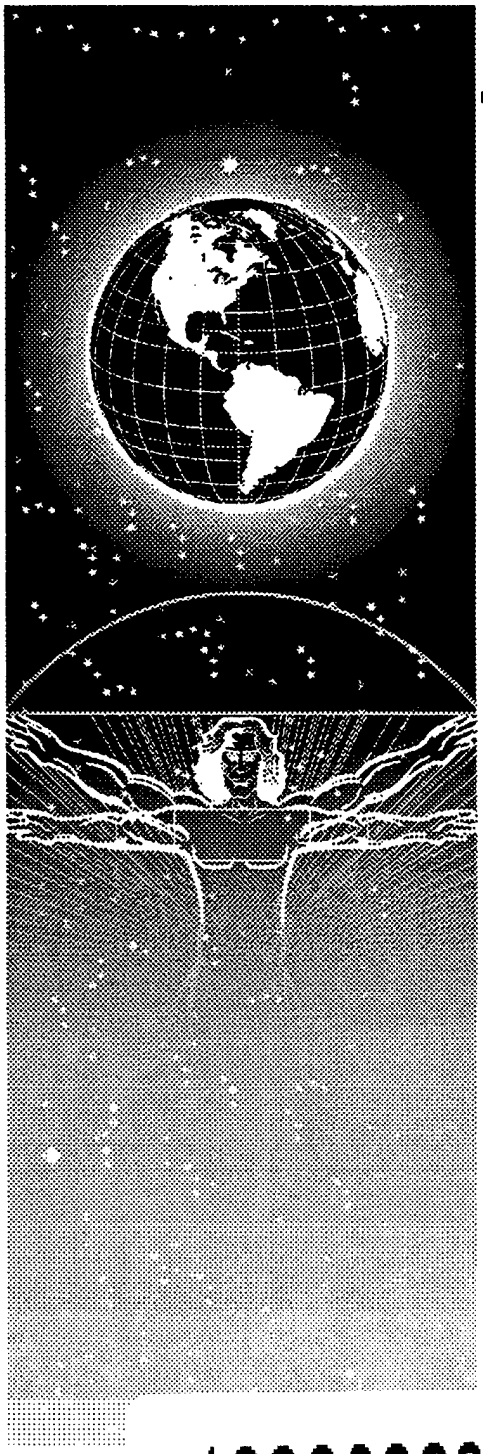
AL/CF-TR-1997-0159



UNITED STATES AIR FORCE
ARMSTRONG LABORATORY

MIDDLE CEREBRAL ARTERY BLOOD FLOW VELOCITY AFTER EXPOSURE TO SUSTAINED +Gz

Manaswee Kovitaya, M.D., M.S.

DEPARTMENT OF COMMUNITY MEDICINE
WRIGHT STATE UNIVERSITY
Dayton OH 45324

Lloyd D. Tripp, Jr.

SYSTEMS RESEARCH LABORATORIES, INC
2800 Indian Ripple Road
Dayton OH 45440

Tamara L. Chelette Ph.D.

CREW SYSTEMS DIRECTORATE
ARMSTRONG LABORATORY
WRIGHT-PATTERSON AFB OH 45433-7008

June 1997

Interim Report for the Period January 1996 to June 1997

Crew Systems Directorate
Biodynamics and
Biocommunications Division
Wright-Patterson AFB OH
45433-7901

NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise, as in any manner, licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use or sell any patented invention that may in any way be related thereto.

Please do not request copies of this report from the Armstrong Laboratory. Additional copies may be purchased from:

National Technical Information Service
5285 Port Royal Road
Springfield VA 22161

Federal Government agencies and their contractors registered with Defense Technical Information Center should direct requests for copies of this report to:

Defense Technical Information Center
8725 John J. Kingman Rd., STE 0944
Ft Belvoir VA 22060-6218

TECHNICAL REVIEW AND APPROVAL

AL/CF-TR-1997- 0159

The voluntary informed consent of the subjects used in this research was obtained as required by Air Force Instruction 40-402.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

Lt Col, Deputy

THOMAS J. MOORE, Chief
Biodynamics and Biocommunications Division
Crew Systems Directorate
Armstrong Laboratory

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1, AGENCY USE ONLY (Leave Blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	June 1997	Interim Report (January 1996 - June 1997)

4. TITLE AND SUBTITLE

Middle Cerebral Artery Blood Flow Velocity After Exposure to Sustained +Gz

5. FUNDING NUMBERS

C: F41624-95-C-6014
PE: 62202F
PR: 7184
TA: 45
WU: 01

6. AUTHOR(S)

Manaswee Kovitaya, Lloyd D. Tripp, Jr.; and Tamara L. Chelette

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Wright State University
Dayton, Ohio 45324

