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DIFFERENCES IN MECHANISM BETWEEN SYNCOPE RESULTING FROM RAPID ONSET ACCELERATION AND ORTHOSTATIC STRESS

A Research Paper

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by

*Maj David A. Self, PhD
Curtis D. White, MS
Robert M. Shaffstall, MS
Benjamin L. Mtinangi, MB, MSC
Jennifer S. Croft, BSC
Roger Hainsworth, PhD, DSC

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Contents

Illustrations

Page

Tables

Page

Preface

The vulnerability of cardiovascular function to head-to-foot (+Gz) inertial loads existing in military aviation environments has spawned a large body of applied research over the past 50 years. Failure of the heart and blood vessels to restore circulation to the brain under acceleration leads to G-induced loss of consciousness (G-LOC), often with catastrophic outcomes for the aviator. Class A mishaps involving G-LOC in aviators is a continuing problem for the Air Force. Each year, there are several incidents of G-LOC during high-G maneuvers, despite recent impressive advances in G-countermeasures equipment and training. The Crew Technology Division at Armstrong Laboratory, Brooks AFB, continues to study the effects of acceleration and use new insights gained in developing improved anti-G garments.

Anti-G suits function by inflating with air during high-G turns. This helps prevent G-LOC by increasing peripheral resistance to blood flow in the blood vessels, which increases the pressure of blood perfusing the brain. This increase in pressure partially offsets the hydrostatic drop in pressure resulting from +Gz acceleration and helps maintain blood flow through the brain. These garments also help prevent pooling of blood in the legs by providing an external resistance to expansion, not unlike the tough skin covering a giraffe's lower legs. Increased pooling of blood during acceleration will also lower the perfusion pressure of blood in the brain and lead to G-LOC.

These phenomena can be compared to fainting. Certain individuals suffer from orthostatic intolerance: they lose consciousness whenever they transition to upright posture. This results from the pooling of blood in the lower extremities inevitably leading to a loss of perfusion pressure at head level necessary to keep blood circulating through the brain. This is what happens in soldiers who pass out on the parade ground after standing at attention for prolonged periods of time. Acceleration frequently has been viewed as an exaggerated case of orthostasis. The principles of design in G-suits make use of our understanding of orthostatic intolerance and infer that the same mechanisms are at play during +Gz acceleration. As we continue striving to produce improved anti-G garments, more mechanistic information about the nature of G-LOC is essential.

This report describes a recent investigation into G-LOC conducted using the centrifuge at Brooks AFB, and orthostatically intolerant patients undergoing treatment at The University of Leeds Medical School in England. The purpose of the project was to determine whether hydrostatic or venous pooling effects predominate during acceleration.

Two different techniques were used in this study that require explanation. Plethysmography is a term given to a group of devices that measure changes in volume of a body segment resulting from the movement of blood. The device we utilized to detect changes in blood volume in the legs and abdomen is an impedance plethysmograph, which passes a very small electrical current through the body segment and then measures resistance to current flow. As blood is an excellent conductor, changes in the amount of blood will be reflected by changes in resistance. The second technique needing explanation is lower body negative pressure (LBNP). This is simply a vacuum cleaner connected to an airtight chamber surrounding the lower half of a subject. This device

quickly produces venous pooling the same way prolonged upright posture does, but is quantifiably reproducible and works in a much shorter period of time. It was used to produce syncope (fainting) in the Leeds patients. The term presyncope merely refers to our technique of terminating the upright tilt and LBNP before the subjects went completely unconscious.

The ultimate aim of this study was to increase the efficacy of next generation anti-G suits. As we anticipate the upper limit of +Gz loads to increase from 9 to 12 with introduction of the F-22, we must also increase the capabilities of aviators to withstand this increased level of physiologic stress.

The authors wish to thank Wayne Isdahl and Charles Kuhnel, the centrifuge operations personnel and the volunteer subjects, without whose efforts, this study would have been impossible. This manuscript has been accepted for publication in late 1996 in *Aviation, Space and Environmental Medicine.* We wish to thank the referees and editors for their invaluable suggestions for its improvement.

Abstract

Background and Hypothesis. Orthostatically-induced syncope is accompanied by venous pooling and vasodilatation. Loss of consciousness during head-to-foot acceleration (G-LOC) in aviators may be caused by a different mechanism, as venous pooling should be prevented through the use of an anti-G suit. This research was conducted to test the hypothesis that in individuals wearing a well-fitted anti-G garment, there are no important changes in volume of dependent regions during loss of consciousness resulting from rapid onset acceleration stress. Furthermore, this work compares venous pooling patterns in G-LOC subjects to patterns seen during syncope in volunteers and patients subjected to orthostatic stress. The tilt/LBNP tests were conducted to establish what level of venous pooling was required to induce syncope in the absence of a hydrostatic component (other than 1 G) and to confirm that our equipment was sensitive enough to detect volume changes large enough to cause syncope.

Methods. Shifts in blood volume to the calf, thigh and abdominal segments were compared in subjects with G-LOC to those in subjects taken to presyncope with orthostatic stress created by upright tilt and lower body negative pressure (LBNP). Centrifuge subjects were exposed to a 15-sec rapid onset (6 G/sec) +5 Gz exposure on the centrifuge while remaining relaxed and wearing a well-fitting anti-G suit, but with the anti-G suit pressure inactivated.

Results. Blood volume decreased an average of 14.9 (± 22.1) ml in the calf segment; increased an average of 64.1 (± 7.9) ml in the thigh segment, and decreased an average of 80.1 (± 29.7) ml in the abdominal segment. The mean net change in volume of the three combined regions was not significantly different from zero. Presyncope was induced in subjects by a progressive exposure to upright tilt, and then addition of LBNP at -20 mm Hg and -40 mm Hg. In the tilt/LBNP group, there was a net increase of 1022 (±269.8) ml for the combined segments. Changes in all 3 segments were significantly different than the mean segmental volume changes seen in centrifuge subjects at G-LOC endpoints. Significant changes from baseline mean arterial pressure, but not heart rate were also seen within, but not between the 2 groups, with mean eye level blood pressures (ELBP) falling an average of 45.6 (±7.7) mm Hg in the tilt/LBNP group at syncope and 105.1 (±15.5) mm Hg in the centrifuge subjects at G-LOC.

Conclusions: These differences suggest that G-LOC may be due entirely to hydrostatic effects, with venous pooling being prevented by the wearing of an anti-G garment, even when it remains uninflated.

Chapter 1

Introduction

Orthostatically-induced syncope is characterized by increased pooling of blood in the capacitance vessels in dependent regions. This leads to reduction in stroke volume and finally, a decline in arterial pressure below that required to maintain cerebral perfusion. Loss of consciousness resulting from acceleration stress has sometimes been described as an exaggerated case of orthostatic stress.[1] However, since syncope during acceleration is observed in aviators and centrifuge subjects wearing anti-G suits that are designed to prevent venous pooling, other mechanisms may be responsible. An alternative explanation is that the cephalid pressure drop during acceleration is due entirely to the effects of gravity on hydrostatics.

The influence of gravity on a column of fluid is such that the pressure at any point in the column of fluid is given by the relationship

$$P=\rho*G*h$$

where ρ is the density of the fluid, G is the strength of the gravitational field and h is the height of the column. When the column is closed at both ends, a hydrostatic indifference point (*HIP*) is created in the middle of the tube. Pressures at points equidistant above and below the *HIP* will be equal, but algebraically opposite in sign.[2] A drop in pressure can occur without any movement of fluid by simply increasing the value of the gravitational

vector. During acceleration, the pressure at eye level declines linearly with increasing +Gz inertial loads.[3] We can demonstrate that this is possible without any fluid displacement, by setting a rigid tube system rotating on a centrifuge (Figure 1-1). Pressure transducers placed above and below the *HIP* reflect changes in the absence of a changing volume. As anti-G garments provide a degree of external rigidity to dependent regions, this mechanism may dominate, making venous pooling only a minor component.

