navy, and Canadian Forces accidents, which remain unexplained solely on the basis of high +Gz exposure from a +1 Gz baseline (17). Although the cardiovascular reflexes surrounding this aerial maneuver are beginning to be understood as a result of investigations using an animal model (4), only one study has incorporated measurements of human physiological responses other than heart rate and BP (26).

Doe et al. (4) described the delay in vasoconstrictor tone (as measured by limb and abdominal perfusion pressure and flow) development during carotid sinus unloading (simulated "pull"), with isolated carotid sinus perfusion (simulated "push") in a dog model. It is this delay in development of peripheral vascular resistance which is implicated in the exaggerated +Gz intolerance following −Gz exposure. Whether this response occurs in the intact human, however, has not been tested.

Tilt tables are also used to study cardiovascular responses. They offer a convenient and cost-effective method of studying human cardiovascular responses to transitions in gravitational stress by exposure to alternating head-down (HDT = −Gz) or head-up tilt (HUT = +Gz). Although the total ±Gz envelope available is limited, specialized measurements of cardiovascular status not feasible during in-flight or centrifuge experimentation may be more easily obtained (11,21,26).

The primary aim of this investigation was to study cardiovascular reactions/reflexes in more detail during a low-intensity tilt table simulation of the push-pull maneuver using an HUT — HDT — HUT model. The main hypothesis tested was that the delay in the development of peripheral vasoconstrictor tone as observed by Doe et al. (4) in the animal model, would also be

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This manuscript was received for review in July 2001. It was revised in March 2002 It was accepted for publication in June 2002.

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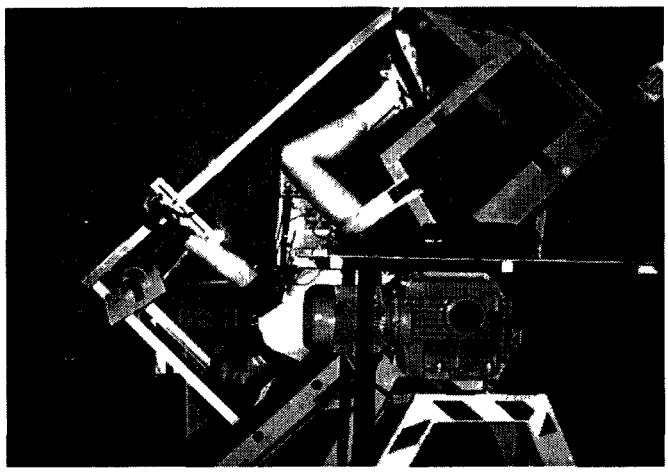


Fig. 1. Illustration of the DCIEM electronic tilt table with subject in the −45° HDT position

observable in humans. We also tested two additional hypotheses in this study: 1) that the severity of the transient hypotension during HUT (+G_z) after HDT (−G_z) increases with the magnitude of the preceding −G_z tilt angle; and 2) that the severity of the transient hypotension occurring during rapid HUT after HDT will increase with the duration of the preceding −G_z tilt exposure.

METHODS

A customized, electronically controlled tilt table was constructed for these experiments (**Fig. 1**). The tilt table can accommodate a seated or standing subject. Conversion of the tilt table to the seated configuration was accomplished by attachment of an adjustable bench-like seat to the tilt table. Restraint systems were provided for subject safety. These included adjustable head and shoulder supports, and quick-release straps for the shoulders, thorax, waist, and legs. The initial +75° HUT position was selected in order to simulate the typical 15° seat-back flying posture.

The tilt table can be rotated through a range of +75° HUT through to −45° (referenced from vertical = +90°). It can be rotated at angular velocities from 5 to 45° · s^{-1}. A transducer attached to the tilt table measures tilt angle, the record of which may be used to temporally correlate with recorded physiological variables obtained during each experiment. The start angle, stop angle, tilt rotation rate, and tilt position dwell time for each run is performed by entering these data in an alpha-numeric keypad/controller box mounted on the tilt table. The device is equipped with emergency interlocks and over-travel safety features.

Subjects

There were 20 subjects, 4 female and 16 male DCIEM and civilian employees between the ages of 20 and 59 yr, who volunteered for this experiment. All procedures involving safety and ethical issues when working with human volunteers were adhered to. Each subject was provided with an information package outlining the experimental protocol containing the consent forms to be signed. All subjects were examined by a medical officer/physician prior to participation. Female subjects were tested for pregnancy prior to the experiment as required by the DCIEM Human Ethics Committee. All subjects attended a training session on a separate day, before actual experiments commenced. During this session, subjects were exposed to several tilting maneuvers for familiarization with the sensations of the tilt-induced push-pull maneuvers, and to determine the seating and restraint device positions. At this time, they were also familiarized with the biomedical instrumentation. Subjects were instructed to avoid alcohol 48 h, exercise 24 h, and caffeine 4 h prior to the experiment.

Experimental Design

The experiment was conducted in one session for each subject and no later than 7 d after the familiarization session. Each session lasted approximately 2 h. Subjects underwent a total of 12 randomized tilt sequences ('runs') divided into 2 sets of 6 runs. Each tilting maneuver was followed by 2-min of rest, and a 20-min rest period was inserted between the 2 sets of 6 runs. During this 20-min rest, subjects were assisted with dismounting the tilt table, and were allowed to move freely about the lab with biomedical instrumentation/electrodes still attached. This physical activity allowed for the desired re-distribution of body fluid compartments and a return to the physiologic baseline status in preparation for the next 6 tilts. Consumption of 200–300 ml of water was allowed at this time. The individual tilt runs consisted of HUT — HDT — HUT sequences to simulate +1 G_z baseline condition, the −G_z "push" phase, and the subsequent transition to the +G_z "pull" phase, respectively. The second HUT phase was divided into three sub-phases, which are referred to in this investigation as: HUT_1 (0–10 s), HUT_2 (11–20 s), and HUT_3 (21–30 s). The experimental factors manipulated in this study were: a) absolute −G_z/HDT angle (0°, −25°, −45°); b) dwell-time at −G_z/HDT (7 s, or 15 s); and c) time ($HUT_{control}$, HDT, HUT_1, HUT_2, HUT_3). Therefore the total number of experimental tilt runs = (3 −G_z HDT levels) × (2 −G_z dwell times) = 6 run types (x 2) = 12 runs total/subject.