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

Armstrong Laboratory, Crew Systems Directorate
Biodynamics and Biocommunications Division
Human Systems Center
Air Force Materiel Command
Wright-Patterson AFB OH 45433-7008

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

AL/CF-TR-1997-0159

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

Anecdotal information has been available for many years that G training over time increases a human's ability to tolerate G. However, little data exist to corroborate the observation. The main thrust of this study was to quantify the accumulative physiological effects of +Gz exposure on cerebral blood flow using transcranial Doppler. A total of six male and six female subjects participated in this study. The subjects experienced numerous G exposures ranging from 2.5 to 5.2 G during three days of centrifuge training. Total time at G >1 was 5.3 minutes. Changes in middle cerebral artery blood flow velocity during a squat-stand orthostatic challenge test before and after G exposures and then within seven days after each day of G exposure were observed. No significant changes in middle cerebral artery blood flow velocity were found. Further studies with more subjects, higher G levels, and more repeated G exposures of longer duration are suggested.

14. SUBJECT TERMS

Transcranial Doppler Sonography, High G, Squat-Stand, Middle Cerebral Artery, Pulsatility Index, Blood Flow Velocity

15. NUMBER OF PAGES

38

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UNLIMITED

THIS PAGE LEFT BLANK INTENTIONALLY

PREFACE

Technical support and equipment for this research were provided by the Combined Stress Branch, Biodynamics and Biocommunications Division, Crew Systsems Directorate, Armstrong Laboratory, Wright-Patterson AFB, Ohio.

The authors would like to acknowledge and thank Robert Esken, Jr., Col Raymond Ten Eyck, Steve Bolia and Rudolph A. Cartwright for their invaluable assistance with this project.

We would also like to thank the members of the Sustained Acceleration Test Panel for their efforts and patience with this program.

THIS PAGE LEFT BLANK INTENTIONALLY

TABLE OF CONTENTS

Page

INTRODUCTION 1

BACKGROUND 1

Transcranial Doppler 1

Cerebral Hemodynamics 2

Cerebral Artery Blood Flow Velocity 3

Gender Difference 4

Normal Velocity 4

Indices of Pulsatility 4

Normal Pulsatility 6

Cerebrovascular Autoregulation 6

METHODS 7

Subjects 7

Equipment and Facilities 8

G Exposure 8

Dynamic Environment Simulator 8

Centrifuge Run 9

Squat-Stand Test 9

Laboratory Setup 9

Experimental Procedure 10

Data Collection 11

Data Analysis 11

TABLE OF CONTENTS (CONTINUED)

Page

RESULTS 12

VMCA-Squat 12

VMCA-Stand 14

Percent Change of VMCA 16

Pulsatility Index-Squat 17

Pulsatility Index-Stand 19

Percent Change of Pulsatility Index 21

DISCUSSION 22

CONCLUSION 25

REFERENCES 26

LIST OF TABLES

Table Page

1. Subjects' Characteristics 7

2. First Three Days of Centrifuge Indoctrination of the Subjects 9

3. Means and Standard Deviations of VMCA-Squat (cm/s) 12

4. Summary of ANOVA for VMCA-Squat 13

5. Means and Standard Deviations of VMCA-Stand (cm/s) 14

6. Summary of ANOVA for VMCA-Stand 15

7. Means and Standard Deviations of Percent Change of VMCA 16

8. Summary of ANOVA for Percent Change of VMCA 16

9. Means and Standard Deviations of PI-Squat 17

10. Summary of ANOVA for PI-Squat 18

11. Means and Standard Deviations of PI-Stand 19

12. Summary of ANOVA for PI-Stand 20

13. Means and Standard Deviations of Percent Change of PI 21

14. Summary of ANOVA for Percent Change of PI 22

LIST OF FIGURES

Figure Page

1. Diagram of the Zygomatic Arch Area from which Doppler Transducer Signals are Obtained.... 2

2. Dynamic Environment Simulator.... 8

3. Subject in (a) Squatting Posture and (b) Standing Posture.... 10

4. Screen Illustrates Subject's Posture (Right Side View) and TCD data.... 11

5. Means of VMCA-Squat.... 12

6. VMCA-Squat of Female Group and Male Group.... 13

7. Means of VMCA-Stand.... 14

8. VMCA-Stand of Female Group and Male Group.... 15

9. Means of Percent Change of VMCA.... 16

10. Percent Change of VMCA of Female Group and Male Group.... 17

11. Means of PI-Squat.... 18

12. PI-Squat of Female Group and Male Group.... 18

13. Means of PI-Stand.... 19

14. PI-Stand of Female Group and Male Group.... 20

15. Means of Percent Change of PI.... 21

16. Percent Change of PI of Female Group and Male Group.... 22

INTRODUCTION

Historically, high performance aircraft pilots and experienced centrifuge test subjects have reported a progressive increase in Gravity (G) tolerance when exposed to gravitational forces >1 G several days in a row. The aerospace medical community has named this phenomenon the G training effect and has incorporated G tolerance training into all acceleration research protocols to abate any G intolerance which may be attributed to this effect. Conversely, anecdotal evidence suggests that G layoff may cause a decrease in the G training effect. Although 50 years of anecdotal evidence describes the G training phenomenon, there are no quantitative data that characterize the physiological mechanisms of the G training effect.