The model (designed to approximate a seated human form) was made of rigid PVC 1" tubing with high fidelity pressure transducers placed within the lumen, that was completely filled with degassed saline. The device was placed on the centrifuge such that rotation created a 3G inertial load in the +Gz axis. Top trace: outputs from the 4 transducers when the "calf" segment had a rigid element. The 2 transducers above the putative *HIP* registered a fall in pressure, with the transducers below this point, reporting an increase. Bottom trace: records of another experiment where the "calf" segment was replaced with a distendible element that allowed a small change in volume under acceleration. In reality, the *HIP* does not occur at the midpoint of the arterial system, as there is greater compliance in the footward end of the system.

Technology for measuring shifts in blood volume during acceleration has only recently been introduced and utilized in centrifuge studies.[4] No previous work has quantitatively evaluated the extent to which venous pooling occurs during rapid onset G exposure leading to G-LOC. Although acceleration workers have argued for the predominance of a hydrostatic mechanism, their findings have been largely inferential as there have been no direct measurements of venous pooling under acceleration during G-LOC incidents.[5] Furthermore, previous research has measured changes in total leg

volume during short periods of LBNP, using water displacement plethysmography, impedance plethysmography and radioactive iodinated serum albumin.[6] However, the tests were terminated prior to presyncope.

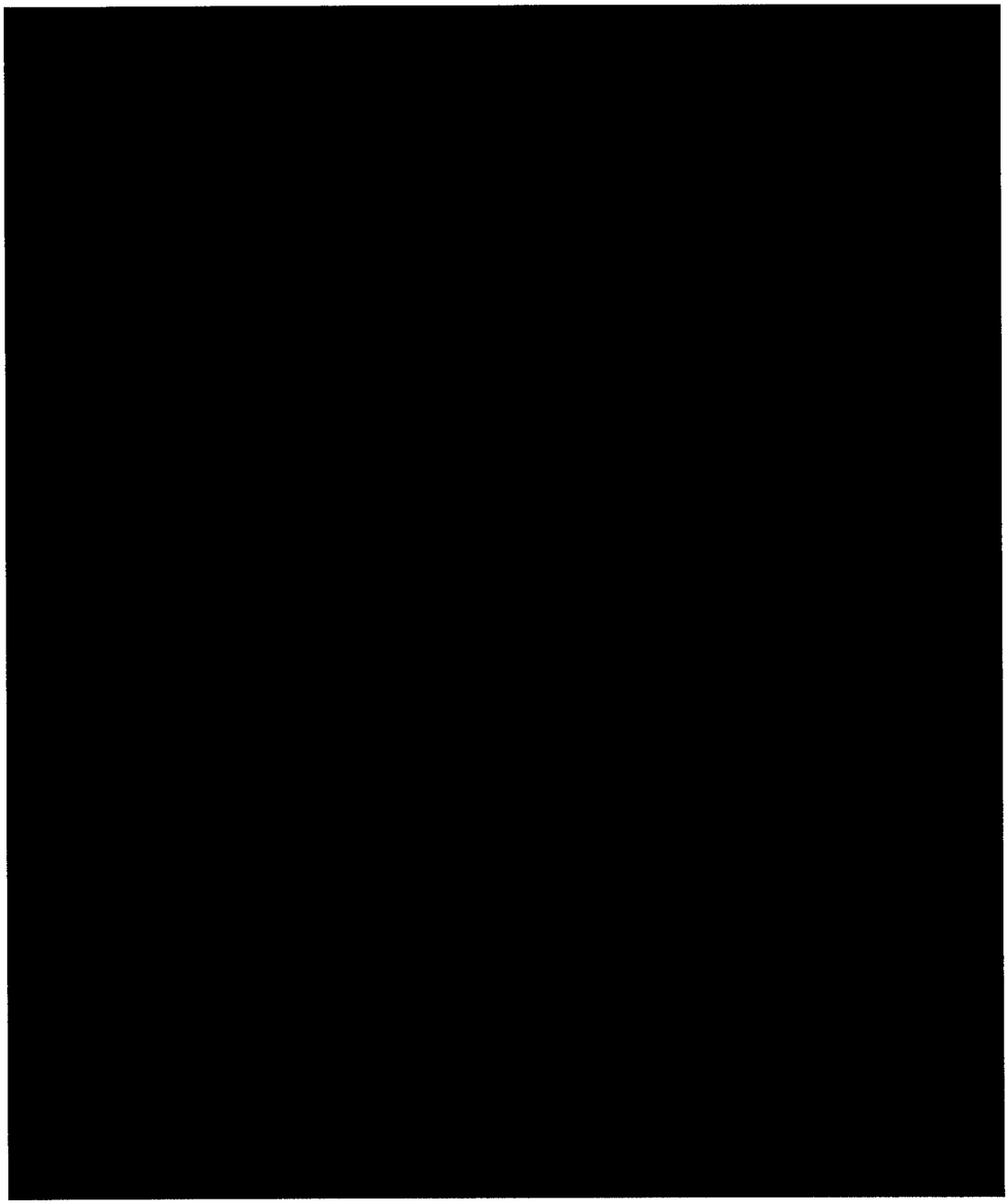

Figure 1-1. Recordings of hydrostatic pressure inside the device pictured on right.

This research was conducted to test the hypothesis that in individuals wearing a well-fitted anti-G garment, there are no important changes in volume of dependent regions during loss of consciousness resulting from acceleration stress. Furthermore, this work compares venous pooling patterns in G-LOC subjects to patterns seen during syncope in volunteers and patients subjected to orthostatic stress. We conducted the tilt/LBNP tests to establish what level of venous pooling was required to induce syncope in the absence of a hydrostatic component (other than 1 G) and to confirm that our equipment was sensitive enough to detect volume changes large enough to cause syncope.

Earlier studies that compared acceleration and orthostatic stress in humans have been limited to gradual onset (GOR) acceleration, where +Gz increased by 0.1G/sec or less. As a gravitational stimulus presented this slowly allows for reflexogenic mechanisms to become activated, this technique more closely mimics orthostatic stress and is appropriate for mechanistic studies. However aviators do not typically fly GOR profiles in high performance military aviation (onset rates are 6G/sec or greater for most maneuvers). Furthermore, with the exception of the T-37, aircrew flying fighter type aircraft wear anti-G garments during flight. In this study, we have constrained our methods to reflect actual flight conditions at the expense of applicability to a wider discussion of physiology.

Notes

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Chapter 2

Materials and Methods

Impedance Plethysmography

Subjects were instrumented with disposable EKG electrodes that were connected to a THRIM IV/SP 1 tetrapolar impedance plethysmograph (UFI, Morro Bay, CA) that defined calf, thigh and abdominal segment volumes. Passive electrodes were placed at the lateral maleolus, lateral aspect of the knee at mid-patellar level, hip (trochanteric prominence) and on the lateral 12th rib. Active electrodes were placed on the dorsal surface of the foot and in the axillary region and conveyed a 1 milliamp 50 KHz alternating current. The plethysmograph continuously reported resistance (r) and reactance (x) to the applied current across each measured segment. The Impedance vector (R) was calculated by the relationship

$$R = \sqrt{(r^2+x^2)}$$

The theory and validation of impedance plethysmography has been described previously.[1] Briefly, resistance of any conductor is directly related to its length (L) and an effective resistivity constant (p), and inversely related to its cross-sectional area (A) such that

$$R = pL/A$$

This can be expressed in terms of resistance and volume by multiplying the right side of the equation by L/L yielding:

$$R = pL^2/V$$

and rearranged such that

$$V = pL^2/R$$

The effective resistance constant (p) can be determined by measuring a baseline volume (V_o) and resistance (R_o). In practice, each subject was measured in the standing position and a geometric volume was calculated by treating the calf, thigh and abdominal segments as conical volumes where:

$$V_o = \Sigma[1/3*\pi*L(radius_1^2 + radius_1*radius_2 + radius_2^2)]$$

Measurements were taken every 3 cm and V_O was incrementally calculated with a computer program. After the subjects were instrumented, they stood outside the centrifuge gondola or for the tilt subjects, were tilted upright and R_O was measured. The effective resistivity constant in Ohm*cm was computed for each subject from the relation

$$p = R_o*V_o/L^2$$

Changes in volume ($\Delta V = V-V_o$) were continuously estimated from the impedance (R) of the segment to current flow.