After instrumentation and set-up, subjects were positioned on the tilt table, and all harnesses tightened. The subject was then rotated to +15° HUT (upright) at 5° · s^{-1}, and held for 120 s, while data collection was started and verified. The subject was then rotated at 5° · s^{-1} to the supine (0°) rest position for 120 s. Following this rest, subjects were then rotated back to the +75° HUT position, the starting position for the tilt push-pull maneuver, which was held for 60 s. The subjects were then rotated to one of the three experimental HDT angles at a rotation rate of 45° · s^{-1}, and held in this position for 7 or 15 s. Following HDT, the subject was rotated at a rate of 45° · s^{-1} to +75° HUT and held for 30 s. Each tilt run was followed by 120 s of rest in the supine position in preparation for the next tilt run. The purpose of this supine position was to create a reliable physiological baseline condition prior to each tilt run by allowing redistribution of body fluids and avoiding

progressive blood pooling in dependent capacitance regions.

Physiological Measurements

Continuous arterial blood pressure (BP) was measured using Finapres™ (Model 2300, Ohmeda Inc., Englewood, CO). The finger cuff was placed around the middle phalanx of the second digit of the left hand and the arm was passively suspended and fixed using a custom Velcro™ glove positioned at the level of the aortic root. The height of the hydrostatic column (h) from the heart (3rd intercostal space) to eye was measured using a level-equipped ruler. The column was measured with the subject in the +75° HUT position vertically from the Finapres™ cuff to the pupil, and was used to calculate eye level BP using the equation:

$$\text{eye level BP} = \text{heart level BP} - (pgh),$$

where p = density of blood ($g \cdot cm^{-2}$); g = gravitational units ($9.8\ m \cdot s^{-2}$); h = reference column height (cm). The pgh calculation was also applied at −25° and −45° HDT positions, to account for the different magnitude and sign of the height between heart and eye, (i.e., as the head became lower than heart-level). At the 0° HDT position, head-level was considered equal to heart-level, and no correction was applied. Heart-level mean arterial pressure (MAP, mm Hg) was calculated as diastolic pressure +0.33 (systolic BP − diastolic BP). Immediately before each tilt run, the Finapres™ auto-calibration function was disabled to avoid interruptions in measurements. Heart rate (HR) was monitored and displayed continuously (Tektronix ECG monitor model 408, Beaverton, OR). ECG electrodes were placed on the front of each shoulder, two on the abdomen 5 cm above the iliac crests, and one in the V_5 position.

Thoracic impedance cardiography was used to estimate changes in thoracic blood/fluid volume and to estimate stroke volume. A Minnesota Impedance Cardiograph Model 304B (Instruments for Medicine Inc., Greenwich, CT) measured Z_o and dZ/dt signals, which were acquired on a beat-to-beat basis. The subject was instrumented using four disposable Mylar™-backed tape electrode bands. Two bands were placed around the neck 3 cm apart and two were placed at the xiphoid process and below with 5-cm of separation. Blood resistivity (ρ) was determined directly from fingertip blood samples obtained from the subjects. Thoracic baseline impedance (Z_o, Ω) was used as an index of thoracic interstitial and vascular fluids. dZ/dt ($\Omega \cdot s^{-1}$) was derived automatically from the ΔZ waveform and used for the estimate of stroke volume (SV, $ml \cdot beat^{-1}$) using the Kubicek equation (13):

$$SV = \rho \cdot [L^2]/[Z_o^2] \cdot dZ/dt \cdot t$$

where SV = stroke volume estimate ($ml \cdot beat^{-1}$), ρ = electrical resistivity of blood ($\Omega \cdot cm^{-1}$), L = distance between electrode 2 and 3 (cm), Z_o = average thoracic basal impedance (Ω), dZ/dt = peak value of dZ/dt wave ($\Omega \cdot s^{-1}$), and t = ventricular ejection time (s). An estimate of cardiac output (Q, $L \cdot min^{-1}$) was derived as the product of HR * SV.

Venous occlusion plethysmography (22) was used to measure forearm blood flow (FBF). Subjects were instrumented with a double-stranded mercury-in-silastic strain gauge (Hokensen model EC-4, Bellevue, WA) fitted around the right forearm approximately 15 cm from the elbow with 10–15% pre-stretch of the gauge. The venous occlusion pressure cuff was placed around the upper arm and was set to inflate to 50 mm Hg using a rapid cuff inflator unit (Hokenson EC-20, Bellview, WA). The gauge was electronically calibrated prior to each measurement. The arm was suspended in front of the subject 3 cm above heart level using a modified Velcro™ glove, which was attached to a bracket on the tilt table. For the +75° HUT position, the hydrostatic distance from heart level to the strain gauge was recorded in centimeters for calculation of forearm-level systolic arterial BP using the pgh equation. Since the arm was suspended in a fixed position on the tilt table, the distance from heart-level to the gauge was different (in magnitude and sign) for each of the three HDT angles. To correct for this, the distance (h) from the mid-axillary line/aortic root level to the mid-arm gauge level was recorded at each HDT tilt angle, and trigonometric calculations and the pgh equation were then used to correct for the differences in heart to arm distance at these positions. Slopes of the blood flow tracings were obtained directly from chart recordings, and measured by hand, then entered into a Microsoft Excel™ macro to calculate FBF as:

$$\text{FBF } (ml/100\ ml \text{ of tissue} \cdot min^{-1}) = \text{change in slope/min/deflection for 1\% change in voltage,}$$

as described by Whitney (22). Five blood flow measurements were taken during each tilt run: control HUT, HDT (15-s duration only), HUT_1, HUT_2, and HUT_3. Blood flow measurements were not obtained during the 7-s duration due to the short duration of HDT. The time needed to take the blood flow measurement varied from approximately 6–10 s. Consequently, FBF and FVR data are reported only for 15s HDT duration conditions.

