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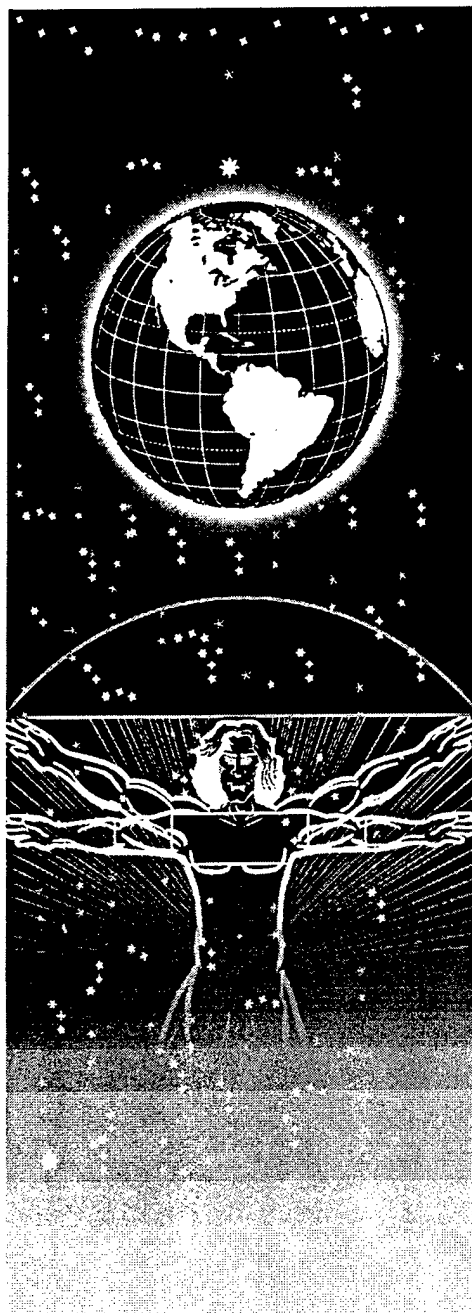
**FEMALE EXPOSURE TO HIGH G:
CHRONIC ADAPTATIONS OF
CARDIOVASCULAR FUNCTIONS**

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FINAL REPORT

September 1998

19981014 001



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Victor A. Convertino

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REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE September 1998	3. REPORT TYPE AND DATES COVERED Final Report, 1998		
4. TITLE AND SUBTITLE Female Exposure to High G: Chronic Adaptations of Cardiovascular Functions			5. FUNDING NUMBERS PE: 61102F PR: 2300 TA: AC WU: 52	
6. AUTHOR(S) Victor A. Convertino, Lloyd D. Tripp, David A. Ludwig, Juano Duff, Tamara L. Chelette				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Air Force Research Laboratory (AFMC) Human Effectiveness Directorate Flight Stress Protection Division, Physiology Research Branch 2507 Kennedy Circle Brooks AFB TX 78235-511			8. PERFORMING ORGANIZATION REPORT NUMBER AFRL-HE-BR-TP-1998-0079	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)			10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES To be published in Aviation, Space, and Environmental Medicine, Vol 69.				
12a. DISTRIBUTION AVAILABILITY STATEMENT Approved for public release; distribution unlimited.			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) Introduction: Exposure to microgravity is associated with increased leg venous compliance and reductions in cardiac output, baroreflex functions, and tolerance to orthostatism. However, the effects of chronic exposure to high-G environments are unknown. In addition, there is evidence that females have lower orthostatic tolerance than males, although the underlying mechanisms are unclear. Therefore, we tested the hypotheses that high-G training will enhance baroreflex and orthostatic functions and that females will demonstrate similar adaptations compared with males. Results: G-training increased calf compliance in both men and women. Stroke volume and cardiac output were increased during the squat-to-stand test in the males, but not in the females, following G-training and provided protection against the development of acute hypotension in the men. Conclusions: G-training caused adaptations in orthostatic functions opposite to those observed following exposure to microgravity environments. However, adaptations to G-training were limited in females, a finding that may provide a physiological basis for their lower simulated combat tracking performance during simulated aerial combat maneuvers compared with males.				
14. SUBJECT TERMS microgravity orthostatic baroreflex			15. NUMBER OF PAGES 15	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT UNCLASSIFIED	18. SECURITY CLASSIFICATION OF THIS PAGE UNCLASSIFIED	19. SECURITY CLASSIFICATION OF ABSTRACT UNCLASSIFIED	20. LIMITATION OF ABSTRACT UL	

Female Exposure to High G: Chronic Adaptations of Cardiovascular Functions

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CONVERTINO VA, TRIPP LD, LUDWIG DA, DUFF J, CHELETTE TL. *Female exposure to high G: chronic adaptations of cardiovascular functions.* *Aviat Space Environ Med* 1998; 69:000-000.

Introduction: Exposure to microgravity is associated with increased leg venous compliance and reductions in cardiac output, baroreflex functions, and tolerance to orthostatism. However, the effects of chronic exposure to high-G environments are unknown. In addition, there is evidence that females have lower orthostatic tolerance than males, although the underlying mechanisms are unclear. Therefore, we tested the hypotheses that high-G training will enhance baroreflex and orthostatic functions and that females will demonstrate similar adaptations compared with males. **Methods:** Calf venous compliance, baroreflex function, and orthostatic performance were measured in six men and seven women before and after repeated exposures on the centrifuge (G-training) for 4 weeks, 3 times/week, with gradual levels of G starting with +3 Gz without G-suit protection during week 1 and advancing to +9 Gz with G-suit protection by the end of week 4. Calf venous compliance was measured by occlusion plethysmography using impedance rheographic recordings of volume change. Baroreflex function was assessed from beat-by-beat changes in heart rate (HR) and mean arterial pressure (MAP) that were measured before, during, and after a Valsalva maneuver strain at 30 mmHg expiratory pressure. The orthostatic performance of reflex responses was assessed from beat-by-beat changes in HR, MAP, stroke volume (SV), cardiac output (Q; by impedance plethysmography), and systemic peripheral resistance during the last 10 cardiac beats of a 4-min squat position and during the initial 10 cardiac beats in a standing position. **Results:** G-training increased calf compliance in both men and women. SV and Q were increased during the squat-to-stand test in the males, but not in the females, following G-training and provided protection against the development of acute hypotension in the men. **Conclusions:** G-training caused adaptations in orthostatic functions opposite to those observed following exposure to microgravity environments. However, adaptations to G-training were limited in females, a finding that may provide a physiological basis for their lower simulated combat tracking performance during simulated aerial combat maneuvers compared with males.

FAILURE TO EFFECTIVELY regulate blood pressure (BP) and cerebral perfusion during high-G aircraft maneuvering could lead to reduced performance in pilots. Regular training at high G enhances G-performance, while prolonged layoff from exposure in high-G profiles (G-layoff) can result in reduced G-endurance (23). However, physiological mechanisms associated with adaptation to chronically repeated high-G exposure (G-training) and subsequent G-layoff have not been identified. Since impaired BP regulation following exposure to conditions of low gravity is associated with increased compliance of the lower leg (7,24), the impairment of cardiac baroreflex responses (6,8,10,13), and lower stroke volume (3,9), it is reasonable to hypothesize that improved performance

with high-G training may be associated with enhanced autonomic and cardiovascular functions. However, the assumption that training in combat-oriented aerial maneuvers in high-performance aircraft improves cardiovascular mechanisms associated with BP regulation lacks experimental evidence.

Although females have been included in the training for and command of fighter aircraft, little or no data exist on female adaptation to the high-G environment. Recent data reported from several investigations provide evidence that females have lower tolerances to various orthostatic challenges than males (15,20,25) and that these lower tolerances are associated with differences in BP regulation in females (12,26). A lower orthostatic capacity could clearly compromise the performance of the female warrior under combat conditions, especially in high-performance aircraft. Based on their lower orthostatic tolerances, it is reasonable to hypothesize that females may benefit, to the same degree or higher than males, from training in high-G environments.

In conjunction with the female performance study described by Chelette et al. (5), we measured changes in baroreflex function, limb compliance, and hemodynamic responses to an orthostatic challenge before and after training at high-G acceleration in men and women. The purpose of this research was to test the hypothesis that physiological functions associated with BP regulation are enhanced by increased G-exposure and are independent of gender.

METHODS

Subjects: Seven women with a mean (\pm SE) age of 27 \pm 2 yr, a weight of 58.9 \pm 3.1 kg, and a height of 165 \pm

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This manuscript was received for review in July 1997. It was revised in January 1998. It was accepted for publication in January 1998.