Geddes and Hoff, showed that the relationship[2]

$$\Delta R/R_o = \Delta V/V_o$$

will hold for biological conductors if differences in the resistivity of blood and non-blood tissues are accounted for. This relation for analysis purposes was expressed as:

$$\Delta V = [(p*L^2/R) - V_o] * X$$

where X, the correction factor for the resistance change due to the movement of blood, is the ratio of the effective resistance of blood (150 Ω*cm) to p. Calculated volumes were expressed as changes from baseline, with negative values reflecting decreases in volume.

Centrifuge Experiments

Subjects used in this study were male members of the Armstrong Laboratory human-use centrifuge subject panel who had passed a Class II USAF flying physical. Experiments were carried out on the 6.1 meter radius human-use centrifuge, Armstrong Laboratory, Brooks AFB, TX. Seven G-LOC incidents are included in this data set, and were inadvertent, occurring during a human-use committee-approved protocol that was designed primarily to evaluate relaxed tolerance to rapid +Gz maneuvers. The suits were unpressurized because we were comparing the effects of increasing the amount of material coverage in the new Advanced Technology Anti-G Suit (ATAGS) to the coverage provided by the standard CSU 13-B/P anti-G suit. These seven G-LOC incidents were the only such events out of a much larger subject pool who underwent several hundred +5 Gz exposures. All ocurred in subjects wearing the CSU 13-B/P garment. All subjects were exposed to the same +5 Gz profile with suit pressurization turned on just prior to or following their unpressurized ride.

Subjects wore two sets of EKG leads and were observed at all times via closed-circuit color television. Each subject, the central observer and the medical monitor could stop the centrifuge at any time. Voice and video contact was maintained throughout the study. Subjects were instrumented with a cuff for the continuous monitoring of finger

arterial blood pressure using a Finapres monitoring system (Ohmeda model 2300, Madison, WI). A water column mounted on the subject's head referenced finger arterial pressure at heart level to eye level (ELBP). In practice, the changing weight of the water column was subtracted from the Finapres signal after the data was A/D converted, creating a hybrid signal. Mean arterial pressure was estimated by:

$$P_{mean} = P_{diast} + 1/3(P_{syst} - P_{diast})$$

The subjects were exposed to rapid onset (6-G/sec) head-to-foot inertial loads (+Gz) of 15 sec (maximum) duration. However, the exposures were immediately terminated whenever a subject experienced G-LOC. A data collection period always began with a +3 Gz exposure, followed by exposures in increasing +1 Gz increments. Each exposure was separated by a 2 min rest period. The subjects were instructed to remain relaxed during the exposures. All exposures presented here were to +5 Gz. All subjects were wearing a standard CSU-13B/P well-fitted anti-G suit. In the 7 G-LOC incidents, the subjects were taken to G with the pressurization inactivated. Continuous records of the +Gz exposures were made, with physiological measures being evaluated just prior to +Gz onset and at G-LOC.

Finapres, Impedance plethysmography, EKG and centrifuge accelerometer signals were recorded on analog tape (Racal Inst.) and A/D converted at 200 Hz with LabView software (National Instruments, Austin, TX). Digitized signals were analyzed using DaDISP waveform analysis software (DaDISP Development Corp, Cambridge, MA). Video Images of the centrifuge subjects were recorded on 3/4 inch tape and used to temporally establish G-LOC. Heart Rate (HR) was calculated from EKG R-R intervals.

Tilt/LBNP Studies

Results were obtained from two normal subjects and four patients who were shown to have reduced orthostatic tolerance. This study was approved by The Leeds Teaching Hospitals Research Ethics Committee. None of the four subjects showing reduced tolerance had an apparent organic cause for their syncopal attacks. The tests were conducted at The Leeds General Infirmary, UK, under the medical supervision of Dr. Roger Hainsworth. Each subject underwent a progressive series of orthostatic challenges. The tests began with a 30-min period at supine, followed by 30 minutes of upright posture (tilted 60°). The tests then progressed while still tilted, to 10 minutes of lower body negative pressure (LBNP) at -20 mm Hg, followed by 10 min at -40 mm Hg LBNP. The apparatus for applying LBNP enclosed the subjects' legs and pelvis to the level of the iliac crests and has been described previously.[3] Both upright tilt and LBNP were immediately terminated at the onset of presyncopal symptoms (a rapidly falling blood pressure or unconsciousness), and the subject returned to supine posture. The magnitude of the stimulus necessary to produce presyncope varied, with no subject going beyond 8 minutes of -40 mm Hg LBNP. As with the centrifuge subjects, each tilt subject was instrumented with Finapres, EKG and impedance plethysmography. ELBP in the Leeds subjects was simply calculated by subtracting 22 mm Hg (average 30 cm heart-eye distance) from the mean heart level blood pressure. Standing baseline segmental volume and impedance measurements were taken immediately upon the initial tilt to upright.

Experimental subjects in both the centrifuge and tilt/LBNP groups were briefed on the intent of the experiments and signed informed consent releases, including the right to withdraw from the experiments without prejudice at any time.

Notes

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Chapter 3

Results

Standing baseline segment volumes, heart rate (HR) and ELBP did not differ significantly between the groups of seven centrifuge subjects and six tilt/LBNP subjects (student's t test for a difference between means). Geometric volume measurements were made with both groups upright. The baseline HR and ELBP measurements were made in the tilt subjects, immediately after the 60° upright tilt. For the centrifuge subjects, measurements were made with them standing, just prior to climbing into the centrifuge gondola. These values are presented in Table 3-1 and in Figures 3-1 and 3-2.