Two EMG electrodes were placed over the rectus abdominus muscle 5 cm from the midline of the body and 3 cm apart and amplified (Gould™ isolated preamplifier Model 11-5407, Cleaveland, OH). A third electrode was fixed on the anterior superior iliac crest to function as the ground. EMG was monitored on an oscilloscope in order to confirm that all subjects remained relaxed during the tilt maneuvers.

Data Collection and Reduction

The following signals were continuously displayed on a computer monitor: ECG, BP, EMG, and tilt angle. All data with the exception of forearm blood flow and EMG were acquired using electronic data acquisition software (LabVIEW v. 1.1, National Instruments Inc.), using a sampling rate of 100 Hz. Waveform data reduction and analysis software was used off-line to analyze each channel of physiological data, to record the timing of physiological events, and to automatically calculate physiological variables from raw BP and impedance cardiography waveforms. Raw ECG, Z_o, and dZ/dt data were used to derive measures of HR, SBP, DBP, SV and CO. Forearm MAP was calculated as $DBP_{forearm}$ +

$0.33(SBP_{forearm} - DBP_{forearm})$. An index of total peripheral resistance (TPR) was calculated as: $TPR = MAP_{heart}/CO$ (mm Hg · L^{-1} · min^{-1}). Forearm vascular resistance (FVR) was calculated as: $MAP_{forearm}/FBF$ (mm Hg · ml^{-1} · 100 ml $tissue^{-1}$ · min^{-1}). The mean values for all variables were calculated and used for statistical analysis in each phase of the tilt maneuver. A 10-s window 10 s prior to tilt was taken as the mean $HUT_{control}$. The mean values of HR, BP, SI, CI, and TPR were determined during the time periods corresponding to the blood flow measurements.

Statistical Tests

Physiological variables were compared using a three-way repeated measures analysis of variance (ANOVA). A 5 (Time) * 3 (Tilt Angle) * 2 (Tilt Duration) repeated measures ANOVA was conducted on data. The data for FBF and FVR were compared using a two-way repeated measures ANOVA (5 tilt times * 3 tilt angles). The 0.05 α level was used to establish statistical significance. Post-hoc tests were performed using a Tukey HSD post-hoc test with an α level of 0.05.

RESULTS

All but 1 subject tolerated the 12 tilt runs without symptoms of orthostatic intolerance. This subject reported a mild peripheral vision dimming and lightheadedness, which dissipated within 10 s after HUT_1.

Systolic Blood Pressure

During 7 s of HDT, there was an insignificant decrease in SBP_{heart}, but a significant decrease was observed during 15 s of HDT (**Fig. 2**; $p < 0.01$). When subsequently tilted to 75° HUT_1, SBP_{heart} decreased markedly for the 7 s HDT condition ($p < 0.001$), and was maintained at the previously decreased HDT level during the 15 s HDT condition. The decline during the 7 s HDT condition at HUT_1 was significantly greater for the −45° HDT angle condition vs. −25° and 0° conditions ($p < 0.001$). SBP_{heart} recovered to $HUT_{control}$ levels by HUT_2. There were no differences at HUT_2 and HUT_3 in SBP_{heart} across HDT angle or duration conditions.

Head-level SBP (SBP_{head}) results are presented in **Fig. 3**, and illustrate a distinctly different pattern of response. In contrast to heart-level SBP, head-level BP increased significantly during HDT, and then decreased during the subsequent HUT_1 phase with respect to the $HUT_{control}$ level for all HDT angles and dwell time conditions ($p < 0.001$). The decrease in SBP_{head} during HUT_1 was greatest for the −45°/7-s HDT condition ($p < 0.01$) (Fig. 3a). There were no differences between the three HDT angle conditions for the 15-s HDT condition (Fig. 3b). By HUT_2, SBP_{head} had returned to $HUT_{control}$ levels.

Heart Rate

Heart rate fell significantly during HDT for both the 7- and 15-s HDT conditions ($p < 0.001$). The reduction in HR during HDT was greatest for −45°/7-s HDT duration condition ($p < 0.01$). For the 15-s HDT condition, however, HR was lowest for the −25° and −45° vs. the 0° HDT condition (**Fig. 4**; $p < 0.01$). There was a significant increase in HR in response to HUT_1 with respect to $HUT_{control}$ for only the −45°/7 s condition ($p < 0.01$). Heart rate had recovered to the $HUT_{control}$ level by HUT_2 and HUT_3 for all HDT dwell time/angle conditions.