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3 cm and six men with a mean age of 24 ± 1 yr, a weight of 76.7 ± 4.3 kg, and a height of 177 ± 4 cm served as subjects. Each subject received medical clearance and gave their written voluntary consent to participate. Experimental procedures and protocols were approved by the Human Utilization Research Committee at Armstrong Laboratory, Wright-Patterson Air Force Base.

Protocol: Subjects underwent a series of tests for the assessment of baroreflex function, limb compliance, and hemodynamic responses to an orthostatic challenge before and after training at high-G acceleration. A detailed description of the G-training is presented elsewhere (1). Briefly, each subject underwent a total of 8 d of high-G exposure with peak acceleration plateaus at 4 to 5 G on days 1 through 4, followed by a gradual increase to peak acceleration plateaus at 6, 7, 8, and 9 G on days 5, 6, 7, and 8, respectively. Training profiles on days 4 to 8 involved four open-loop simulated aerial combat maneuvers with the subjects wearing a standard G-suit on day 4 and a positive-pressure breathing system (COMBAT EDGE) plus standard G-suit on days 5 through 8. These training profiles were 100 to 135 s in duration. After the 8 d of indoctrination training, subjects had been exposed to over 45 min of G-acceleration greater than +2 Gz.

On experimental days, subjects reported to the laboratory wearing a T-shirt and jogging shorts in order to undergo their tests for cardiovascular function. After each subject was placed on an 8-ft exam table in a supine position, band electrodes were placed on the upper and lower left calf and were secured with Aquasonic electrode gel. This provided better coupling between the electrode and the subjects' skin. A BP cuff was placed on the thigh just above the left knee. The electrodes then were connected to a Minnesota Impedance Cardiograph (model 304B; Minneapolis, MN). A continuous heart rate (HR) was recorded using a modified five-lead electrocardiogram. In addition, an Ohmeda 2300 Finapres® photoplethysmographic finger BP cuff was placed on the middle finger of the subject's left hand. HR and BP responses were saved as digital data.

Following the initial instrumentation procedure, subjects performed Valsalva maneuvers at an expiratory pressure of 30 mmHg in the supine posture to provide an index of baroreflex function according to a technique previously described (22). Each trial included a 30-s baseline period that was followed by a 15-s strain period and a 2-min poststrain period. A small leak in the system prevented the subjects from maintaining the expiratory pressure by occluding the glottis. Trials were separated by 2 min of rest. The average of three trials was calculated to represent the response for each subject. Subjects were instructed to remain quiet and still during both the baseline and the poststrain collection periods. Following baseline collection, the subjects were asked to give a ready signal at the end of a normal inspiration. At this point, the subject began blowing into a mouthpiece connected to a calibrated pressure transducer (Propper Analog Manometer). After 15 s at 30 mmHg expiratory pressure, the subject released pressure and breathed normally after the mouthpiece was removed. An aneroid gauge positioned in front of the subject provided feedback on the expiratory pressure. Expiratory pressures were measured continuously, and beat-to-beat HR and

mean arterial pressure were estimated with the Finapres® finger plethysmographic device. Excellent estimates of directly measured intra-arterial pressures during Valsalva maneuvers have been demonstrated with this device (16).

Following the Valsalva maneuver test, calf compliance was measured by applying venous occlusion with an impedance plethysmographic technique (18). Subjects remained in the supine position, and an occlusion cuff was placed around the thigh, just above the knee, and was inflated to 60 mmHg for 120 s. The subjects were instructed to remain as still as possible during this procedure. Changes in impedance, i.e., volume, were recorded using a two-channel brush recorder (Mark 220; Cleveland, OH). Leg compliance was calculated by dividing the volume change at a plateau, i.e., the point at which venous pressure equals cuff pressure, by the cuff pressure and was expressed as milliliters per mmHg. The value for leg compliance was multiplied by 100 for convenience.

Following the leg compliance test, subjects were asked to stand so that they could be instrumented for the squat-stand test. Four silver tape electrodes, two placed around the neck and two placed around the thorax, were attached to a Minnesota Impedance Cardiograph (Model 304B) for non-invasive rheographic determination of beat-to-beat stroke volume (18) during the final 10 s of squat and the initial 10 s of standing. This instrument introduced a frequency of 50 KHz at a low constant current (1 mA R.M.S.) into the thorax through the outside electrodes and detected changes in electrical impedance of the thorax with each pulse beat across the inner pairs of receiving electrodes. Cardiac output was calculated as the product of HR and stroke volume, and systemic peripheral resistance was calculated by dividing mean arterial pressure by cardiac output. Subjects remained instrumented from the previous test and were asked to place the hand with the Finapres® finger BP unit on their chest at heart level. Subjects were instructed to assume a squatting position for 4-min. Impedance and BP data were collected continuously throughout this test. The subjects then were instructed to stand erect as quickly as possible without using their hands to assist them. Data were collected for 30 s after standing. All physiological data were stored on a Tandy 4000 microprocessor.

Measurement of baroreflex responses to Valsalva maneuver: Data from the three trials were averaged in a phase-by-phase manner for baseline, phase I, early phase II, late phase II, and phase IV (22). BP responses (change in mean arterial pressure [Δ MAP]) for each phase were calculated as follows: for phase I, peak MAP during early straining - baseline MAP; for early phase II, peak phase I MAP - lowest midstrain MAP; for late phase II, peak late strain MAP - baseline MAP; and for phase IV, peak poststrain MAP - phase III MAP. Changes in HR were calculated using the same phase-by-phase method employed for Δ MAP. For phase I, Δ MAP was used in the analyses as an index of vascular volume (22). For late phase II, Δ MAP was used in the analyses as a marker for sensitivity of baroreflex-mediated control of peripheral vascular resistance (17). The Δ HR/ Δ MAP ratio was used in the analyses for early phase II and phase IV

because of its usefulness in describing integrated cardiac baroreflex responsiveness (17).

Statistical analysis: Analysis of covariance (ANCOVA) was used to analyze the male and female groups using two repeated measures, pre-G-training and post-G-training. This approach to the analysis of experiments with simple pre- and post-G-training repeated measures identifies the differences in pre- and post-G-training gain scores between males and females after adjusting for pre-G-training variation. As suggested by Laird (19), this statistical model attempts to correct for changes in pre- and post-G-training measures that are influenced by initial pretreatment values (i.e., regression toward the mean). The result is a mean gain score for each gender that is statistically adjusted for the baseline level (pre-G-training) of each subject. Confidence intervals are placed around the adjusted means and were used to evaluate differential changes from pre- to post-G-training between males and females.

RESULTS

The results for hemodynamic responses to the squat-stand test are presented in Table I and in Figs. 1 and 2. The change in posture from squat to standing reproduced an average reduction in total peripheral resistance of 8 to 12 pru (Fig. 1), which did not differ between males and females before and after G-training (Table I). Likewise, the elevation in HR caused by standing was similar before and after G-training (Fig. 2) in both males and females (Table I). During the move from squat to standing, males increased stroke volume and cardiac output after G-training compared with the pre-G-training response, while these responses remained relatively unchanged from pre- to post-G-training for females (Table I). The increased stroke volume and cardiac output in males during standing after G-training was associated with 10 mmHg less reduction in MAP compared with the females who demonstrated a similar hypotension both pre- and post-G-training (Fig. 2). No differential changes in the $\Delta\text{HR}/\Delta\text{MAP}$ ratio induced by standing were observed between males and females, although both groups demonstrated a moderate increase in $\Delta\text{HR}/\Delta\text{MAP}$ after G-training compared with before G-training (Table I).

HR and BP responses to the Valsalva maneuver are presented in Table II, and responses during early phase I and phase IV are presented in Fig. 3. Differences between males and females from before and after G-training were minimal. Although the confidence interval for the change from before to after G-training in the $\Delta\text{HR}/\Delta\text{MAP}$ ratio during early phase I and phase IV included zero (Table II), 8 of 12 male and female subjects demonstrated an increase in their responses (Fig. 3).

Baseline impedance of the calf increased from 23.1 ± 3.8 to 30.9 ± 4.4 ohms in the females, but was reduced from 36.3 ± 4.2 to 30.4 ± 4.0 ohms in the males (Table I). Calf compliance increased by 146% in males and by 90% in females after G-training compared with before G-training (Table I and Fig. 4).