The G training effect is an operational issue which begs addressing. Current Air Combat Command policy for pilots who have been out of the cockpit for an extended period of time is to perform an undefined number of G warm-up maneuvers prior to using full +9 Gz command authority during air-to-air combat maneuvering. With the downsizing of the active duty, full-time Air Force and the increased reliance on Air Force Reserve (part-time) components to fulfill mission requirements, the need for defining the physiological mechanisms that drive G tolerance and the time course in which these changes occur becomes an issue of flying safety from an operational standpoint.

It has been suggested that the G training effect is a conditioned cardiovascular response which may be driven by changes in venous compliance; i.e., increases in peripheral vascular resistance. Another theory is that these effects may be the result of a change in baroreceptor sensitivity secondary to changes in aortic and carotid blood pressure during +Gz acceleration. Both the venous compliance issues and baroreceptor response mechanisms have been investigated by Convertino and Tripp (13); a third issue concerning the cerebral hemodynamic response to G training effect remains.

The main thrust of this investigation was to quantify the accumulative physiological effects of G training on cerebral hemodynamics using transcranial Doppler (TCD). This investigation measured middle cerebral blood flow velocities during a squat-stand orthostatic challenge test at 1 G within seven days after centrifuge exposure. Given the importance of the increasing visibility of women in the modern, high performance, combat aircraft operation, the secondary purpose of this study was to detect any sex-based differences in cerebrovascular system response after G exposure. This study is an add-on experiment to an existing indoctrination protocol currently approved by the Armstrong Laboratory Human Use Review Committee.

BACKGROUND

Transcranial Doppler

For many years, it had been assumed that the cranium was largely impenetrable by ultrasound, making interrogation of the intracranial circulation seem impossible. Aaslid et al. (3) in 1982, however, demonstrated this assumption to be incorrect by describing a noninvasive method of

obtaining the blood flow velocities in the major basal cerebral arteries using 2-MHz pulsed Doppler ultrasound. The technique described subsequently became known as TCD sonography.

Since 1982, the cerebral oximetry technique has been used clinically in neurology and neurosurgery to assess blood flow velocities of the intracranial arteries (9). TCD sonography is used for diagnosis and monitoring of vasospasm in the middle cerebral artery (MCA) after subarachnoid hemorrhage (2), monitoring of the MCA blood flow velocity during carotid endarterectomy (44), and cardiopulmonary bypass (36). In aerospace medicine, the use of TCD has included studies of cerebral blood during +Gz acceleration (33, 50), lower-body negative pressure (8, 16), and correlation with space adaptation syndrome (5).

The TCD technique is based upon measurement of the Doppler frequency shift of reflected ultrasonic waves after the strike moving red blood cell (9). Each of the cerebral arteries has its own characteristic TCD waveform, depth, location, and flow direction. The Doppler spectra obtained from the MCA are characterized by insonation depth of 30 to 60 mm, flow directed toward the transducer, and mean flow velocities of 55 ± 12 cm/sec (39).

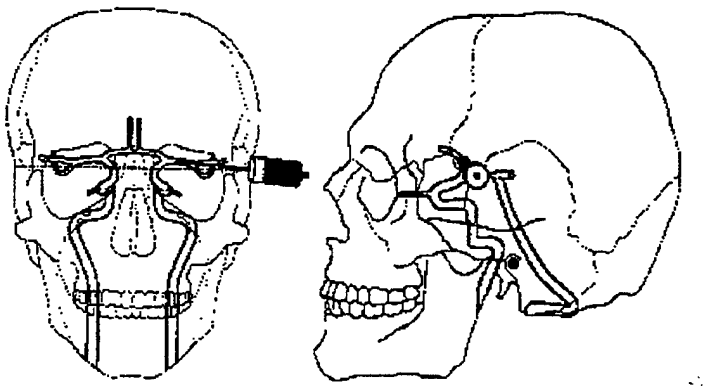


Figure 1. Diagram of the Zygomatic Arch Area from which Doppler Transducer Signals are Obtained

Figure 1 illustrates the position of the TCD probe against the zygomatic arch from 1 to 5 cm in front of the ear. An ultrasonic window in which the signal has maximum amplitude can be found by searching this region.