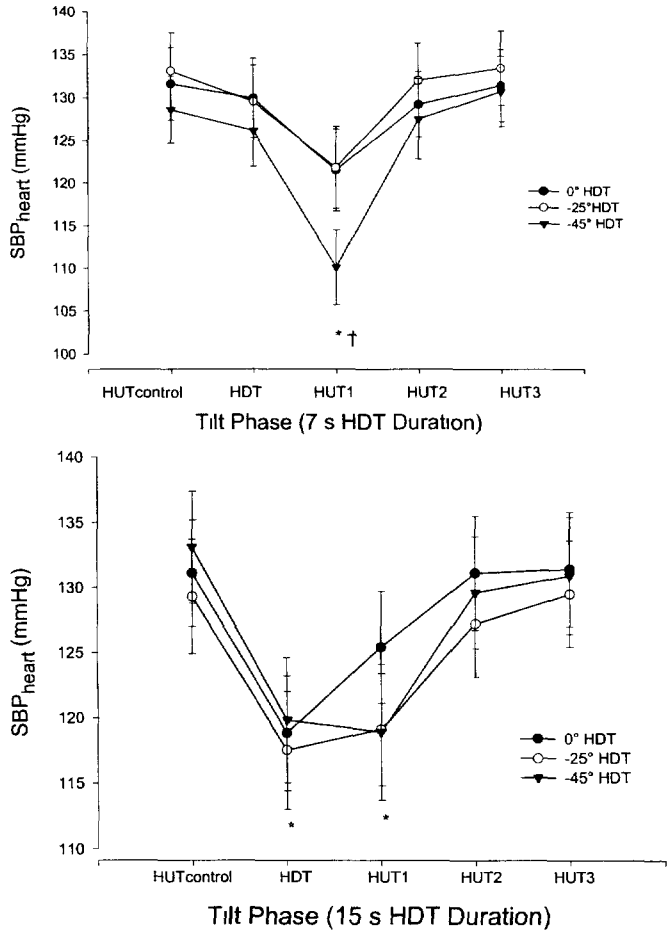


Fig. 2. Systolic BP at heart-level during tilting (SBP_{heart}) (**2a**, upper: 7-s HDT duration), (**2b**, lower 15s HDT duration) Tilt phases are $HUT_{control}$: seated upright 75°, HDT: 0°, −25°, and −45°, HUT_1 75° at 0–10s, HUT_2 at 11–20s, HUT_3 at 21–30s *Significantly different vs $HUT_{control}$, †significantly different vs. 15-s HDT and −25° and 0° HDT conditions Data are expressed as mean ± SEM

Thoracic Impedance, Stroke Volume, and Cardiac Output

Results for Z_o, SV and Q are presented in **Table I**. $HUT_{control}$ were pooled across conditions for comparisons. Z_o generally decreased during HDT with respect to $HUT_{control}$, indicating increasing thoracic blood/fluid volume with greater degrees of HDT ($p < 0.001$). The greatest decreases in Z_o occurred during −25° and −45° HDT vs. 0° ($p < 0.05$). Z_o had not recovered to $HUT_{control}$ levels by HUT_1 ($p < 0.01$), but were not significantly different than $HUT_{control}$ by HUT_2 and HUT_3.

There was a general trend for SV to increase significantly during HDT with respect to $HUT_{control}$ ($p < 0.001$), and remain significantly elevated during HUT_1 and HUT_2 ($p < 0.01$). SV was not significantly elevated with respect to $HUT_{control}$ at HUT_3. The largest increases

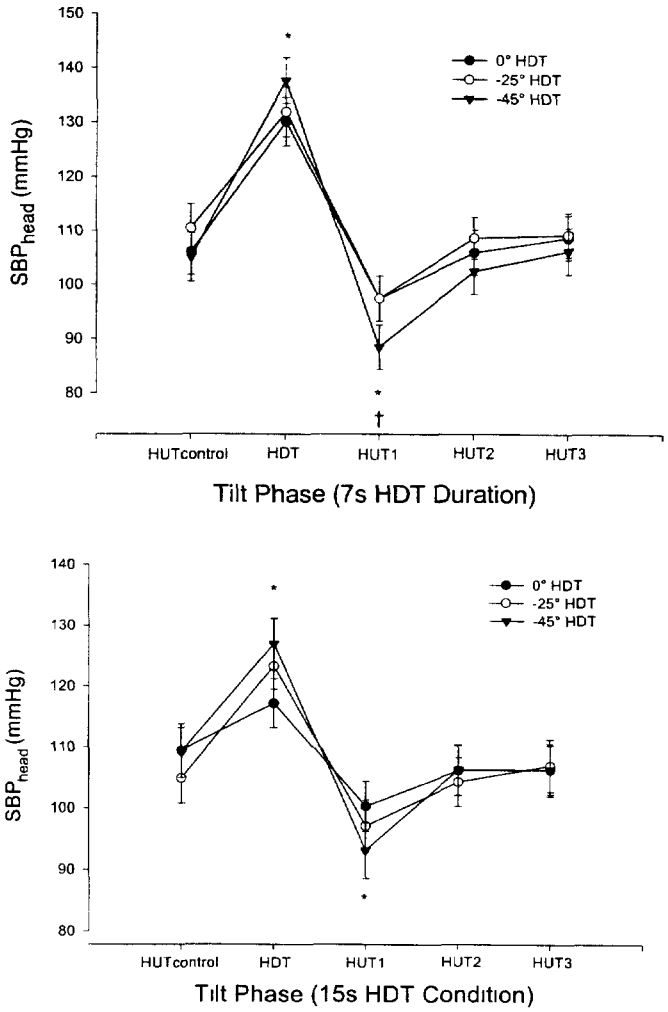


Fig. 3. Systolic BP at head-level during tilting (SBP_{head}) (**3a**, upper: 7-s HDT duration), (**3b**, lower 15-s HDT duration) See Fig. 2 for tilt phases * Significantly different vs $HUT_{control}$; †significantly different vs −25° and 0° HDT conditions Data are expressed as mean ± SEM.

in SV (32%) during HDT occurred in the −45°/15-s and −25°/15-s conditions ($p < 0.01$).

Q changes generally reflected SV changes during tilting, and increased significantly during HDT ($p < 0.01$). The largest increases in Q occurred during −45° HDT vs. −25° and 0° ($p < 0.05$). Q was significantly elevated with respect to $HUT_{control}$ during the HUT_1 period ($p < 0.05$), but returned to baseline for the remainder of the HUT_2 and HUT_3 phases.

Total Peripheral Resistance

Total peripheral resistance index during tilting is presented in **Fig. 5**. There was a significant decrease in TPR during HDT regardless of HDT angle or dwell-time ($p < 0.001$). However, the magnitude of the decrease was related to the HDT angle, with the decrease greatest at −45° (28%) and −25° (27%) vs. 0° (17%) ($p < 0.05$). After tilting upright to HUT_1, TPR remained depressed below control for all conditions ($p < 0.001$). However, for the −45°/7-s condition, TPR decreased further to a value 34% below the $HUT_{control}$ level. At HUT_2, TPR was significantly lower for the −45°/7-s HDT condition vs. −25°/7-s and 0°/7-s conditions ($p < 0.01$). For the 15s HDT condition TPR also remained depressed with respect to $HUT_{control}$ levels for all HDT angle conditions ($p < 0.001$). However, both the −45° and −2° HDT angle conditions were significantly lower at HUT_1 vs. the 0° HDT condition ($p < 0.05$). Across all HDT angle/dwell time conditions, HUT_2 and HUT_3 TPR remained lower than $HUT_{control}$, but the decrease was not statistically significant.