DISCUSSION

A major finding of this study was the observation that chronic exposure to high-G acceleration was associated

with alterations in cardiovascular function and the magnitude of orthostatically induced hypotension. G-training increased the stroke volume and cardiac output responses in the men, caused by moving from the squat to the standing posture, and was associated with their ability to ameliorate the magnitude of orthostatic hypotension. In addition, high-G training may enhance cardiac baroreflex responsiveness in some individuals, since most of our subjects demonstrated increased HR response to a given BP change (i.e., $\Delta\text{HR}/\Delta\text{MAP}$) during early phase II and phase IV of the Valsalva maneuver. These findings are directly opposite to the attenuated carotid-cardiac baroreflex response (6,8,10,13) and increased orthostatic hypotension associated with reduced stroke volume following prolonged exposures to space-flight and ground-based simulations of microgravity (3,6). Therefore, the results of the present investigation provide evidence to support the hypothesis that the capacities of cardiovascular functions to regulate BP in the face of orthostatic challenges can be increased by chronic repeated exposure to high-G acceleration.

Another important finding of the present study was that women failed to demonstrate cardiovascular adaptation to high-G training compared with men. While high-G training increased stroke volume and cardiac output and protected against orthostatic hypotension during the squat-stand test in the men, it failed to alter any of these cardiovascular functions in women. This comparison of the influence of high-G-training may be particularly important in that an absence of enhanced cardiovascular functions observed in females compared with males was associated with a lower tracking performance during simulated air-to-air combat at high G in the women compared with the men (5). Together, our data provide indirect evidence that the defense of BP regulation and cerebral perfusion is associated with, and may be an important underlying mechanism for, cognitive task performance during high-G maneuvers. Perhaps as important is the possible implication that female pilots may have less physiological potential for their cardiovascular functions to adapt during training to support optimal performance during aerial combat.

In the present study, we used the beat-to-beat hemodynamic response during the initial time interval (less than 10 s) of standing immediately following 4 min of a squat posture as an orthostatic challenge designed to assess cardiovascular function before and after G-training. We are unaware of any previous documentation that describes the use of this test in research or clinical application. An immediate pronounced reduction in total peripheral resistance occurred when standing, which represents an apparent reactive hyperemia induced by a tourniquet effect of the squat position. Since the initial response of sympathetically mediated peripheral vasoconstriction requires 2 to 3 s to occur (11), with maximum effect requiring approximately 10 to 15 s (4), hemodynamic responses within 10 s of standing probably were not influenced by baroreflex functions during this procedure. As a result, the squat-stand protocol provided a highly reproducible cardiovascular stimulus (i.e., reactive hyperemia-induced hypotension) before and after G-training in both males and females (Fig. 1). These data suggest that this orthostatic protocol could provide an

TABLE I. MEAN DIFFERENCES BETWEEN PRE- AND POST-G TRAINING IN HEMODYNAMIC RESPONSES TO STANDING IN MALES (N = 6) AND FEMALES (N = 7).

	Post-/Pre-Stand Test Differences	SE	95% CI
Total Peripheral Resistance, pru			
Males	-4.0	2.6	[-9.9, 1.8]
Females	0.5	2.4	[-4.9, 5.9]
Heart Rate, bpm			
Males	-0.3	2.5	[-5.84, 5.22]
Females	3.0	2.3	[-2.1, 8.1]
Stroke Volume, mL			
Males	14.0	5.3	[2.2, 25.9]
Females	-0.5	4.9	[-11.5, 10.5]
Cardiac Output, L/min			
Males	1.3	0.5	[0.1, 2.4]
Females	0.4	0.5	[-0.7, 1.4]
Mean Arterial Pressure, mmHg			
Males	-10.0	3.9	[-1.4, -18.6]
Females	-5.5	3.6	[2.5, -13.4]
Δ HR/ Δ MAP, bpm/mmHg			
Males	0.2	1.6	[-0.2, 0.6]
Females	0.3	1.5	[-0.1, 0.6]
Baseline Calf Impedance, ohms			
Males	-2.6	4.7	[-13.0, 7.9]
Females	6.3	4.3	[-3.2, 15.8]
Calf Compliance, Δ mL/ Δ mmHg			
Males	15.0	4.5	[4.9, 25.2]
Females	7.3	4.2	[-2.0, 16.6]

Note: Bolded confidence intervals do not include zero. Mean differences are adjusted for pre-G-training differences (ANCOVA). SE = standard error of the mean and 95% CI = 95 percent confidence interval.

excellent repeatable diagnostic or screening technique for clinical application and field operations in addition to its research potential.

Reduced total peripheral resistance when standing in the present study caused an immediate reduction in MAP, although the males were better able to ameliorate the magnitude of this orthostatic hypotension after G-training than the females (Fig. 2). The HR reflex response was similar between both gender groups before and after training, but in the presence of a smaller hypotension stimulus in the males after G-training. This result supports the notion that males may have had greater inte-

grated baroreflex-mediated cardiac chronotropic responsiveness after G-training than females, although this difference could not be discerned statistically.

Since central venous pressure and cardiac filling are reduced during standing (2), it was somewhat unexpected that stroke volume was maintained or increased during movement from squatting to standing postures in our subjects. Although a mechanism was unclear, the defense of stroke volume immediately on standing after squatting may reflect that lowered myocardial afterload (i.e., reduced arterial BP) was similar or greater than the magnitude of reduced preload during this transient pos-

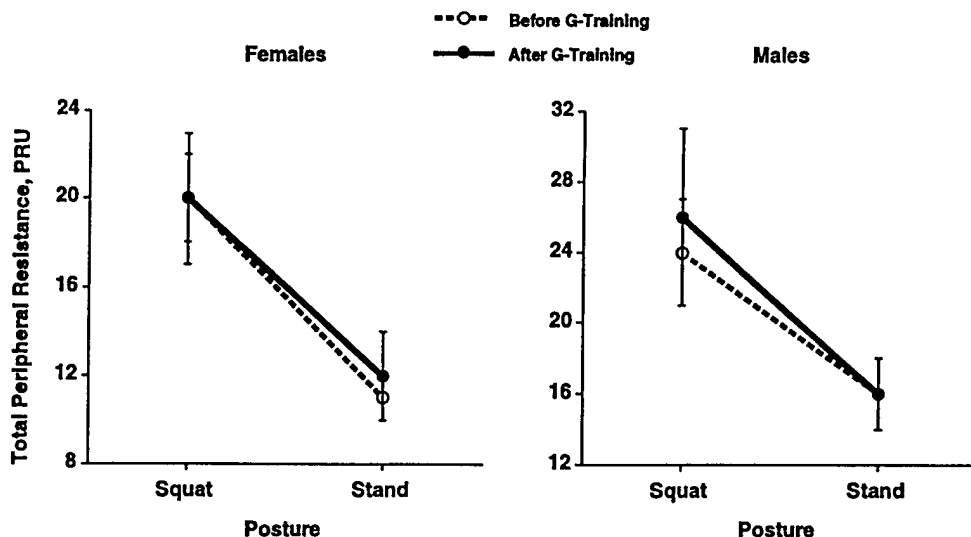


Fig. 1. Total peripheral resistance during squat and stand postures in females (left panel) and males (right panel) before and after G-training. Circles represent the mean, and bars represent \pm SEM values.

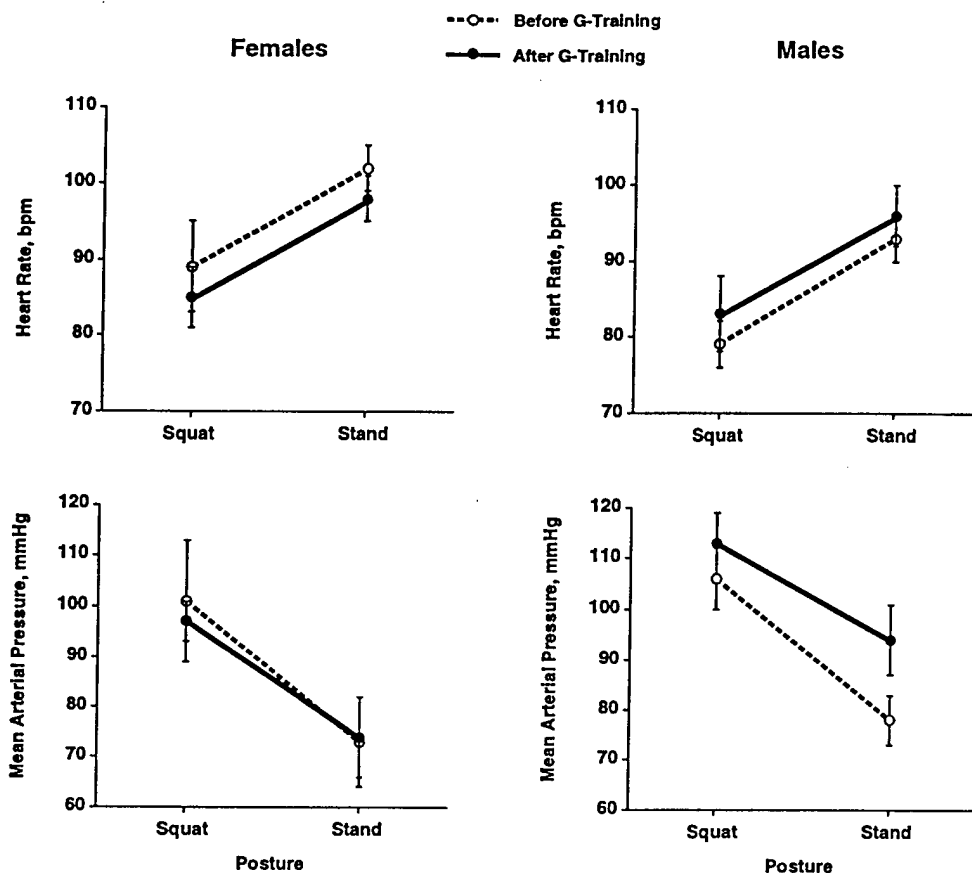


Fig. 2. HR and mean arterial BP during squat and stand postures in females (left panel) and males (right panel) before and after G-training. Circles represent the mean, and bars represent \pm SEM values.