Cerebral Hemodynamics

The mechanics of flow in a vascular bed are usually simplified to three concepts:

(1) Perfusion pressure: the pressure differential between the inflow side and the outflow side.

(2) The resistance to flow.

(3) The resultant flow volume.

In the cerebral circulation, the perfusion pressure is the difference between the arterial blood pressure (ABP) and the intracranial pressure (ICP) because the venous pressure inside the dura cannot possibly be lower than the ICP as a result of the collapsible walls of the veins. The venous sinuses do not collapse completely because of their stiff walls. This is of little help to the intradural part of the cerebral circulation, and only results in a large energy loss in the vein bridges leading into the sinuses when the ICP is significantly elevated above the venous pressure in the jugular veins.

The concept of cerebrovascular resistance (CVR) is sometimes thought of as borrowed from electrical theory (Ohm's Law), but the basis for this concept is Poiseuille's Law for steady laminar flow in long cylindrical tubes. According to this concept, cerebral blood flow (CBF) at any time should be given by:

$$CBF = (ABP - ICP) / CVR = CPP / CVR$$

Assuming constant CVR (no autoregulation or other factor changing the caliber of the resistance vessels), flow and pressure are perfectly proportional. For changes in cerebral perfusion pressure (CPP) so short-lasting that the autoregulation does not react, this theory assumes that the relationship between pressure and flow would follow exactly the appropriate thin line in the graph. A 20 percent drop in pressure would lead to a 20 percent drop in flow. This is the dynamic pressure-flow relationship. In contrast, the static pressure-flow relationship is the familiar autoregulation curve (35). This allows vascular resistance to change in order to compensate for variations in perfusion pressure

Cerebral Artery Blood Flow Velocity

The human brain receives blood through defined cerebral artery systems; each system consists of a cerebral artery with its branches extending down through the level of the capillaries. When investigating the cerebral circulation, we examine the behavior of the blood flow at certain points along these transmission lines. However, the various methods examine the blood flow at different levels. Electromagnetic flow-meter measures the blood flow in precerebral arteries in the neck, in highly-selected cases also in the basal cerebral arteries (41, 42, 43), while TCD records the blood velocities in precerebral neck arteries, as well as in the basal cerebral arteries and their main branches.

In relating blood velocity to blood flow, some expressions need clarification. The blood flow in an artery is expressed as volume units per time unit. Accordingly, the total cerebral blood flow (CBF) should be the blood flow in all inflow brain arteries combined. However, because of the widespread use of indicator methods, the term CBF has usually come to denote the amount of

blood perfusing 100 g of brain tissue per minute. In relating cerebral artery blood velocity to CBF one must, therefore, clearly distinguish between when blood flow expresses the perfusion per 100 g of brain tissue per minute and when it states the blood flow in defined cerebral artery system units, as measured with electromagnetic flow meters.

Gender Difference

Women have higher hemispheric CBF than men (30, 48). This small difference in CBF is reflected in a 3 to 5 percent higher middle cerebral artery velocity (28, 34). The difference in CBF and velocity has been explained on the basis of a lower hematocrit in premenopausal women (28). The gender difference in velocity diminished with age in the study of Vriens et al. (52) which is consistent with this explanation. However, both Adam et al. (4) and Brouwers et al. (10) reported higher velocities in young females than in young males at a time when no hematocrit difference exists.

In the latter study (10), young females had slightly higher resting pCO_2, but such a pCO_2 difference was not found by Vriens et al. (52) in adults. The cause of this small gender difference in velocity requires further investigation.

Normal Velocity

Normal middle cerebral artery mean velocity (VMCA) varied from 41 ± 7 to 94 ± 10 cm/sec. However, most of this variation can be explained by age differences. When the mean velocities are plotted against age, the gradual decline in velocity with age become apparent. VMCA is highest at a setting depth of 55 to 60 mm and lowest at 35 to 40 mm using the transtemporal approach (40).

Indices of Pulsatility

Pulsatility analysis, the investigation of the excursions of the blood velocity waveform during one cardiac cycle, is commonly used in clinical and scientific work. Unlike the absolute blood velocity, the pulsatility does not depend on the angle of incidence between the blood flow and the axis of the ultrasound beam (40).

The most frequently used index is based on the work on peripheral arterial disease by Gosling and associates (25, 26):

PI = (Vs - Vd) / Vm (PI = pulsatility index; Vs, Vd, Vm = systolic, diastolic, mean velocity, respectively).

Their index was originally defined as the sum of the energies in the first and subsequent Fourier harmonics of a velocity waveform, divided by the energy in the zeroth harmonic. This was later superseded by the similar but simpler *pulsatility index*, the maximal vertical excursion of the waveform divided by its mean height (26).