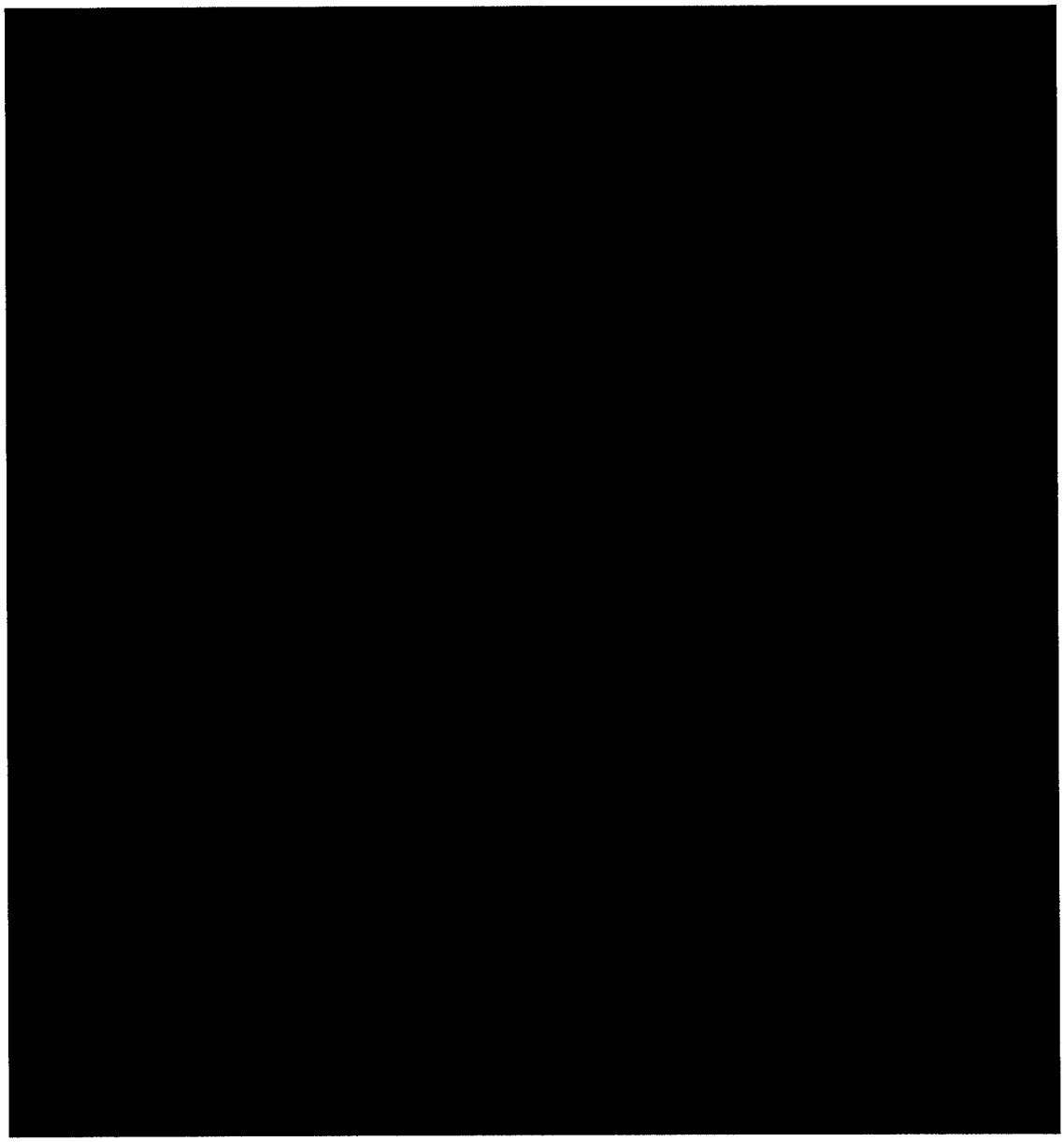

Figure 3-1. Comparison of geometric volume (this figure) and HR and ELBP (Figure 3-2) baseline values for the centrifuge and tilt subjects prior to exposure to either the +Gz or the tilt/LBNP stimulus.

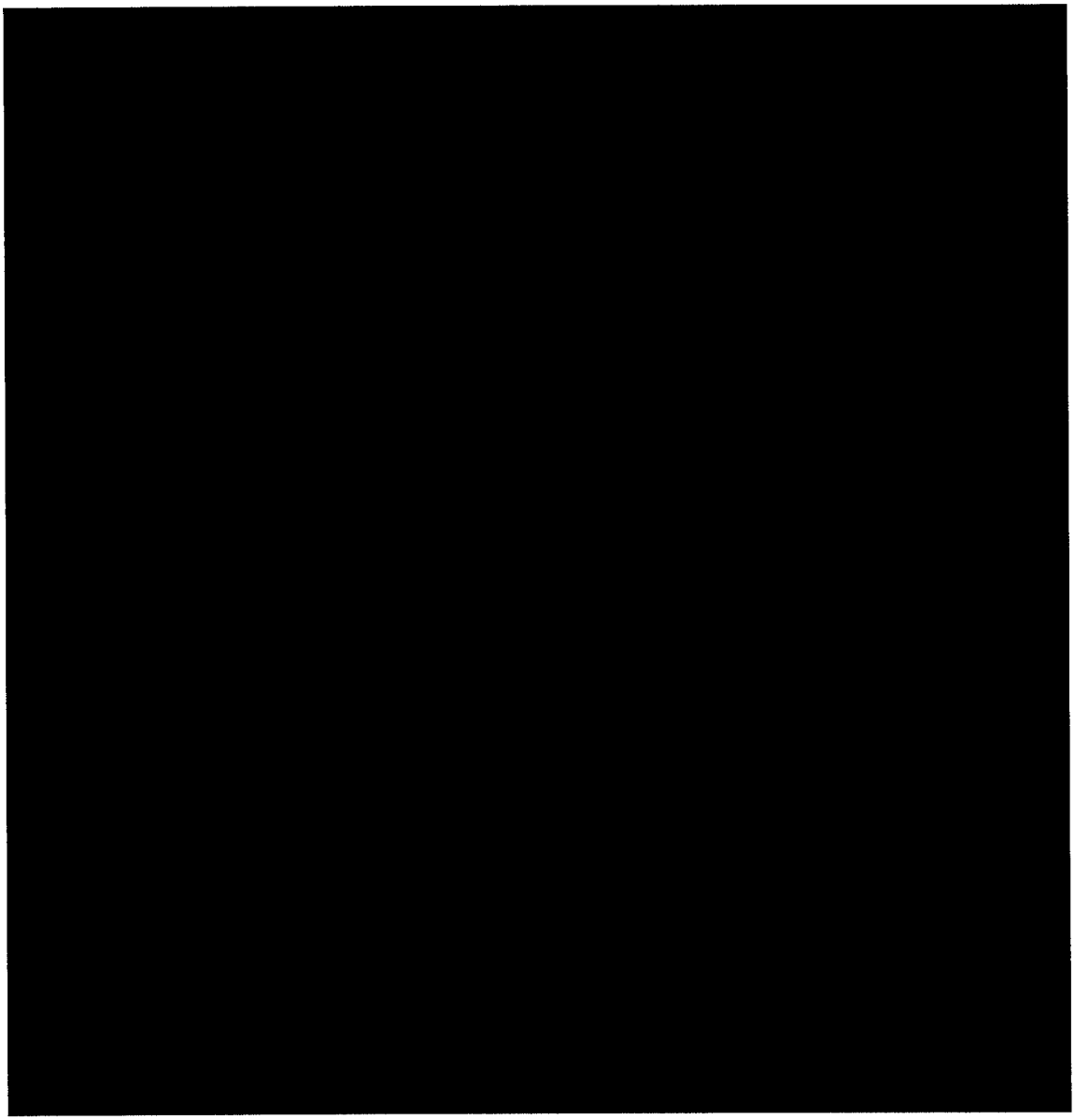

Figure 3-2. Comparison of geometric volume (Figure 3-1) and HR and ELBP (this figure) baseline values for the centrifuge and tilt subjects prior to exposure to either the +Gz or the tilt/LBNP stimulus.

Centrifuge Experiments

All G-LOC incidents included in this data set occurred during a +5 Gz exposure, at a mean of 5.3 (± 0.42; sem) sec after the acceleration plateau was reached. Records from two subjects showing acceleration in +Gz units; eye-level blood pressure in mm Hg; calf, thigh and abdominal segment blood volume in ml changes from standing baseline values (set at zero) are presented in Figure 3-3. Upward deflections of the volume traces reflect increases in blood volume, with downward movement reflecting decreases. Whenever a subject experienced G-LOC, the exposure was terminated. In Figure 3-3, both subjects experienced G-LOC just prior to the point of +Gz decrease. We emphasize that the subjects in this experiment were wearing well-fitted anti-G suits with the pressurization inactivated, and all tried to remain relaxed during the +Gz exposure. Nevertheless, some subjects showed an anticipatory muscle contraction prior to +Gz onset that resulted in a small volume decrease within a limb segment (see subject 4). Immediately prior to +Gz onset, mean values for heart rate (HR) and mean ELBP were 96.1 (± 4.5) bpm and 85.5 (± 5.34) mm Hg, respectively. Onset of +5 Gz produced an average fall in mean ELBP of 105.1 (± 15.5) mm Hg (measured at G-LOC). Heart rate increased by an average of 15.5 (± 3.9) bpm in response to the +5 Gz stimulus. No bradycardic responses were observed before, during or after G-LOC incidents. Mean changes from baseline in blood volume in calf, thigh and abdominal segments for the 7 subjects are presented in Table 3-1. Blood volume decreased an average of 14.9 (± 22.1) ml in the calf segment; increased an average of 64.1 (± 7.9) ml in the thigh segment, and decreased an average of 80.1 (± 29.7) ml in the abdominal segment. However, the mean net change in volume of the three com