ture change. The ability of males to ameliorate orthostatic hypotension during the post-G-training squat-stand test resulted from their ability to increase stroke volume and cardiac output compared with females. This result suggests that G-training may have increased cardiac filling and/or myocardial contractility in male subjects. Cardiac filling can be influenced by increased blood volume, greater filling time, higher preload (central venous pressure), and lower afterload. Although we were unable to

measure blood volume directly in our subjects, the phase I Δ MAP during the Valsalva maneuver has been used as an index of cardiac filling pressure and changes in blood volume (22). Since there was no difference in the phase-I Δ MAP between males and females between pre- and post-G-training (Table II), increased cardiac filling pressure and blood volume does not appear to explain the difference in stroke volume response to post-G-training standing between males and females. The HR re-

TABLE II. MEAN DIFFERENCES BETWEEN PRE- AND POST-G-TRAINING FOR Δ HR AND Δ MAP IN MALES (N = 6) AND FEMALES (N = 6) DURING THE FOUR PHASES OF THE VALSALVA MANEUVER.

Valsalva Maneuver Phase	Pre-/Post-G- Training Differences	SE	95% CI
Phase I Δ MAP			
Males	1.4	1.8	[-2.6, 5.4]
Females	2.6	1.8	[-1.4, 6.6]
Early Phase II Δ HR/ Δ MAP			
Males	0.3	0.2	[-0.2, 0.7]
Females	0.2	0.2	[-0.2, 0.6]
Late Phase II Δ MAP			
Males	-0.2	3.9	[-9.0, 8.5]
Females	-3.3	3.9	[-12.0, 5.5]
Phase IV Δ HR/ Δ MAP			
Males	0.4	0.2	[-0.2, 0.9]
Females	0.3	0.2	[-0.3, 0.8]

Note: Mean differences are adjusted for pre-G-training differences (ANCOVA). SE = standard error of the mean and 95% CI = 95 percent confidence interval.

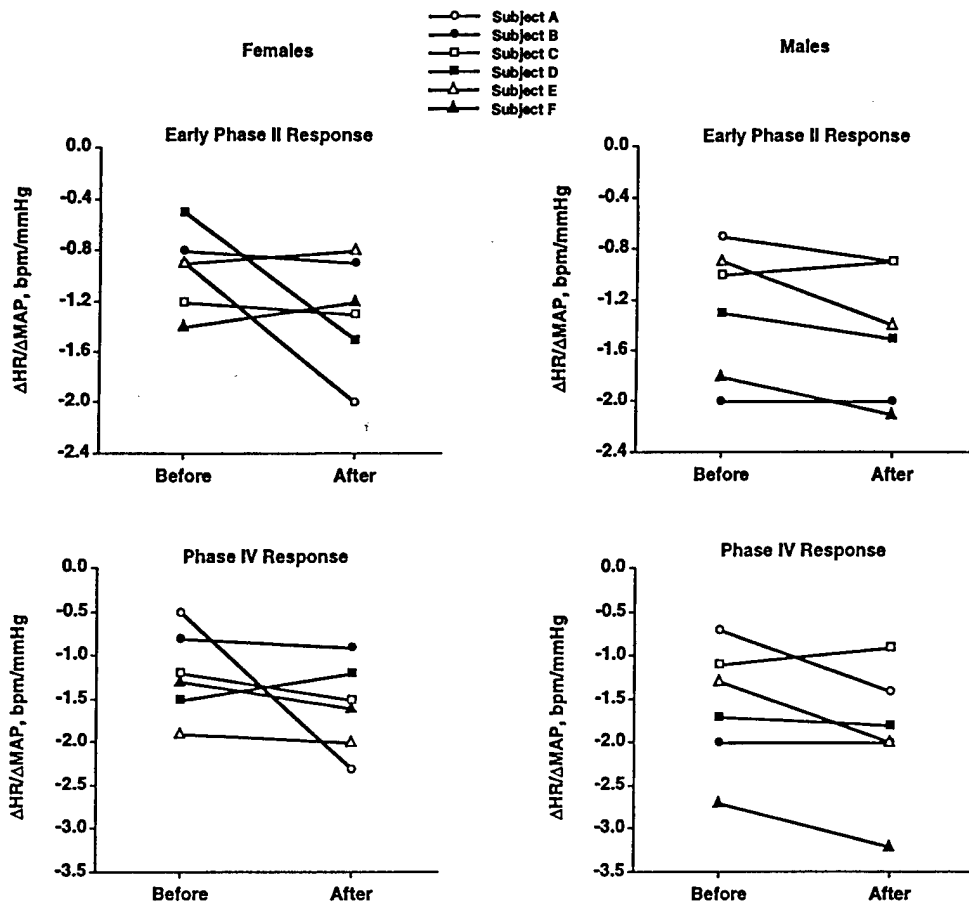


Fig. 3. Ratio of the change in HR to the change in mean arterial BP ($\Delta HR/\Delta MAP$) during early phase II and phase IV of the Valsalva maneuver in females (left panel) and males (right panel) before (open bars) and after (lined bars) G-training. Bars represent the mean, and lines represent \pm SEM values.

sponse to pre- and post-G-training standing also was similar between males and females, suggesting that cardiac filling time could not explain stroke volume differences between genders. Since myocardial afterload was

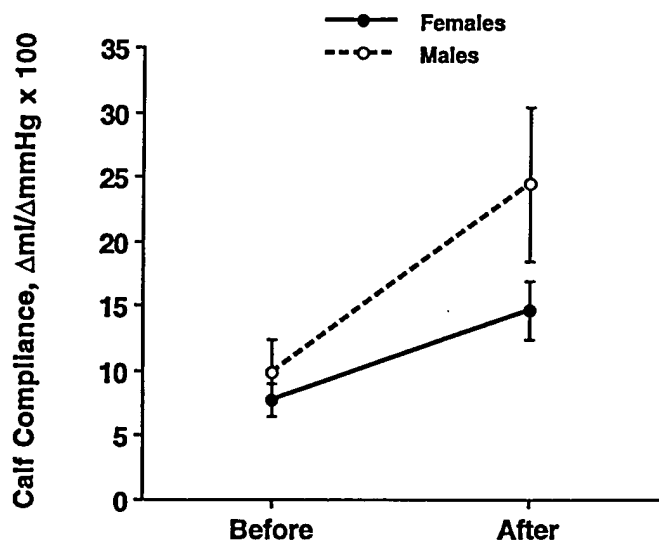


Fig. 4. Calf compliance in females (left panel) and males (right panel) before (open bars) and after (lined bars) G-training. Bars represent the mean, and lines represent \pm SEM values.

greater in males compared with females after G-training (i.e., less hypotension), afterload could not explain stroke volume differences between genders. It, therefore, appears unlikely that enhanced cardiac filling could provide a mechanism by which males increased their stroke volume during the initial 10 s of standing after G-training compared with females. It is, therefore, possible that increased stroke volume during post-G-training standing in males compared with females may have reflected increased myocardial contractility during the orthostatic challenge. The possibility that chronically repeated exposure to high G may enhance cardiac function is a hypothesis that warrants further investigation.