In a defined artery, the shape of the waveform of the blood flow and the blood velocity results from the interaction of the two variables, the input signal and the local and organ-related factors.

(1) The repeated forward compression wave caused by the cardiac contractions moves at a velocity of 5 to 8 m/sec in large arteries. This wave propagation velocity is one order of magnitude larger than the velocity by which the blood constituents are transported. As the wave travels, the shape of the wave changes. The dissipation of energy in viscous flow tends to diminish its amplitude.

(2) The incoming waves from the heart become reflected from the peripheral vascular tree. Reflections are generated wherever the arterial caliber or wall properties change in normal as well as diseased vascular beds. The reflected waves propagate backward and interact with the next forward wave(s), increasing the amplitude in some places and decreasing it in others. The reflections originating distal to a given point of observation are functions of the viscoelastic properties of the distal vasculature and the resistance to flow (viscous friction) through the vascular bed. When investigating the behavior of the blood flow with Doppler techniques, the observer "looks" into a distal system where trains of oscillating pulses propagate.

The input signal and its reflections differ with the point of observation, even when the heart generates an unchanging train of pressure waves. An observed waveform, therefore, contains information about the dynamics of the blood flow both proximal and distal to the point of observation. In the lower aorta, the reflected waves are almost in-phase with the incident waves and the viscous effects are comparatively small (37). The result is an increasing amplitude. In smaller arteries, the viscous effects outweigh the effect from reflection and the amplitudes, therefore, decrease.

The complexity of the vascular system is such that it is very difficult to define its exact state from the resulting waveforms. Disease and other departures from normality compound these difficulties. The methods currently used to analyze blood velocity waveforms are based on observation rather than theory and depend on empirical indices. The initial definition of an index is, thus, motivated by observation, although some justification may be obtained through simplified models of blood flow. The interpretation of these indices is then evaluated statistically in clinical and experimental settings and correlated with existing parameters. Thus, the framework for the interpretation of blood velocity waveforms is based on inferences rather than fluid mechanics.

With this understanding, it is important that the methods used to obtain the waveforms and to calculate the indices be carefully defined.

Normal Pulsatility

An approximate value for normal pulsatility can be derived from the literature. The normal pulsatility index (PI) usually falls between 0.5 and 1.1. An increase in PI with age has been reported in patients with cerebrovascular symptoms (31). In a detailed study of PI variability in normals, Sortgberg et al. (47) found PI to vary between 0.69 and 1.2. Deviations that increase PI include systemic factors such as: bradycardia, aortic valve incompetence, and/or increases in vascular resistance distal to the conductance arteries.

Cerebrovascular Autoregulation

The cerebral circulation displays the phenomenon of autoregulation; that is, cerebral blood flow remains relatively constant despite moderate variations in cerebral perfusion pressure (CPP) (15). Clearly, there exist upper and lower limits beyond which near-constant flow cannot be maintained (8). During hypertensive crisis, vessels constrict until maximal constriction is attained trying to buffer the incoming high systemic pressure. Because further vessel constriction is not possible, subsequent changes in pressure will produce proportional changes in CBF. If CPP is sufficiently high, forced dilatation of vessels will occur, further increasing the level of CBF with loss of cerebral autoregulation and subsequent development of intracranial hemorrhage. Conversely, as the lower limit of autoregulation is approached (as in presyncope), vessels become maximumly dilated to allow greater flow in the cerebral capillaries to compensate for decreased systemic blood flow, causing further decreases in CPP to produce proportional decreases in CBF. Under each of these circumstances, an approximately linear relationship develops between CPP and CBF whereby subsequent pressure changes result in significant changes in flow.

There are three candidates for the principle of cerebral autoregulation (40):

(1) Metabolic autoregulation: mediated by the balance between cerebral metabolism and cerebral blood flow in each local environment.

(2) Myogenic autoregulation: an intrinsic property of vascular smooth muscle that maintains constant muscle fiber tension; when combined with Laplace's Law, results in reduced vessel caliber when transmural pressure increases.

(3) Neurogenic autoregulation: mediated by sympathetic nerve fibers, this would be a "centralized control."

All three mechanisms could possibly be controlling blood flow to some extent and it is difficult to isolate one from the other. Since regulation appears to be local, the metabolic hypothesis enjoys the most widespread support (6) as the dominant mechanism of autoregulation, at least in

the normal physiologic state. The key to this system is a strongly vasoactive substance that is produced in variable amounts depending on the balance between local CBF and the metabolic activity of the cells. The actual substances that could be involved are being researched and the results are not yet fully conclusive. The transmitter substance, in turn, acts on the vascular smooth muscle to restore the balance between supply and demand. One of the amazing facts of the cerebral autoregulation is its speed of reaction and its effectiveness in counteracting any change in CBF during perfusion pressure variation. In terms of a metabolic control system, this means that the potential candidate for transmitter substance must be able to account for this high performance homeostatic control.