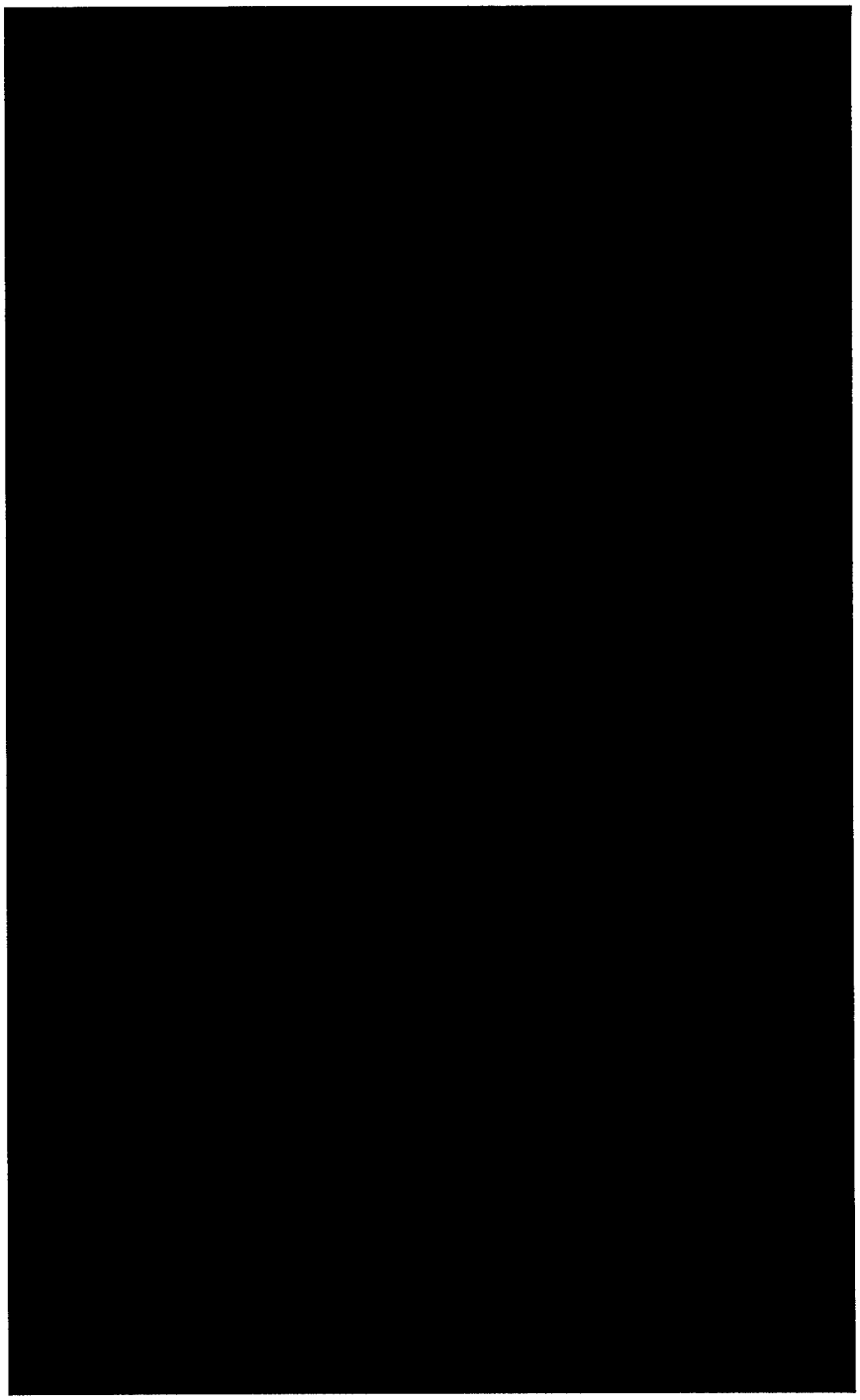

Figure 3-3. Physiological recordings of two relaxed subjects undergoing a +5 Gz exposure. EKG is shown in the bottom panel: R-R interval was used to compute HR. Time (in sec) is depicted on the abscissa.

bined dependent regions was extremely small (31 ±19.9 ml), and not significantly different from zero. Thus, a redistribution of blood volume was occurring between the compartments, but this did not reflect significant shifting of blood volume into dependent regions.

These responses were compared to +Gz exposures in which the anti-G suit pressurization was activated in the same subjects. Under these conditions, none of the subjects experienced G-LOC. The venous pooling patterns were also different. Calf volume decreased a by a mean of 5 (± 6.9) ml; with thigh and abdominal volume decreasing by means of 329 (± 96.2) and 246 (± 65.7) ml, respectively. This was a decrease in volume of 580 (± 56.3) ml for the three combined segments. Mean ELBP fell an average of 73 (± 7.8) mm Hg with +Gz onset. Figure 3-4 presents records of two subjects experiencing a +5 Gz load with the anti-G suit pressure activated. Shown are acceleration in +Gz units, anti-G suit pressure in psi, eye-level blood pressure (ELBP) in mm Hg, calf, thigh and abdominal segment blood volume in ml changes from standing baseline values (set at zero). None of the subjects experiencing G-LOC on an unpressurized trial lost consciousness at the same level of +Gz stress with a pressurized anti-G suit. Compare pulse pressure under G here with that in Figure 3-3. Although volumes and ELBP were not significantly different from the G-LOC exposures, they were great enough to prevent syncope.