High venous compliance of the lower extremities may contribute to lower orthostatic tolerance in some populations since earlier onset of syncope has been reported to be associated with increased calf compliance (21). However, we found no increase in the development of orthostatic hypotension following G-training despite a dramatic increase of calf compliance in both men and women in the present investigation. Our observation of increased calf compliance with high-G training was unexpected since we hypothesized that high-G acceleration would induce adaptations that would enhance cardiovascular function for BP regulation. The mechanism of increased compliance in our subjects is unclear. Increased compliance has been observed following exposure to low

gravity and was associated with reduction in the muscle compartment (tissue and water) that surrounds the veins (7). However, the absence of statistically discernable changes in baseline impedance in both males and females following G-training (Table I) suggested that increased venous compliance in the calf was not associated with loss of the muscle compartment. An alternative explanation for increased venous compliance following G-training is the possibility that the veins and/or their valves may have become damaged by the repeated exposure to extremely high hydrostatic pressures under acceleration. Our observation that increased calf compliance following G-training may be the first data to support a hypothesis that chronically repeated exposure to high-G acceleration may cause structural damage to veins of the lower extremities and may compromise venous return during orthostatic challenges.

As with any investigation, there were limitations in the experimental design of this study. The statistical power of this experiment was moderate to low because sample size was approximately one-third of that required to detect male-female differences, i.e., adequate statistical power would not be achieved until the number of males and females reached approximately 25 per group. Unfortunately, the recruitment of large numbers of subjects was not possible given the complexity and duration of the experimental training and the limitation of research funding. Thus, the low statistical power inflated the Type-II error rate of the experiment (i.e., it increased the chance of missing a gender effect). However, this does not mean that the results of the present investigation were not valid, but that statistical analyses should not be viewed as deterministic, accept/reject propositions. Considering this limitation, we chose to present our results as confidence intervals that reflect a range of possible outcomes and are more informative than accept/reject conventions (14). Since the pre-G-training measures were taken prior to the post-G-training measures, there may have been an order effect in the cardiovascular alterations observed following G-training that was not considered by our experimental design. However, the amount of change within each group did not confound any comparisons that may be made between males and females since both gender groups received the same experimental manipulations.

Operational Implications: Aircrews of high-performance aircraft have reported that resumption of high +Gz flying after extended time away from +Gz exposure (G-layoff) is accompanied by a period of reduced tolerance or performance (4). Empirical data have been obtained from recent experiments that corroborate these observations (23). The adaptations in cardiovascular function following G-training in the present study may provide a physiological basis for the phenomenon of G-layoff. Since G-training was associated with enhanced baroreflex function, increased stroke volume, and less orthostatic hypotension, it is possible that these mechanisms are attenuated in the extended absence of high-G exposure. This possibility underscores the importance of providing regular physical training at high G or with procedures that can replace the physiological stimuli required to maintain the level of cardiovascular function associated with normal high-G training activity.

Since there is compelling evidence that females have lower orthostatic tolerance than males (15,20,25), we predicted that the cardiovascular function of the female subjects would benefit from G-training. Against expectations, the female subjects showed virtually no change in orthostatic function after G-training. This result may suggest that females have an inherently limited capacity to improve their orthostatic performance. The inability of the female subjects to adapt their cardiovascular functions to high-G training with associated lower combat task performance scores compared with males may provide important insight for pilot selection and training.

Adaptations in cardiovascular function observed in the present study also may provide a physiological basis for cognitive performance under high G. If the maintenance of arterial BP is closely related to cerebral perfusion and consciousness, it is reasonable to predict that individuals with a greater capacity to defend their BP under high-G challenges will perform better in combat conditions. This hypothesis was supported by the observation in the present study that improvement in the protection of BP during the squat-stand test in male subjects was associated with higher performance scores during combat tracking than in their female counterparts (5). A significant finding of this study was that the cardiovascular functions of female subjects demonstrated an inability to adapt to high G and, consequently, that female subjects failed to perform the cognitive tasks of air-to-air combat as well as male subjects following prolonged high-G training, despite females and males having similar G tolerances (5). It is possible that task performance during high-G acceleration may be affected by multiple mental and physical distractions associated with maintaining consciousness. Therefore, our data strongly suggest that G-tolerance alone may not provide an accurate predictor of performance at high G and that measurements of cardiovascular function and adaptation may enhance the sensitivity required for an optimum assessment of operational factors that influence combat performance. Further experiments designed to systematically investigate physiological mechanisms underlying this relationship could prove important in the design of pilot training for future manned as well as unmanned aircraft.

ACKNOWLEDGMENTS

The authors thank Drs. Raymond P. Ten Eyck and Geoffrey W. McCarthy for their medical monitoring of the subjects, Craig Reister and Gary Muniz for their engineering support and technical assistance with data collection, and the subjects for their time and cooperation. This research was supported in part with grants funded by the Air Force Office of Scientific Research and the Defense Women's Health Research Program. The views expressed herein are the private views of the authors and not to be construed as representing those of the Department of Defense or the Department of the Air Force.

REFERENCES

1. Albery WB, Ten Eyck RP, Wolfe M. Echocardiographic monitoring of naive male and female centrifuge subjects for changes in cardiac function. *Aviat Space Environ Med* 1997; (In press).
2. Blomqvist CG, Stone HL. Cardiovascular adjustments to gravitational stress. In: Shepherd JT, Abboud FM, eds. *Handbook of physiology: the cardiovascular system. Peripheral circulation and organ blood flow*, Sect. 2, Vol. 3, Pt. 2, Ch. 28. Bethesda, MD: American Physiological Society, 1983; 1025-63.

3. Buckley JC Jr., Lane LD, Levine BD, et al. Orthostatic intolerance after spaceflight. *J Appl Physiol* 1996; 81:7-18.
4. Burns JW. G-protection capabilities and current G-protection issues. In: Current concepts on G-protection research and development. Neuilly-sur-Seine, France: AGARD. AGARD-LS-202, May 1995, Paper #10.
5. Chelette TL, Albery WB, Esken RL, Tripp LD. Individual performance during high G simulated flight after 24 hours of sleeplessness. *Aviat Space Environ Med* 1997; (In press).
6. Convertino VA. Exercise and adaptation to microgravity environments. In: Fregly MJ, Blatteis CM, eds. *Handbook of physiology: environmental physiology. III. The gravitational environment*, Sect. 1, Ch. 36. New York: Oxford University Press. 1995:815-43.
7. Convertino VA, Doerr DF, Stein SL. Changes in size and compliance of the calf following 30 days of simulated microgravity. *J Appl Physiol* 1989; 66:1509-12.
8. Convertino VA, Doerr DF, Eckberg DL, et al. Head-down bed rest impairs vagal baroreflex responses and provokes orthostatic hypotension. *J Appl Physiol* 1990; 68:1458-64.
9. Convertino VA, Doerr DF, Ludwig DL, Vernikos J. Effect of simulated microgravity on cardiopulmonary baroreflex control of forearm vascular resistance. *Am J Physiol* 1994; 266:R1962-9.
10. Convertino VA. Carotid-cardiac baroreflex: relation with orthostatic hypotension following simulated microgravity and implications for development of countermeasures. *Acta Astronautica* 1991; 23:9-17.
11. Eckberg DL, Sleight P. *Human baroreflexes in health and disease*. New York: Oxford University Press 1992:256-9.
12. Frey MAB, Hoffer GW. Association of sex and age with responses to lower-body negative pressure. *J Appl Physiol* 1988; 65:1752-6.
13. Fritsch JM, Charles JB, Bennett BS, et al. Short-duration spaceflight impairs human carotid baroreceptor-cardiac reflex responses. *J Appl Physiol* 1992; 73:664-71.
14. Garner MJ, Altman DG. Confidence intervals rather than p values: estimation rather than hypothesis testing. *Br Med J* 1986; 292:746-50.
15. Hogan TR, Cubitt M, Ecken MK, Davis JE. Effect of gender on orthostatic tolerance (Abstract). *Med Sci Sports Exerc* 1995; 27:S188.
16. Imholz BPM, Van Montfrans GA, Settels JJ, et al. Continuous non-invasive blood pressure monitoring: reliability of Finapres device during the Valsalva manoeuvre. *Cardiovasc Res* 1988; 22:390-7.
17. Korner PI, Tonkin AM, Uther JB. Reflex and mechanical circulatory effects of graded Valsalva maneuvers in normal man. *J Appl Physiol* 1976; 40:434-40.
18. Kubicek WG, Patterson RP, Witsoe DA. Impedance cardiography as a noninvasive method of monitoring cardiac function and other parameters of the cardiovascular system. *Ann NY Acad Sci* 1969; 170:724-32.
19. Laird N. Further comparative analyses of pretest-posttest research designs. *Am Statistician* 1983; 37:329-30.
20. Ludwig DA, Convertino VA, Goldwater DJ, Sandler H. Logistic risk model for the unique effects of inherent aerobic capacity on +Gz tolerance before and after simulated weightlessness. *Aviat Space Environ Med* 1987; 58:1057-61.
21. Luft UC, Myhre LG, Loeppky JA, Venters MD. A study of factors affecting tolerance of gravitational stress simulated by lower body negative pressure. In: Research report on specialized physiology studies in support of manned space flight. Albuquerque, NM: Lovelace Foundation. NASA Contract Report NAS 9-14472. 1976:1-60.
22. Luster EA, Baumgartner N, Adams WC, Convertino VA. Effects of hypovolemia and posture on integrated baroreflex function. *Aviat Space Environ Med* 1996; 67:308-13.
23. Morgan TR, Hill RC, Burns JW, Vanderbeek RD. Effects of G-layoff on subsequent tolerance to +Gz (Abstract). *Aviat Space Environ Med* 1994; 65:448.
24. Thornton WE, Hoffer GW. Hemodynamic studies of the legs under weightlessness. In: Johnson RS, Dietlein LF, eds. *Biomedical results from Skylab*. Washington, D.C.: National Aeronautics and Space Administration, SP-377. 1977:324-9.
25. White DD, Gotshall RW. Women have lower tolerance to lower body negative pressure compared to men. *J Appl Physiol* 1996; 80:1138-43.
26. White DD, Montgomery LD. Pelvic blood pooling of men and women during lower body negative pressure. *Aviat Space Environ Med* 1996; 67:555-9.