METHODS

Subjects

Participating in this study were 12 adult subjects (6 males and 6 females). All of them were members of the United States Air Force Armstrong Laboratory Sustained Acceleration Stress Panel and had previously undergone medical screening and met Air Force Flying Class II Medical Standards. These were centrifuge naive subjects with no previous exposure to +Gz on the centrifuge. Table 1 provides an overview of the subjects' age, height, and weight.

Table 1. Subjects' Characteristics

SUBJECTS	AGE (Years)	HEIGHT (Inches)	WEIGHT (Pounds)
Female (n=6)			
Range	21-35	60.00-69.75	100.00-188.00
Mean	26.27	64.75	137.50
SD	5.05	3.37	32.15
Male (n=6)			
Range	22-38	64.00-73.00	145.00-202.00
Mean	27.4	68.75	168
SD	6.19	3.72	24.32
All Subjects (n=12)			
Range	21-38	60-73	100-202
Mean	27.00	66.57	151.36
SD	5.31	3.95	31.74

SD = Standard Deviation

All subjects were briefed on the medical risks associated with this research. Informed consent was obtained from all subjects prior to their participation. In addition, a briefing addendum was used for female subjects. This protocol was reviewed and approved by the Armstrong Laboratory Human Use Review Committee and by the Wright State University Review Board.

Equipment and Facilities

This experiment was conducted at the Armstrong Laboratory, Wright-Patterson Air Force Base, Dayton, Ohio. Minimum instrumentation included an Eden Medical Equipment (EME) TCD model TC-64B, Sony closed-circuit video camera and monitor, Panasonic video mixer, and Panasonic VHS video cassette recorder.

G Exposure

Dynamic Environment Simulator (DES)

All G exposures were conducted on the Dynamic Environment Simulator (DES) centrifuge located at Wright-Patterson AFB, Ohio (Figure 2).

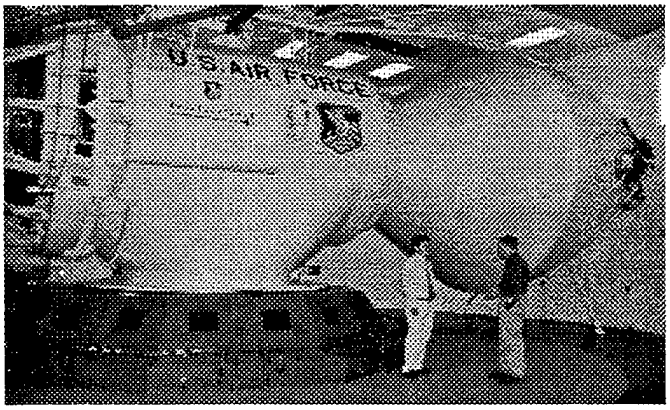


Figure 2. Dynamic Environment Simulator

The DES is a three-axis human centrifuge which can generate high sustained G acceleration. It has a radius of 19 feet to the center of the cab and weighs approximately 180 tons. It is capable of sustained accelerations up to 20 G in one of three independent axes: X, Y, and Z. Maximum onset and braking rates are 1 G per second. The DES is controlled by a digital computer and can be operated automatically by the computer, manually, or by closed-loop. In this experiment the DES was operated automatically. The cab is a 10-foot diameter spherical gondola in which, in this experiment, the seat back angle was 30 degrees from vertical. The DES has been in man-rated operation since 1969.

Centrifuge Run

Table 2. First Three Days of Centrifuge Indoctrination of the Subjects

	+Gz	PEAK DURATION	G SUIT
Day 0	No +Gz exposures		
Day 1	2.2	10 sec	no
	2.8	10 sec	no
	3.0	10 sec	no
	3.3	10 sec	no
Day 2	3.0	10 sec	no
	3.3	10 sec	no
	3.8	10 sec	no
	4.0	10 sec	no
	3.0	180 sec	no
Day 3	3.0	10 sec	yes
	3.6	10 sec	yes
	4.0	10 sec	yes
	4.4	10 sec	yes
	4.6	10 sec	yes
	5.2	10 sec	no
		Total 320 sec = 5.3 minutes	

Each subject was exposed to +Gz over three days (Table 2) with approximately seven rest days between the two exposure days. A minimum rest of one minute was allowed between two consecutive G plateaus. The time at peak was about 10 seconds and each G exposure lasted for about 60 to 90 seconds. An anti-G suit was used on Day 3. Each subject was examined by the medical monitor before and after each acceleration exposure day in the centrifuge.