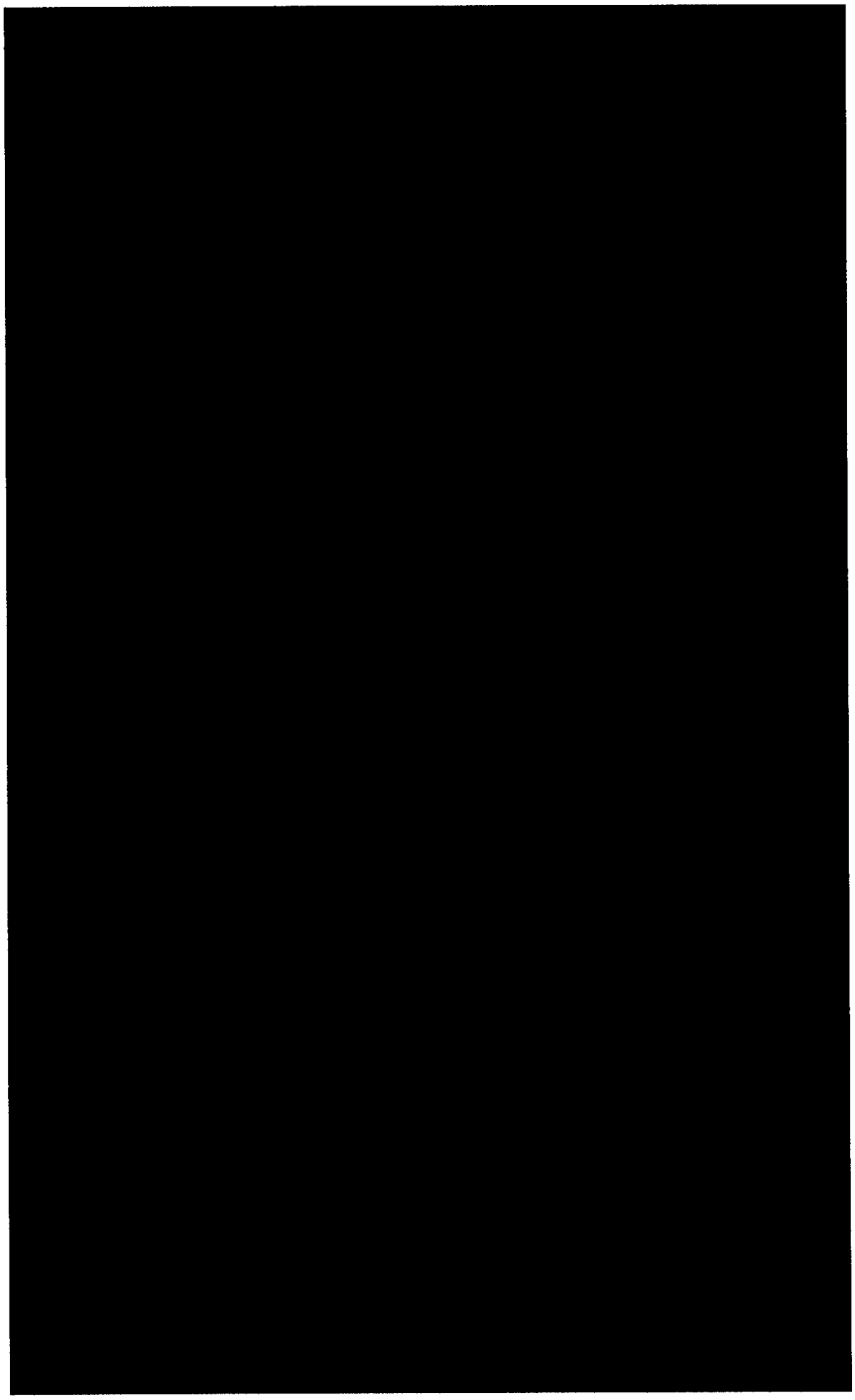

Figure 3-4. Recordings of two relaxed subjects undergoing a +5 Gz exposure with their CSU-13B/P anti-G suits pressurized using a standard ALAR anti-G suit inflation valve.

Tilt/LBNP Studies

We exposed six subjects to orthostatic challenge consisting of 30-min head up tilt, 10 min of -20 mm Hg LBNP, and then -40 mm Hg LBNP presented sequentially. Each subject was taken to a presyncopal end point, that varied temporally, based on the degree of orthostatic intolerance present. The mean end point was 3.5 (±2.5) min of -20 LBNP. Records from two subjects are presented in Figure 3-5. Shown are calf, thigh and abdominal segment volumes in ml change from baseline and Finapres heart level arterial pressure in mm Hg. Only 60° upright baseline and the final level of orthostatic stress that produced presyncopal symptoms are shown. In all subjects, the increase in segmental blood volume followed immediately after each progressive increase in orthostatic stress, and then stabilized. Upon return to supine at presyncope, blood volume decreases were always seen in calf and thigh segments and in the abdominal segments of subjects showing a previous increase in this region. However, during the period of observation, the decreases did not return to baseline, usually retaining 20–30% more volume. This was probably due to loss of plasma into the interstitium.

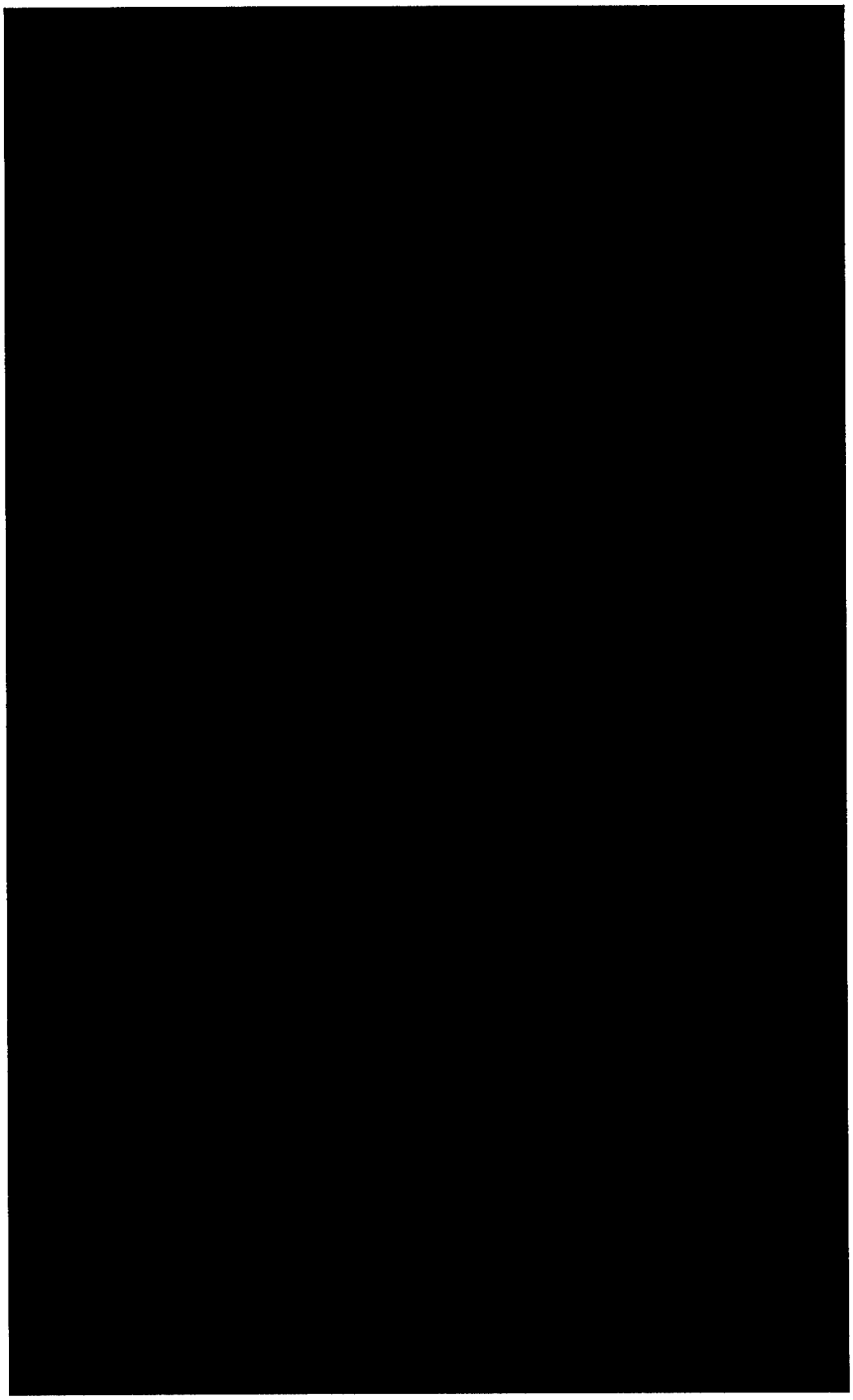

Figure 3-5. Recordings of two of the tilt/LBNP subjects undergoing progressive orthostatic stress. Time (in sec) is not continuous between the baseline recording and the final segment shown.

Upon tilt to 60° upright, baseline HR and ELBP were 93 (±5.6) bpm and 72.2 (±3.1) mm Hg, respectively. At presyncopy, mean ELBP declined 45.6 (±7.7) mm Hg and HR showed a mean increase of 15.8 (±12.2) bpm. At the presyncopal endpoint, segmental blood volumes increased by means of 111 (±30.2) ml in the calf, 672 (±150.8) ml in the thigh, and 239 (±88.8) ml in the abdominal region. This was a total net change of 1022 (±269.8) ml for the combined segments. Changes in all three segments were significantly different than the mean segmental volume changes seen in centrifuge subjects at G-LOC endpoints (Student's t test for the difference between means, $p \leq 0.005$). A graphic comparison of data from both the centrifuge and tilt studies is presented in Figures 3-6 and 3-7.