Forearm Blood Flow and Vascular Resistance

Results for FBF during the 15s HDT conditions are presented in **Fig. 6**. FBF increased during HDT and this increase was proportional to the magnitude of the HDT angle ($p < 0.02$). The hyperemia occurring at −45° HDT was significantly greater than at −25° and 0° ($p < 0.01$). At HUT_1, FBF remained significantly higher vs. $HUT_{control}$ for all HDT tilt angles ($p < 0.001$), however by HUT_2 and HUT_3, FBF was not significantly different from $HUT_{control}$.

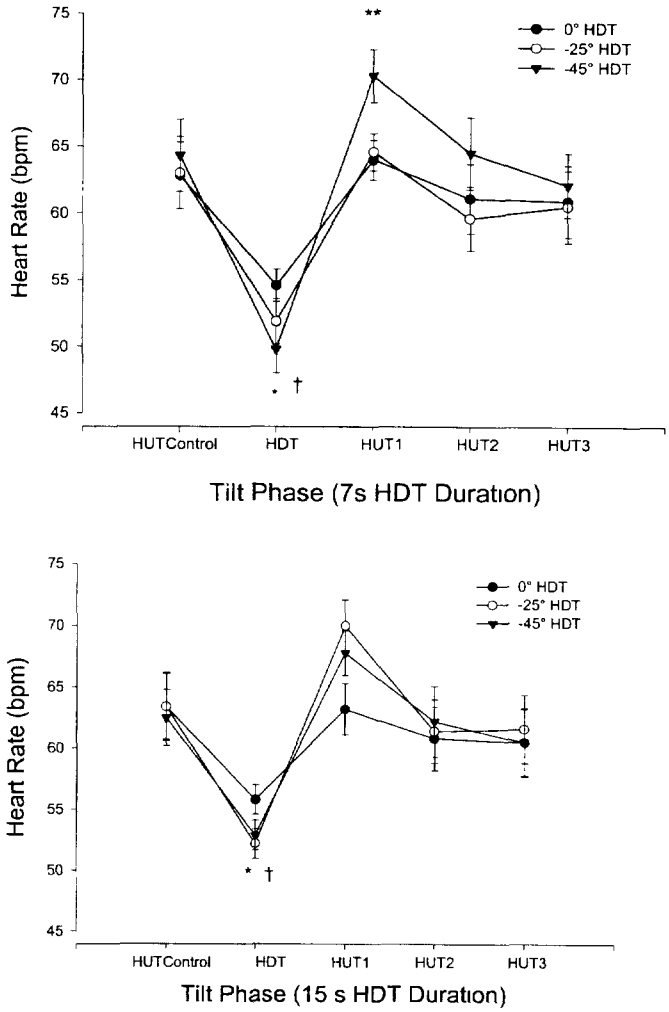


Fig. 4. Heart rate during tilting. (**4a**, upper 7-s HDT duration), (**4b**, lower 15-s HDT duration) See Fig. 2 for tilt phases *Significantly different vs HUTcontrol, all HDT conditions, **significantly different from $HUT_{control}$ at −45° HDT for 7 s; †significantly different −45° vs −25° vs 0° HDT for 7 s, and −45° vs −25° and 0° HDT for 15 s Data are expressed as mean ± SEM

TABLE I. THORACIC IMPEDANCE (Zo), ESTIMATED STROKE VOLUME (SV) AND CARDIAC OUTPUT (Q) AT REST

Tilt Position.		HDT						HUT1					
HDT Angle/Condition (°)		0°		−25°		−45°		0°		−25°		−45°	
HDT dwell time/condition(s):		7	15	7	15	7	15	7	15	7	15	7	15
Variable	$HUT_{Control}$												
Zo (Ω)	28.50	26.7*	26 6*	26 2*†	26 1*†	26.3*†	25 8*†	27 9*	27.9*	27 6*	27 8*	28.2*	27*
(SEM)	0 67	0.61	0 63	0 60	0 62	0 62	0 60	0.66	0 66	0 66	0 66	0.63	0.64
SV (ml · beat $^{-1}$)	79 60	100 2*	103*	110 9*†	13*†‡	108*†	117*†‡	91.3*	90.5*	87 4*	88.1*	86.8*	89.7*
(SEM)	5.00	5 10	5.40	7 30	5.30	5.10	6.20	4 10	4.90	3 60	3 90	3 40	4.50
Q̇ (L · min^{-1})	4.87	5 55*	4.72	5.92*	5.96*	6 32*†	6.51*†	5.8*	5 68*	5 53*	5 9*	6.08*	6 12*
(SEM)	0 23	0.27	0.30	0.38	0 33	0 31	0 35	0.24	0 36	0 20	0.33	0.26	0 34

Statistical Symbols: Zo *Significantly different vs HUT1 Control; †Significantly different vs 0° HDT condition.
SV *Significantly different vs HUT1 Control; †Significantly different vs. 0° HDT condition; ‡Significantly different vs 7s HDT tilt duration condition.
Q̇: *Significantly different vs HUT1 Control; †Significantly different vs 0°, −25° HDT conditions.

FVR was reduced significantly for all conditions during ($p < 0.0001$) when tilted to the HDT position, and was still significantly depressed with respect to $HUT_{control}$ values at HUT_1 ($p < 0.01$). The greatest decrease in FVR (55%) occurred during the −45° HDT condition, and was significantly greater than the decreases for the −0° and −25° HDT conditions ($p < 05$). The recovery of FVR during the "push" phase was proportional to the previous HDT angle magnitude. At HUT_2 and HUT_3, FVR has returned to $HUT_{control}$ levels for the 0° and −25° HDT conditions. Only with preceding −45° HDT was FVR significantly greater than $HUT_{control}$ levels during the subsequent HUT_2 and HUT_3 ($p < 0.01$).