Squat-Stand Test

Laboratory Setup

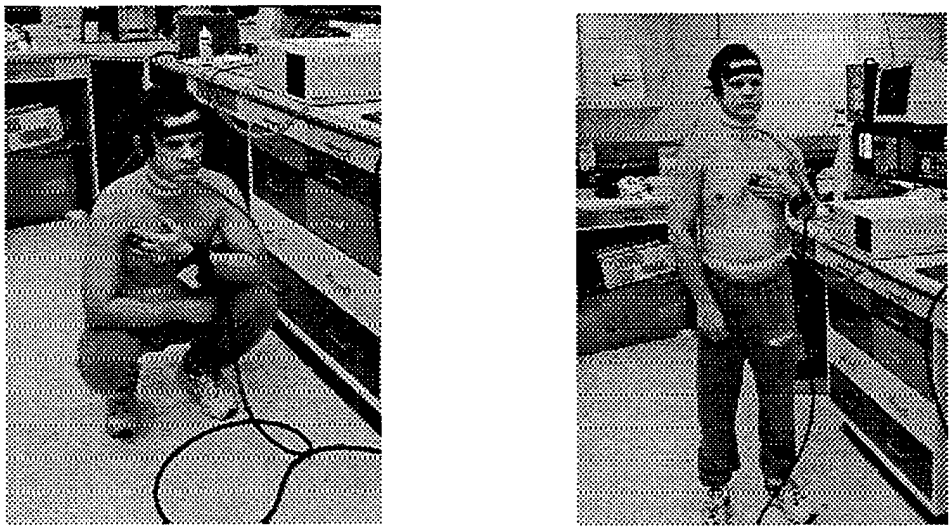
A closed-circuit camera was mounted approximately seven feet from the floor and adjusted at an angle which provided a view of both the subject's head while standing as well as surrounding medical monitoring equipment. The TCD, video monitor, video mixer, and video cassette recorder were placed on a laboratory counter directly across from the video camera. The video

signal from the TCD and of the subject test area were combined by the video mixer, producing a composite image of real-time cerebral blood flow velocity data and of the subject's head upon standing.

Experimental Procedure

The subject entered the laboratory and was seated in a stationary chair. The TCD, video camera, video mixer, and monitor were powered up for the test. Ultrasonic gel was applied to the 2-MHz ultrasonic transducer and the transducer was resting on the superior aspect of the zygomatic process adjacent to the opening of the ear canal. The transducer was then manipulated until a Doppler flow velocity of 65 $\pm$ 12 cm/sec was acquired. Pressure was applied to the transducer and the subject was asked to note the area where the transducer was placed. The investigator then noted the angle of the transducer prior to removing the transducer from the head. The transducer was then placed into a bracket which was positioned on the head. Once the Doppler flow signal was re-obtained, the bracket was then secured to the head.

At this point, the instrumentation was complete and the subject was asked to assume a squatting position for four minutes (Figure 3a). Thirty seconds prior to the end of the four minutes, data collection was initiated by starting the videotape. At the four-minute point, the subject was requested to stand erect from the squatting position (Figure 3b). Data collection continued for an additional 20 to 30 seconds after standing.



(a) (b)

Figure 3. Subject in (a) Squatting Posture and (b) Standing Posture

Data Collection

The cerebral blood flow velocity data were collected prior to the first training day of G exposure (Day 0) and again within seven days after each of the G exposure days (Day 1, 2, and 3). The data include sensor-signal depth in millimeters, mean time averaged blood velocity in centimeters per second, and pulsatility index.

The EME TCD unit that was used did not allow direct input of data into the computer. As a result, the cathode ray tube display image was routed from a video output. This was located on the back panel of the TCD and was merged with the laboratory view from the video camera onto a split screen by the video special effects generator unit. The combined video camera/TCD screen were then recorded on a standard VHS video cassette recorder. These screens are illustrated in Figure 4. After the experiment was completed, the data were manually transcribed from the VHS videotape into a computer data file for subsequent analysis.

Figure 4. Screen Illustrates Subject's Posture (Right Side View) and TCD Data

Data Analysis

Because the middle cerebral artery blood flow velocity (VMCA) and pulsatility index (PI) data from the TCD screen were changed approximately every 4.5 seconds in this study, data from the last three screens during squatting and the first three screens during standing were used for analysis. These data were averaged and defined as VMCA-Squat, PI-Squat, VMCA-Stand, and PI-Stand, respectively.

The percent change of VMCA was defined as (VMCA-Stand - VMCA-Squat) / VMCA-Squat x 100. The percent change of PI was defined as (PI-Stand - PI-Squat) / PI-Squat x 100.

An ANOVA with repeated measures was used to analyze the statistical differences in the effect of day of G exposure in centrifuge training, according to G-run profile (Table 2). The student's *t*-test was also used for "between gender" comparisons. Statistical significance was defined as $p \leq 0.05$. All data analysis was conducted by using Microsoft Excel software.