HIGH SUSTAINED +Gz ACCELERATION: PHYSIOLOGICAL ADAPTATION TO HIGH-G TOLERANCE

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INTRODUCTION

Since the early 1940s, a significant volume of research has been conducted in an effort to describe the impact of acute exposures to high-G acceleration on cardiovascular mechanisms responsible to maintaining cerebral perfusion and consciousness in high performance aircraft pilots during aerial combat maneuvers [1]. The value of understanding hemodynamic characteristics that underlie G-induced loss of consciousness has been instrumental in the evolution of optimal technology development (e.g., G-suits, positive pressure breathing, COMBAT EDGE, etc.) and pilot training (e.g., anti-G straining maneuvers).

Although the emphasis of research has been placed on the development of protection against acute high +Gz acceleration effects, recent observations suggest that adaptation of cardiovascular mechanisms associated with blood pressure regulation may contribute to a protective 'G-training' effect. Regular training at high G enhances G tolerance in humans, rats, guinea pigs, and dogs [1] while prolonged layoff from exposure in high G profiles (G-layoff) can result in reduced G endurance [10]. It seems probable that adaptations in physiological functions following chronically-repeated high G exposure (G training) or G-layoff could have significant impacts on performance during sustained high-G acceleration since protective technology such as G-suits and anti-G straining maneuvers are applied consistently during these periods of training.

The purpose of this paper is to present a review of new data from three experiments that support the notion that repeated exposure on a regular basis to high sustained +Gz acceleration induces significant physiological adaptations which are associated with improved blood pressure regulation and subsequent protection of cerebral perfusion during orthostatic challenges.

CARDIOVASCULAR RESPONSES OF PILOTS

In a recent study, heart rate and arterial blood pressure responses during rapid (over a time course of 4 seconds) 75° head-up tilt were measured in 8 fighter pilots and compared to the responses in 12 non-pilots [9]. The tilt tests in the pilots were conducted within one to two days after the conclusion of a period of high +Gz flying (i.e., air-to-air missions such as basic fighter or air combat maneuvers) in F/A-18 Hornet fighter aircraft or Macchi MB326H advanced jet trainer. The non-pilots required a significantly greater stimulus (i.e., reduction in systolic blood pressure) to induce a similar elevation in orthostatic heart rate [Fig. 1]. Although confined to methodological limitations, this experiment provides indirect evidence that high performance aircraft pilots demonstrate higher arterial baroreflex sensitivity associated with their exposure to high G acceleration compared to non-pilots. Theoretically, increased sensitivity of this mechanism would provide pilots greater compensatory tachycardia and maintenance of cardiac output before mean arterial blood pressure was reduced to critically low levels.

EFFECTS OF LONGITUDINAL +Gz EXPOSURE

In a more recent study [2], 6 men underwent 8 consecutive days of exposure to high +Gz (G training) with peak acceleration plateaus at 4-5 G on days 1 through 4, followed by gradual increase to peak acceleration plateaus at 6, 7, 8, and 9 G on days 5, 6, 7, and 8, respectively. Mean arterial blood

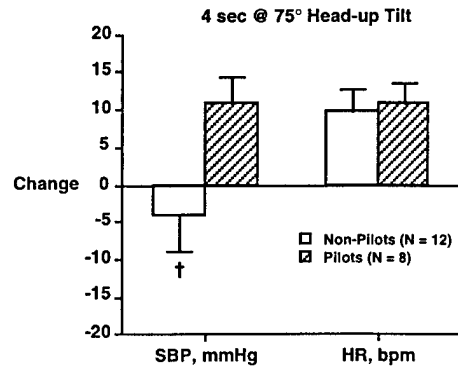


Fig. 1. Change in systolic blood pressure (SBP) and heart rate (HR) during the initial 4 seconds of 75° head-up tilt in non-pilots (open bars) and pilots (hashed bars). Values are mean (bars) \pm 1SE (lines) and † indicates $P < 0.05$ versus pilot value. Data modified from Newman et al. [9].

pressure (MAP) and heart rate (HR) responses were assessed in each subject during a squat-to-stand orthostatic test and Valsalva maneuver before and after G training. During the initial 10 sec on moving from the squat-to-stand posture, hypotension was less after compared with before G training with similar elevations in heart rate [Fig. 2]. These responses are virtually

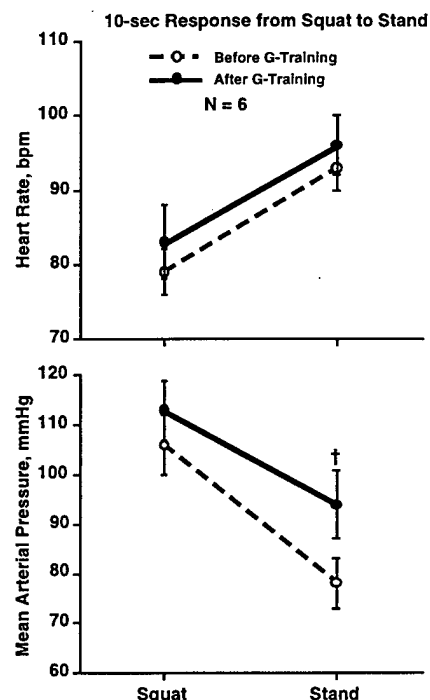


Fig. 2. Heart rate and blood pressure responses during a squat-to-stand maneuver before (open circles and broken line) and after (closed circles and solid line) G training. Values are mean \pm 1SE and † indicates $P < 0.05$ versus before value. Data modified from Convertino et al [2].

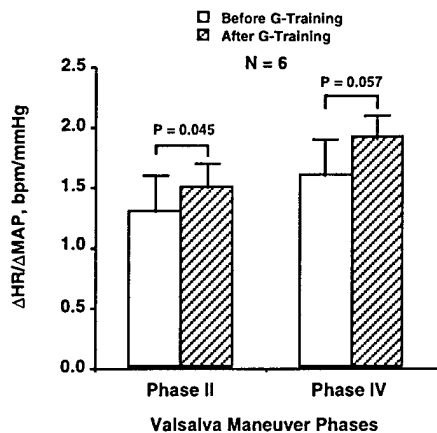


Fig. 3. Ratio of the change in heart rate to the change in mean arterial blood pressure ($\Delta HR/\Delta MAP$) during early phase II and phase IV of the Valsalva maneuver before (open bars) and after (lined bars) G training. Bars represent mean and lines represent ± 1 SEM. Data from Convertino et al. [2].

identical to the comparisons between fighter pilots and non-pilots [Fig. 1] and suggest that G training induced an increase in baroreflex sensitivity. Support for increased arterial baroreflex responsiveness was evident by higher $\Delta HR/\Delta MAP$ responses during phase II and IV of the Valsalva maneuver [Fig. 3]. The ability to reduce the hypotensive response, i.e., defend mean arterial pressure, during orthostatism following G training could be attributed to the greater stroke volume and cardiac output in response to the squat-to-stand maneuver [Fig. 4]. Thus, the G-training study extended the preliminary results of the comparison between pilots and non-pilots by corroborating increased integrated baroreflex control of heart rate through the Valsalva responses and identifying higher stroke volume and cardiac output as an underlying mechanism for defense of mean arterial pressure during orthostatism.