DISCUSSION

This experiment focused on the cardiovascular responses to a mild simulation of the "push-pull" maneuver using alternating HUT – HDT – HUT. Apparent in these results are the marked, acute changes in cardiovascular state when transitioning rapidly from the upright, seated position, to a head-down position, and returning to an upright position. These results clearly support the findings of other investigations which described BP and heart rate responses during the push-pull maneuver. This study extends these findings to uncover in greater detail, the associated vasomotor response to the push-pull maneuver.

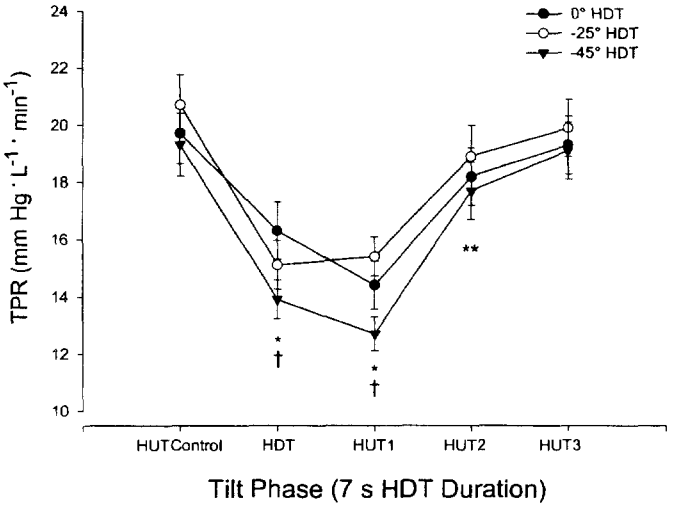
The physiological responses to alternating G_z (historically described by head-up/head-down tilting) have been known for some time. Wilkins et al. (23) described the abrupt slowing of HR on head-down tilting. Similarly, Ryan et al. (21) observed a rapidly evolving 30 bpm decrease in HR on HDT. Fletcher and Girling (10) described a similar pattern, and observed that cardiac deceleration during HDT was more rapid than cardiac acceleration during HUT.

The studies by Banks et al. using a Coriolis acceleration platform device demonstrated that the magnitude (2) and duration (1) of preceding $-G_z$ proportionately influenced tolerance to subsequent $+G_z$. Subjects initially exposed to -2 G_z baseline conditions reacted with an initially large fall in systolic BP of 22 mm Hg during exposure to $+2.5$ G_z, and exhibited a marked delay in the recovery of BP during the baroreceptor adjustment phase. Prior et al. (18) also described the same pattern of response during in-flight and centrifuge studies, where the subsequent $+G_z$ was greater. More recent studies conducted in multi-gimballed centrifuges (24) and in-flight environments (25) confirmed the exacerbating effects on $+G_z$-induced head-level hypotension and G-tolerance when $+G_z$ was preceded by $-G_z$ exposure.

The mechanisms surrounding this extended latency in BP responses after $-G_z$ exposure have been extrapolated mainly from animal studies, and some work using pharmacological and/or neck suction mechanical interventions in humans. These studies point to strong activation of arterial baroreceptors which drive the physiological responses to alternating $\pm G_z$. Neck suction (mimicking $-G_z$) causes abrupt, albeit, transitory R-R interval lengthening due to stimulation of carotid baroreceptors (7–9,14,15,19). Furthermore, arterial BP is modified by such stimulation, such that decreases in carotid transmural pressure (CTP) evokes BP to increase, while elevation of carotid transmural pressure causes BP to decrease. However, these changes are less marked than R-R interval changes since the aortic baroreceptors are excluded from these perturbations. More salient to the discussion of responses to alternating G_z, however, is the classically observed latency effect. Increases in arterial BP (driven by baroreceptor-mediated increases in sympathetic tone) require longer time frames than decreases in BP (driven by withdrawl of sympathetic tone). This has been confirmed in many studies, using animal and human subjects. Rae and Eckberg (19) measured sympathetic nerve activity in humans during neck suction and pressure, and found that positive neck pressure, reducing CTP, resulted in a sluggish BP elevation despite a rapid neural muscle sympathetic activity. Neck suction produced a brisk fall in heart rate and BP. In a recent study examining these latencies to BP responses, Doe et al. (4) mimicked a push-pull maneuver in catheterized dogs, by holding central and peripheral vascular bed blood flow constant while manipulating carotid sinus perfusion pressure. Increases in carotid sinus perfusion pressure resulted in rapid fall in peripheral vascular perfusion pressure at a faster rate than the increases in peripheral vascular perfusion pressure elicited by decreases in carotid sinus

(HUT CONTROL), AND DURING TILTING.

HUT2						HUT3					
0°		−25°		−45°		0°		−25°		−45°	
7	15	7	15	7	15	7	15	7	15	7	15
28.20	28.20	28.00	28.10	28 50	28 00	28 30	28 40	28 10	28 30	28.50	28.10
0 66	0 68	0 66	0.67	0.63	0 65	0 66	0 69	0 67	0 67	0 64	0.66
86.2*	87.7*	87 1*	86.7*	83.2*	87 4*	83.60	86 80	84 10	84 80	81.30	86 70
4 50	4.50	4 30	4.30	3 50	4.80	4 90	5 00	4 70	4 80	3 80	5 10
5.18	5.30	5.31	5.27	5.20	5.22	4 96	5 09	4 95	5 05	5 12	5.12
0 27	0.30	0.27	0.30	0.27	0 26	0.23	0 25	0.23	0.26	0.26	0.24