Table 3-1. Results

	Leeds Patients (n=6)		Centrifuge Subjects (n=7)	
	Baseline	**Change at presyncope**	**Baseline**	**Change at G-LOC**
Volumes (ml)				
calf	3279 ±229	+111 ±30.2	3628 ±168	-14.9 ±22.1
thigh	9707 ±1131	+672 ±150.8	8288 ±527	+64.1 ±7.9
abdomen	14930 ±1467	+239 ±88.8	15325 ±302	-80.2 ±29.6
ELBP (mm Hg)	72.2 ±3.11	-45.6 ±7.7	85.5 ±5.3	-105.1 ±15.5
HR (bpm)	93 ±5.6	+15.8 ±12.2	96.1 ±4.5	+15.5 ±3.9

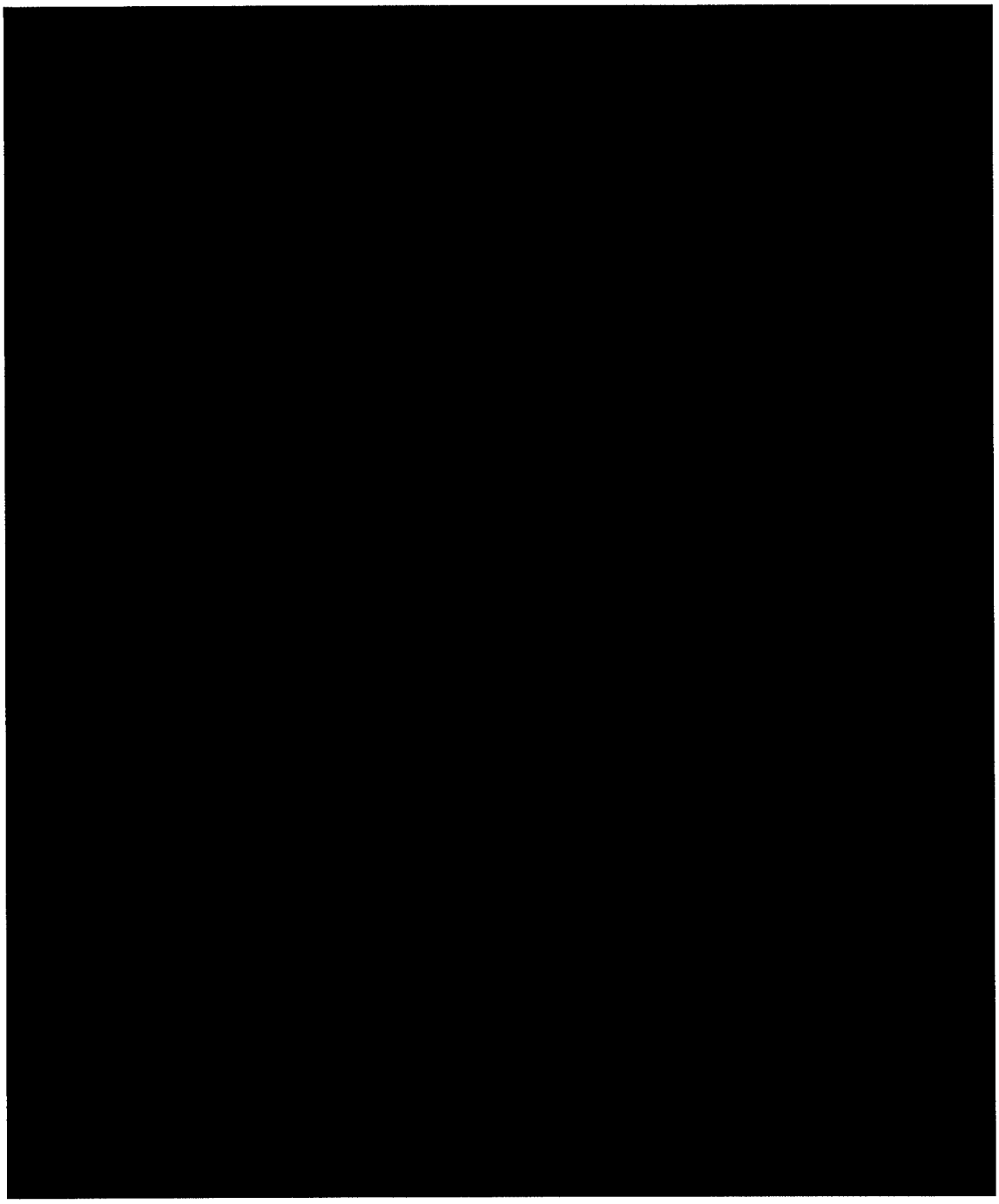

Figure 3-6. Comparison of venous pooling (this figure) and HR and ELBP (Figure 3-7) data between G-LOC and presyncope in the two experimental groups. Differences in changes from baseline seen in HR and ELBP were not significant.

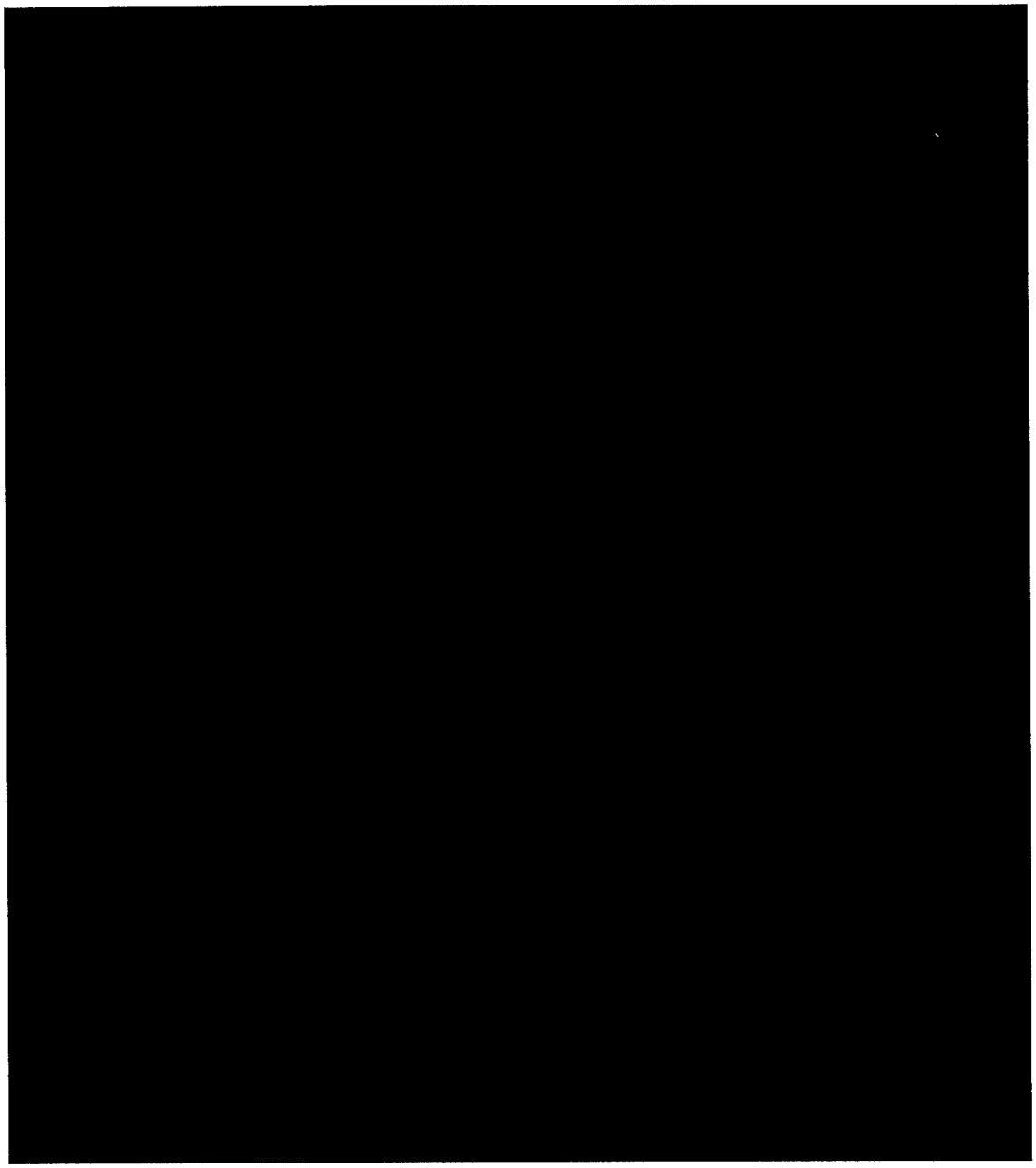

Figure 3-7. Comparison of venous pooling (Figure 3-6) and HR and ELBP (this figure) data between G-LOC and presyncope in the two experimental groups. Differences in changes from baseline seen in HR and ELBP were not significant.