CHARACTERISTICS OF G-TRAINED SUBJECTS

Although the studies on high performance aircraft pilots and G training effects provided new insight into physiological adaptation associated with repeated exposure to high sustained +Gz acceleration, the limited measurements provided little information about underlying mechanisms of improved blood pressure regulation. Since mean arterial pressure is the product of heart rate, stroke volume and peripheral resistance, it is reasonable to hypothesize that exposure to high-G training may

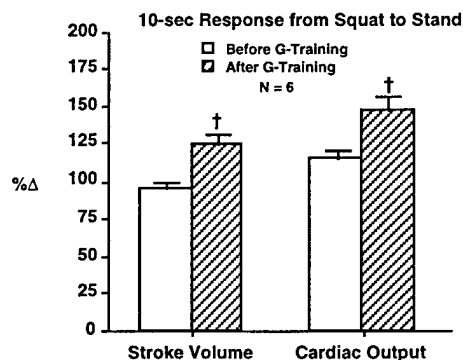


Fig. 4. Percent change (% Δ) in stroke volume and cardiac output during during a squat-to-stand maneuver before (open bars) and after (lined bars) G training. Values are mean ± 1 SE and † indicates $P < 0.05$ versus before value. Data modified from Convertino et al [2].

be associated with enhanced functions of mechanisms that control these cardiovascular responses. In a recently completed experiment, functions of carotid and aortic baroreflex control of heart rate, cardiopulmonary baroreflex control of vascular resistance, adrenoceptor responsiveness, indices of baseline vagal and sympathetic tone, circulating blood volume, and venous compliance of the lower extremities were measured in men after they underwent G-training to test the hypothesis that exposure to high +Gz acceleration would be associated with enhanced functions of specific mechanisms of blood pressure regulation. Heart rate, stroke volume, cardiac output, mean arterial blood pressure, central venous pressure, forearm and leg vascular resistance, and changes in leg volume were measured during various protocols of lower body negative pressure (LBNP), carotid stimulation, and infusions of adrenoceptor agonists in 10 males following a 3-day training exposure on a human centrifuge (G-trained) and compared to the same measurements in 10 males (controls) matched for age, height, weight, and fitness.

Similar to the previous studies [2,9], arterial blood pressure was maintained at a higher level during graded LBNP in the G-trained subjects compared to the controls despite similar heart rate elevations. The lesser hypotension during LBNP in the G-trained subjects was associated with smaller decrements in stroke volume and cardiac output, a similar response as that observed in subjects following G-training [2].

Mechanisms of stroke volume control. Several mechanisms could contribute to the enhanced ability of G-trained subjects to maintain stroke volume. Venous pooling in the lower extremities, which is dependent on compliance of the veins, can limit venous return. Although total leg volume of the G-trained subjects (12.5 ± 0.5 liters) and the controls (12.1 ± 0.5 liters) was similar ($P = 0.49$), an unexpected finding of this study was that calf compliance of the G-trained group (4.8 ± 0.2 ml/mmHg) was significantly less ($P = 0.02$) than that of the controls (6.2 ± 0.5 ml/mmHg). The lower calf compliance measured in the G-trained subjects was associated with less venous pooling during orthostatism reflected by smaller leg volume increases during graded LBNP compared to the control group [Fig. 5].

In addition to less pooling of blood, venous return, cardiac filling and stroke volume could be enhanced with expanded circulating blood volume. Although plasma volume was similar between the two groups, we found that total circulating blood volume in G-trained subjects was 17% greater ($P = 0.09$) than controls as a result of larger circulating red blood cell volume [Fig. 6]. The larger red blood cell volume was reflected in a higher ($P = 0.05$) hematocrit in G-trained (47 ± 1) compared to control subjects (43 ± 1).

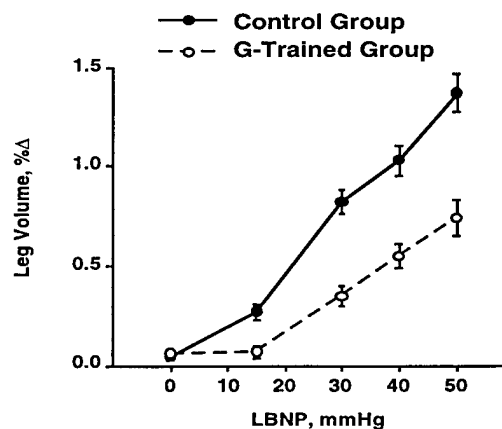


Fig. 5. Percent change (% Δ) in leg volume during graded LBNP in the control (closed circles and solid lines) and G-trained (closed circles and solid lines) subjects. Values are mean ± 1 SEM (lines).

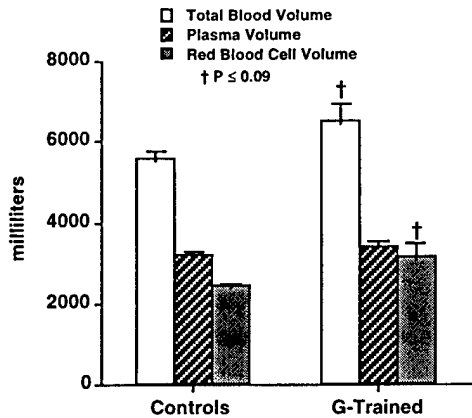


Fig. 6. Total circulating blood, plasma and red blood cell volumes in control and G-trained subjects. Values are mean (bars) \pm 1 SEM (lines). † indicates $P \leq 0.09$ vs. control group value.

Mechanisms of heart rate control. Another mechanism that contributes to the orthostatic regulation of arterial blood pressure involves the elicitation of compensatory tachycardia with the stimulation of arterial baroreceptors in response to hypotension. Studies that have provided comparisons between high performance aircraft pilots and non-pilots, and before and after G training have indicated that repeated exposure to high sustained +Gz acceleration may induce increased heart rate responsiveness in response to arterial baroreceptor stimulation. We applied graded pressure stimuli to carotid baroreceptors and measured beat-to-beat heart rate (R-R intervals) in an effort to directly assess the stimulus-response relationship of the carotid-cardiac baroreflex. A prominent feature associated with G training was a shift of the carotid-cardiac stimulus-response relationship upward and to the left, producing a higher gain (greater maximum response slope), particularly in the hypotension region [Fig. 7]. This indicates that for a given reduction in arterial pressure, there will be a greater compensatory elevation in heart rate (decrease in R-R interval) after adaptation to G training. We found that the average carotid-cardiac baroreflex responsiveness, i.e., maximum slope of the stimulus-response relationship, was greater ($P = 0.02$) in G-trained subjects (7.3 ± 1.2 ms/mmHg) compared to that in the controls (3.9 ± 0.4 ms/mmHg). Aortic-cardiac baroreflex sensitivity was virtually equal ($P = 0.97$) in the G-trained (-0.72 ± 0.20 bpm/mmHg) and control subjects (-0.71 ± 0.20 bpm/mmHg).

Adaptation of the carotid-cardiac baroreflex may be particu-

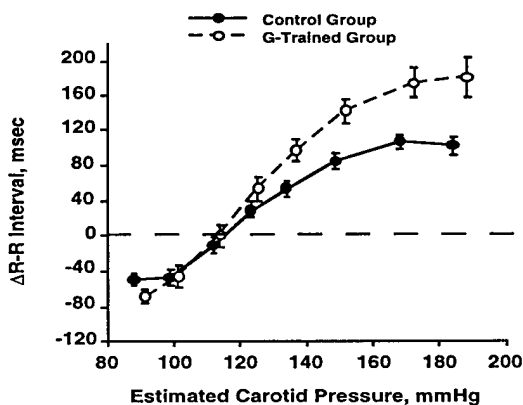


Fig. 7. Average carotid-cardiac baroreflex stimulus-response relationships in G-trained subjects (open circles and broken line) and non-trained controls (closed symbols and solid line). Symbols are means \pm 1 SEM ($N = 10$ in each group).

larly important because its sensitivity has been a predictor of orthostatic functions [3-5,8]. A particularly intriguing finding was based on the fact that, of the ten subjects who trained at high +Gz acceleration, 7 trained on a centrifuge capable of rapid onset rates (ROR = 6 G/sec) of acceleration while the remaining 3 subjects trained on a centrifuge limited to gradual onset rates (GOR = 1 G/sec). Carotid-cardiac baroreflex function of the ROR-trained subjects was dramatically higher (8.4 ± 1.5 msec/mmHg) than of the GOR-trained subjects (4.8 ± 0.6 msec/mmHg). This finding may reflect that adaptation of this mechanism may be dependent on the rate of change of its physiological stimulus as well as its magnitude.