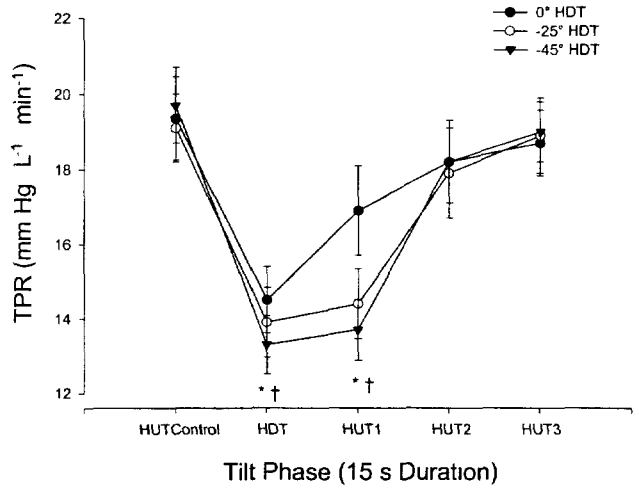


Fig. 5. Total peripheral resistance (TPR) during tilting (**5a:** 7s HDT duration, left panel); (**5b:** 15s HDT duration, right panel). See Fig. 2 for tilt phases. *Significantly different vs. $HUT_{control}$; **significantly different vs. $HUT_{control}$, −45° 7-s HDT condition; †significantly different −45° vs. −25° vs 0° HDT conditions Data are expressed as mean ± SEM.

pressure. Limb vasoconstriction (by decreased CTP) occurred with a time constant of 11.4 s vs. 5.5 s for vasodilation caused by experimental increases in CTP.

Earlier push-pull studies in humans have suggested that these same mechanisms were responsible for the exaggerated +G-intolerance observed after $-G_z$ exposure (1,2). However since only BP and heart rate data were reported in these studies, the hypothesis implicating a delay in peripheral vasoconstrictor response could not be directly confirmed. Recently, Xing et al. (26) described cerebrovascular alterations during a tilt simulation of push-pull. A protective cerebral vasoconstriction observed during HDT was prolonged well into the subsequent HUT "pull" phase, leading the investigators to suggest that this continued vasoconstriction might contribute to an exacerbated cerebral under-perfusion during the "push" phase. While this is an important finding, the mechanisms occurring in the central and peripheral circulations during the push-pull maneuver are still poorly understood.

In the present study, heart-level BP decreased only modestly during HDT regardless of HDT duration. The

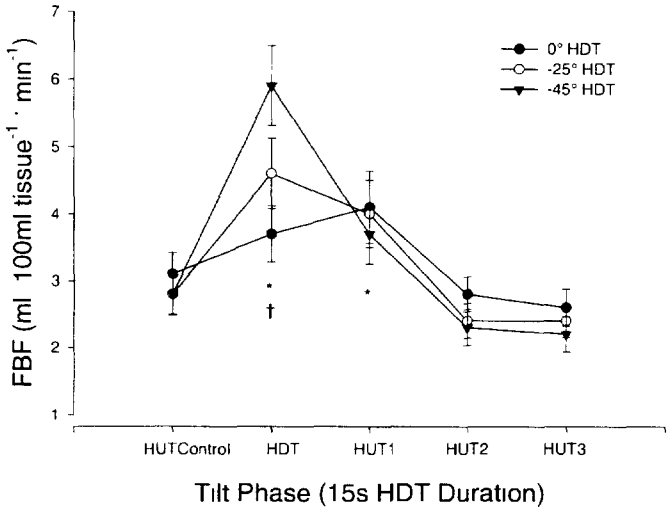


Fig. 6. Forearm blood flow (FBF) during tilting. See Fig 2 for tilt phases. HDT duration conditions are pooled *Significantly different vs $HUT_{control}$, all HDT conditions; †significantly different −45° vs. −25° vs. 0° HDT conditions Data are expressed as mean ± SEM

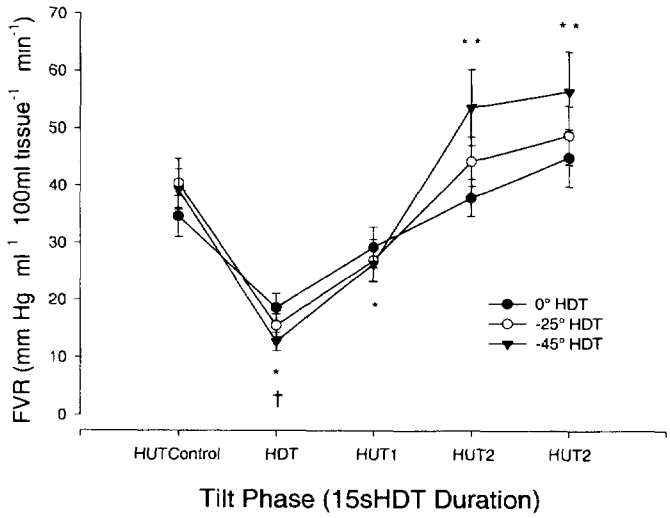


Fig. 7. Forearm vascular resistance (FVR) during tilting. See Fig 2 for tilt phases. Data are for 15-s HDT conditions only * Significantly different vs $HUT_{control}$, all HDT/duration conditions; **significantly different vs $HUT_{control}$ for −45° HDT condition, †significantly different −45° vs −25° vs 0° HDT conditions. Data are expressed as mean ± SEM

modest decrease in heart-level BP (more pronounced during 15 s of HUT) is most probably related to the abrupt decrease in heart rate (Fig. 4) in association with a significantly elevated venous return to the heart. This is supported by the significantly decreased Z_o in conjunction with a marked elevation of $\dot{Q}$ and SV (Table I). Not unexpectedly, head-level BP is elevated during HDT due to the inversion of the hydrostatic column during HDT (Fig. 3). The elevation during HDT is less pronounced during the longer 15-s HDT duration, due to baroreceptor adaptation effects (3,6,21). However, the significant fall in both heart (Fig. 2) and head-level (Fig. 3) systolic BP during the early subsequent HUT phase (HUT_1) strongly suggests that the BP recovery delay mechanism resides largely in the periphery. Indeed, there was no fall in SV or Q from control HUT levels during HUT_1, and SV and Q were actually normalized with respect to control HUT values (Table I). This defense of SV and $\dot{Q}$ is most probably attributable to increases in sympathetic signaling and corresponding elevation in myocardial contractility.