Chapter 4

Discussion

All methods employed in this investigation were noninvasive. Previous work has validated the use of Finapres under acceleration against the behavior of an arterial catheter.[1] In general, Finapres correlated well with arterial measurements (correlation above 0.8), but tended to underestimate systolic and diastolic pressures. This tendency however, does not impact the essential nature of our findings, as it would decrease an already insignificant difference between centrifuge and tilt subjects. This method of calculating ELBP was idealistic, in that actual pressures may not have fallen to as low a level indicated by the hybrid signal (heart level pressure minus the weight of the fluid column). Once arterial pressures became sub-atmospheric, non-tethered neck vessels would tend to collapse, breaking the hydrostatic column, and preventing further decreases.

Although impedance plethysmography has been extensively validated at 1 +Gz, the device used in this study was not validated under acceleration, as results from all other acceptable techniques are either invasive or influenced by centrifugation themselves.[2] We did however test the performance of the device in the centrifuge by connecting it to known resistances of 10, 20 100 and 200 Ω and then monitoring its voltage output through a range of +Gz loads. The circuitry appeared unaffected by acceleration. A

possible source of error may have been introduced if acceleration deformed the calf, thigh and abdominal segments of our subjects away from a conical geometry. In the case of calf and thigh regions that are entirely circumferentially covered by the anti-G garments we believe this was unlikely, as the fabric is strong enough to function as an exoskeleton. We are less confident that the abdominal region is not deformed at G.

This work has shown that loss of consciousness caused by acceleration stress is not accompanied by increased venous pooling in subjects wearing a well fitting anti-G suit, even when it is not pressurized. In this study, venous pooling during acceleration stress was prevented purely as a result of wearing the anti-G garments, even during G-LOC. Loss of consciousness was not seen during trials in which anti-G suit pressurization was activated. Krutz et al. demonstrated that inflation of the anti-G suit "milks" a portion of the initial volume existing in the capacitance vessels prior to +Gz onset.[3] In their study, volumes in calf, thigh and abdominal segments were decreased between 5 and 10% after the G-valve activated, and tended to remain depressed for the duration of the exposure. Our results are in agreement with these findings, with volume decreasing in all three segments, displacing around 1/2 litter. Assuming an identical process was occurring in the leg not measured, this value approaches a liter. Furthermore, with the anti-G suit pressure activated, mean ELBP declined an average of 32 mm Hg less than in the unpressurized G-LOC trials, with pulse pressure declining very little compared to the G-LOC exposures. This was due to both increases in peripheral resistance provided by the inflated anti-G suit and to a larger circulating volume of blood. This work confirms earlier conclusions that G-LOC resulting from rapid onset acceleration is due primarily to

hydrostatic effects, which can be offset by the action of garments that can increase resistance to flow and venous return.[4]

This pattern differs significantly from that of syncope resulting from orthostatic stress induced by head up tilt and LBNP. The results from the six subjects show pronounced increases in blood volume occurring in the calf, thigh and abdominal regions at presyncopal endpoints. There was no difference between results obtained from subjects with normal and those with reduced orthostatic tolerance except that the less tolerant subjects developed symptoms earlier.

It is interesting to note that the rapid fall in mean blood pressure and pulse pressure at presyncope in the tilt/LBNP group was not accompanied by further increases in venous pooling, suggesting the absence of venodilatation. This possibility is lent credence by the work of Epstein et al., who studied forearm venous and arterial tone in patients experiencing vasovagal syncope.[5] They found the large decreases in forearm vascular resistance during the abrupt fall in arterial pressure were accompanied by venoconstriction rather than venodilitation. They concluded that since central venous pressure did not change prior to or during syncope, it was unlikely that dependent capacitance vessels were dilating. The present work provides evidence that the circulatory events that immediately precede syncope involve a changing arterial resistance in the face of a relatively constant volume in the dependent veins.

In Figure 3-5, pulse pressure and mean pressure were increased upon tilt to supine, but to much lower levels than existed during standing baseline. As core blood volume was instantaneously increased with supine tilt, the pressures should have shown a more robust increase. This behavior is in sharp contrast to seen in the centrifuge subjects. At

G-LOC, the centrifuge was rapidly stopped and arterial and pulse pressures were restored, but always to higher levels than prior to the exposure to increased G (see Figure 3-3). As this was not accompanied by changes in segmental blood volume, it suggests the increases were due almost entirely to an increase in vascular resistance. Wood et al., reporting essentially the same finding in 1946, correctly reasoned that blood pressure recovery seen after G-onset would not be possible if the initial fall in pressure were the result of venous pooling. [6]

Thus, G-LOC following rapid onset to +5Gz in subjects wearing anti-G suits and orthostatic presyncopal mechanisms appear to differ in two important ways. During presyncope, the resistance vessels are dilating, whereas in G-LOC they appear to be actively constricting. Secondly, increased venous pooling did not occur as ELBP fell with +Gz onset, while the orthostatically stressed subjects showed simultaneous decreases in ELBP and increases in calf, thigh and abdominal blood volume. This may be due to a failure of orthostatic stress in general, and LBNP in particular to trigger carotid baroreflexes. Vukasovic et al., concluded after studying the effects of LBNP on carotid baroreceptor responses that there is no interaction between carotid baroreflexes and the reflexes elicited by LBNP.[7]

These differences would tend to confirm that LBNP effects are not sufficiently similar in nature to the acceleration environment seen in military aviation to serve as a 1G surrogate research tool for studying the effects of +Gz. If anti-G suits were not worn by the centrifuge subjects, significant venous pooling may have occurred in response to +Gz loads. However, the intent of this study was to examine G-LOC mechanisms under conditions relevant to operational military flying.

Furthermore, these results may have been more compelling, if the same group of subjects had experienced both the acceleration and the tilt/LBNP conditions, allowing us to use the more sensitive paired measures design in our analysis. This was geographically impossible, however, requiring us to assume that both groups were random samples of the same population. This assumption is supported by the lack of significant differences between the two groups in initial baseline measures of geometric volume, mean arterial pressure and heart rate.

Notes

[1] McKenzie, I. Non–invasive blood pressure measurement under G. *SAFE J.* 1991; 2126–30.

[2] Geddes, L.; Hoff, H. The measurement of physiologic events by electrical impedance. *Am. J. Med. Electron.* 1964; 1(1): 1–15.

[3] Krutz, R.W. Jr.; Burton, R.R.; Forster, E.M. Physiologic correlates of protection afforded by anti–G suits. *Aviat. Space Environ. Med.* 1990; 61:106–111.

[4] Howard, P. The physiology of positive acceleration. in: *A Textbook of Aviation Physiology*, J.A. Gilles ed. 1965; pp. 551–687. Pergamon Press, London.

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[5] Epstein, S.E.; Stampfer, M.; Beiser, G.D. Role of capacitance and resistance vessels in vasovagal syncope. 1968; *Circulation* 37:524–533.

[6] Wood, E.H.; Lamber, E.H.; Baldes, E.J.; Code, C.F. Effects of acceleration in relation to aviation. 1946 *Fed Proc* 5: 327–343.

[7] Vukasovic, J.L.; Al–Timman, A.; Hainsworth, R. The effects of lower body negative pressure on baroreceptor responses in humans. 1990; *Experimental Physiol* (75): 81–93.

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