Mechanisms of peripheral resistance control. The capacity to increase total systemic peripheral resistance represents an important mechanism for buffering against the development of hypotension during an orthostatic challenge. We applied low levels of LBNP (i.e., -5 to -20 mmHg) in an attempt to selectively stimulate cardiopulmonary baroreceptors and measured central venous pressure (CVP) in order to assess the stimulus-response relationship of baroreflex control of peripheral forearm vascular resistance (FVR). G training was associated with a reduced responsiveness (maximum slope) of the $\Delta CVP / \Delta FVR$ stimulus-response relationship [Fig. 8]. This relationship indicates that for a given reduction in orthostatically-induced CVP, there was less compensatory vasoconstriction (increase in peripheral vascular resistance) associated with adaptation to G training. We found that average $\Delta FVR / \Delta CVP$ of the cardiopulmonary baroreflex response was 54% less ($P = 0.01$) in the G-trained subjects (-1.4 ± 0.2 pru/mmHg) compared to the controls (-2.6 ± 0.3 pru/mmHg).

A lesser response, i.e., slope, of the cardiopulmonary baroreflex control of peripheral vascular resistance has been interpreted to indicate larger reserve for vasoconstriction since hypovolemia and hypervolemia elicit greater and lesser vascular resistance, respectively, for equal reductions in venous pressure [11]. Vasoactive reserve is defined as the baseline vasoconstrictive state subtracted from the maximum vasoconstrictive capacity [6]. This notion is consistent with the observation that G-trained subjects in this study had greater blood volumes and demonstrated less vasoconstriction at similar levels of LBNP compared to the controls [Fig. 8]. These responses have been interpreted to represent less utilization of vasoconstrictive reserve such that greater reduction in central blood volume is required to induce maximal pressor response [11]. It is therefore reasonable to expect that individuals trained with sustained high +Gz acceleration will gain protection from a hypervolemic adaptation that enhances cardiac

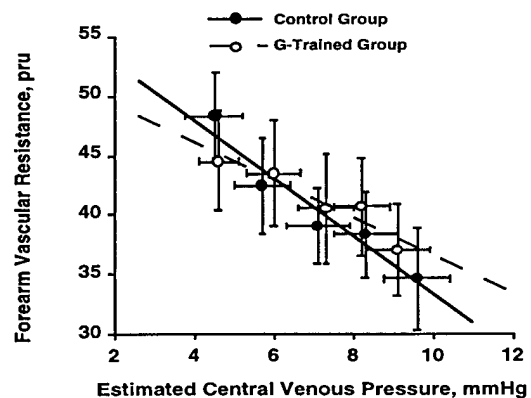


Fig. 8. Cardiopulmonary baroreflex stimulus-response relationship between forearm vascular resistance and estimated central venous pressure in control subjects (closed circles and solid lines) and G-trained subjects (open circles and broken lines). The linear equation for the mean control response is $y = -2.46x + 57.8$ ($r^2 = 0.933$) and for the mean G-trained response is $y = -1.57x + 52.3$ ($r^2 = 0.907$). Symbols are means \pm 1 SEM ($N = 10$ in each group).

filling and the capacity to increase systemic resistance under high-G conditions.

The capacity to buffer reductions in arterial blood pressure by increasing vascular resistance could also reflect changes in end-organ responsiveness. We found that subjects who trained at high +Gz and control subjects had similar vascular resistance responses to graded infusions of isoproterenol, suggesting that β -adrenoreceptor responsiveness (vasodilator effect) was not altered by G training. However, G-trained subjects did demonstrate higher ($P = 0.04$) elevations in peripheral resistance to phenylephrine infusion. This finding suggests that G training may enhance the capacity for peripheral vasoconstriction through increased sensitivity of α -adrenoreceptors.

SUMMARY

Ludwig and Convertino [8] have demonstrated that blood volume and carotid-cardiac baroreflex sensitivity represent two primary predictors for the capacity of the cardiovascular system to defend against the onset of loss in consciousness. These mechanisms are separate and distinct [11], with blood volume affecting the stroke volume and peripheral resistance and carotid baroreceptor sensitivity affecting heart rate. It is interesting that both of these physiological functions were elevated in pilots or subjects who had undergone exposure to high sustained +Gz acceleration compared to control subjects.

Results from the studies presented in this review demonstrated that repeated exposures to high sustained +Gz acceleration was associated with lesser orthostatic hypotension, lower venous compliance and blood pooling in the legs, higher carotid-cardiac baroreflex sensitivity, lesser decline in stroke volume and cardiac output during orthostatism, increased α -adrenoreceptor responsiveness, lesser vasoconstriction under equal LBNP, and larger total blood and red blood cell volume. The data also indicate that these adaptations are rapid, occurring with only a few exposures. The results of these investigations support the hypothesis that high sustained +Gz acceleration has a significant impact on improving the function of mechanisms that underlie blood pressure regulation.

The observations from these studies provide important perspective to understanding the contribution of gravity to the evolution and adaptation of cardiovascular function. Lower venous compliance and blood pooling in the legs, higher carotid-cardiac baroreflex sensitivity, greater stroke volume and cardiac output, larger vasoconstriction reserve, and larger total circulating vascular volume are associated with increased orthostatic performance. Therefore, it is possible that similar changes in these physiological functions after G training represent a partial explanation for increased performance during high sustained +Gz acceleration. Similarly, results from these studies might provide a physiological explanation for G-layoff since development of orthostatic intolerance following exposure to reduced gravity is associated with reductions in these functions. This perspective is best supported by the observation that the majority of nonpresyncopal astronauts in the U.S. space program were career pilots of high-performance aircraft [7]. It has been hypothesized that these individuals would not have been successful in their career if they had not developed high tolerance to G forces. The data presented in this review

support this notion and suggest that greater tolerance to high sustained +Gz acceleration is in part a result of chronic adaptation of physiological mechanisms that underlie blood pressure regulation.

REFERENCES

1. Burton, R.R., and A.H. Smith. Adaptation to acceleration environments. In: *Handbook of Physiology: Environmental Physiology. III. The Gravitational Environment*. M.J. Fregly & C.M. Blatteis (eds). New York, NY:Oxford University Press. Section 4, Chapter 40, 1995, p. 943-970.
2. Convertino, V.A., L.D. Tripp, D.A. Ludwig, J. Duff, and T.L. Chellette. Female exposure to high G: chronic adaptations of cardiovascular functions. *Aviat. Space Environ. Med.* (in press).
3. Convertino, V.A. Conditions of Reduced Gravity. In: *Clinical Autonomic Disorders*, 2nd ed., Chapter 33. P.A. Low (ed). Philadelphia:Lippincott-Raven Publishers, 1997, p. 429-440.
4. Convertino, V.A., D.F. Doerr, D.L. Eckberg, J.M. Fritsch, and J. Vernikos-Danellis. Head-down bedrest impairs vagal baroreflex responses and provokes orthostatic hypotension. *J. Appl. Physiol.* 68:1458-1464, 1990.
5. Convertino, V.A. Exercise and Adaptation to Microgravity Environments. In: *Handbook of Physiology: Environmental Physiology. III. The Gravitational Environment*. M.J. Fregly & C.M. Blatteis (eds). New York, NY:Oxford University Press. Section 1, Chapter 36, 1995, p. 815-843.
6. Engelke, K.A., D.F. Doerr, C.G. Crandall, and V.A. Convertino. Application of acute maximal exercise to protect orthostatic tolerance after simulated microgravity. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol.)* 271: R837-R847, 1996.
7. Fritsch-Yelle, J.M., P.A. Whitson, R.L. Bondar, and T.E. Brown. Subnormal norepinephrine release relates to presyncope in astronauts after spaceflight. *J. Appl. Physiol.* 81:2134-2141, 1996.
8. Ludwig, D.A., and V.A. Convertino. Predicting orthostatic intolerance: physics or physiology? *Aviat. Space Environ. Med.* 65:404-411, 1994.
9. Newman, D.G., S.W. White, and R. Callister. Evidence of baroreflex adaptation to repetitive +Gz in fighter pilots. *Aviat. Space Environ. Med.* 69: 446-451, 1998.
10. Morgan, T.R., R.C. Hill, J.W. Burns, and R.D. Vanderbeek. Effects of G-layoff on subsequent tolerance to +Gz. *Aviat. Space Environ. Med.* 65:448, 1994 (abstract).
11. Thompson, C.A., D.L. Tatro, D.A. Ludwig, and V.A. Convertino. Baroreflex responses to acute changes in blood volume in man. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol.)* 259:R792-R798, 1990.