An examination of Fig. 5 illustrates the abrupt fall in TPR during HDT, with a prolonged depression during HUT_1 and HUT_2 — a total duration of 30 s before it is normalized to $HUT_{control}$ values. This result agrees with Doe et al.'s data from instrumented experimentally perfused dogs, in that the time frame required for full vasoconstriction was longer than that required for vasodilation (4). It is also of note that the magnitude of HDT is related to the decrease in TPR observed during subsequent HUT_1.

What direct evidence exists to verify that prolonged peripheral vasodilation in the skeletal muscles and splanchnic regions contributes to the delay in BP restoration during the PPE? Fig. 6 illustrates hemodynamic measurements obtained from the forearm during the tilting maneuver. It is apparent from Fig. 6 that FVF doubles during HDT, and this increased flow is proportional to the magnitude of HDT, although the duration of HDT was not a factor. Of note, and in agreement with our concurrent TPR measures, this skeletal muscle bed hyperemia persists into the HUT_1 phase, and does not normalize until the HUT_2 period, where it is maintained at levels lower than HUT control indicating some degree of sympathetically mediated vasoconstriction had finally occurred. The same pattern of response is reflected in the forearm vascular resistance results (Fig. 7): FVR during HDT falls precipitously, but remains below control conditions during HUT_1. However, evidence of vasocontriction by HUT_2 and HUT_3 is reflected by the values greater than control levels, particularly for the 135° HUT condition. These data correspond closely to results presented by Mengasha and Bell (16) who tilted subjects +60° HUT and −60° HDT, and measured FBF and FVR using mercury strain gauge plethysmography. As found in the present investigation, they observed large increases in FBF of up to100% from baseline during HDT, with concomitant decreases in FVR of up to 100% from baseline. The authors concluded that these changes were indeed baroreflex-mediated changes (16), vs. simple mechanical effects that could be explained by local hydrostatics at the arm. To strengthen the argument, they pointed to studies that demonstrated that peripheral vasodilation does not occur in sympathectomized or nerve-blocked subjects (20). On the other hand, these responses to limb blood flow have also been attributed to myogenic autoregulatory responses, since Johnson (12) concludes that in addition to neurogenic and humoral effects, myogenic factors can override baroreceptor-induced changes in arteriolar tone.

These results follow from the work of Doe et al. (4). Using non-invasive techniques to study the changes in arterial BP, cardiac hemodynamics, as well as peripheral vascular control, our data agree with their findings in several respects. Firstly, the speed of vasoconstriction after $-G_z$ is slower than the vasodilatory response which occurs in response to placing an individual in the $-G_z$ vector. Secondly, the antecedent $-G_z$ baseline condition determines the physiological responses to subsequent $+G_z$. In this case, exposure to −0.71 G_z caused a marked bradycardia, increase in SV, and abrupt fall in peripheral vascular resistance (as verified by arm venous occlusion plethysmography and measures of TPR). It is these changes during $-G_z$ that feed- forward during the subsequent $+G_z$ phase, and cause the exacerbated $+G_z$ intolerance. Thirdly, both the magnitude and duration of the antecedent $-G_z$ was related to the physiological responses observed during subsequent $+G_z$, in agreement with the data from Banks et al. (1,2).

A limitation of this study relates to the reduced $+G_z$ stress of the second HUT after HDT, or "pull" phase of the maneuver. Although the HDT stress of nearly −1.0 G_z is typical of $-G_z$ encountered during tactical flight maneuvers, the subsequent +1 G_z is not. A typical push-pull maneuver would involve transition to well above +2 G_z, and possible as high as +7 G_z at onset rates approaching 10 $G_z \cdot s^{-1}$ vs. the current 0.5 $G_z \cdot s^{-1}$ on the tilt table. It is thus conceivable that the marked cardiovascular responses observed in this study would be highly magnified after high $+G_z$ levels following

exposure to $-1G_z$. Therefore, the mild gravitational stress encountered in a tilt simulation of push-pull describes the least hazardous physiological outcome. Future work should include direct measurements of sympathetic nervous activity in skeletal muscles to further ascertain the peripheral vasomotor responses. In addition, this should be combined with measures of peripheral vascular blood flow that yield greater temporal resolution than the technique of venous occlusion plethysmography used in this investigation

In conclusion, we used a low-intensity tilt table simulation of the push-pull maneuver using human subjects to demonstrate that antecedent $-G_z$ occurring before $+G_z$ causes a rapid fall in total peripheral resistance as measured continuously with impedance cardiography and forearm vascular resistance/blood flow measures. This decline in vascular resistance persists into the "pull" phase, and delays baroreceptor-mediated recovery of head-level arterial BP. These results parallel data from animal work that showed that the withdrawl of sympathetic tone during $-G_z$ is rapid, while the development of sympathetic tone during subsequent $+G_z$ is delayed. It is this delay, which contributes to the impaired maintenance of head-level BP during excursion to high levels of $+G_z$, leading to worsening of G-tolerance. Accordingly, life support equipment strategies designed to counteract these physiological effects must function rapidly to increase peripheral vascular resistance ahead of the delayed rise in TPR and BP.

ACKNOWLEDGMENTS

The authors wish to gratefully acknowledge the technical support of Mr Jim Maloan, Mr. Ted Larson, and Mr. Tom Gee for instrumentation set-up, electronics support, and electronic data acquisition advise and support, respectively The authors also wish to recognize Dr. Robert Banks, past Head of Aerospace Life Support, DCIEM, for providing the leadership and inspiration necessary for the creation of this tilt table laboratory research program

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