RESULTS

VMCA-Squat

Table 3. Means and Standard Deviations of VMCA-Squat (cm/s)

GROUP		DAY 0	DAY 1	DAY 2	DAY 3
All	Mean	54.56	47.33	50.56	50.00
	SD	10.98	9.69	11.81	11.26
Female	Mean	57.33	49.67	55.00	49.78
	SD	12.64	9.56	12.94	11.15
Male	Mean	51.78	45.00	46.11	50.22
	SD	9.33	10.11	9.77	12.43

Table 3 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 5.

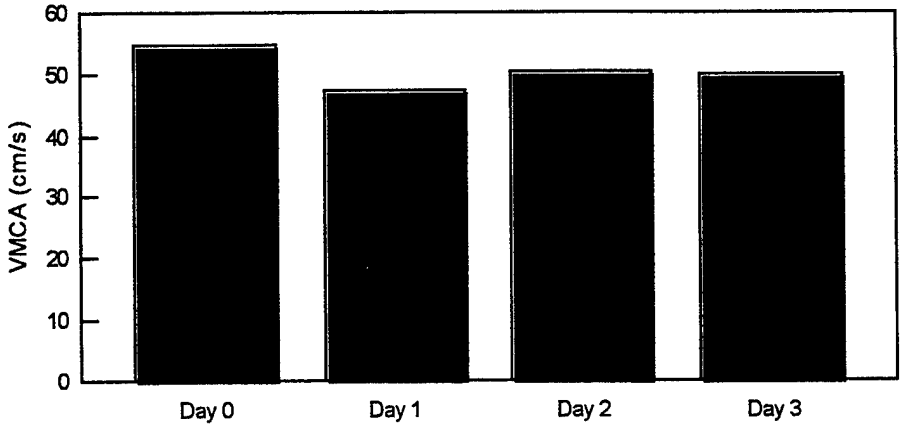


Figure 5. Means of VMCA-Squat

Table 4. Summary of ANOVA for VMCA-Squat

SUBJECT	F	P-VALUE	F-CRITICAL
All	2.2067	0.1058	2.8916
Female	1.7646	0.1970	3.2874
Male	1.3312	0.3014	3.2874

ANOVA with repeated measures was used to compare VMCA-Squat among days of G exposures for all of the subjects (female group and male group). Table 4 shows that there are no significant changes in VMCA-Squat among days of G exposures for all groups.

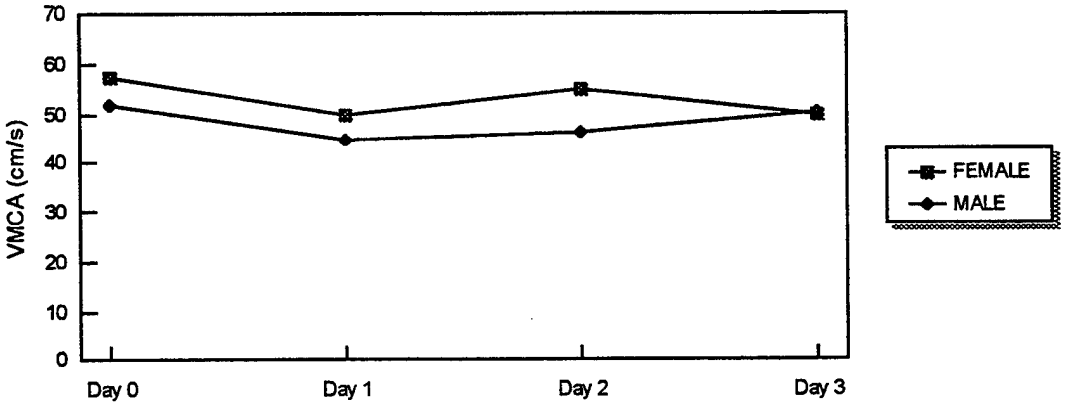


Figure 6. VMCA-Squat of Female Group and Male Group

VMCA-Squat means are illustrated in Figure 6. To determine if there are any significant differences between gender, a *t*-test was accomplished. The p-values at each day of G exposure are 0.4067, 0.4306, 0.2061, and 0.9493.

VMCA-Stand

Table 5. Means and Standard Deviations of VMCA-Stand (cm/s)

GROUP		DAY 0	DAY 1	DAY 2	DAY 3
All	Mean	40.28	35.61	37.06	36.56
	SD	9.32	8.03	10.23	7.49
Female	Mean	44.78	37.67	40.67	35.78
	SD	9.24	8.31	10.46	5.11
Male	Mean	35.78	33.56	33.44	37.33
	SD	7.56	7.92	9.46	9.79

Table 5 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 7.

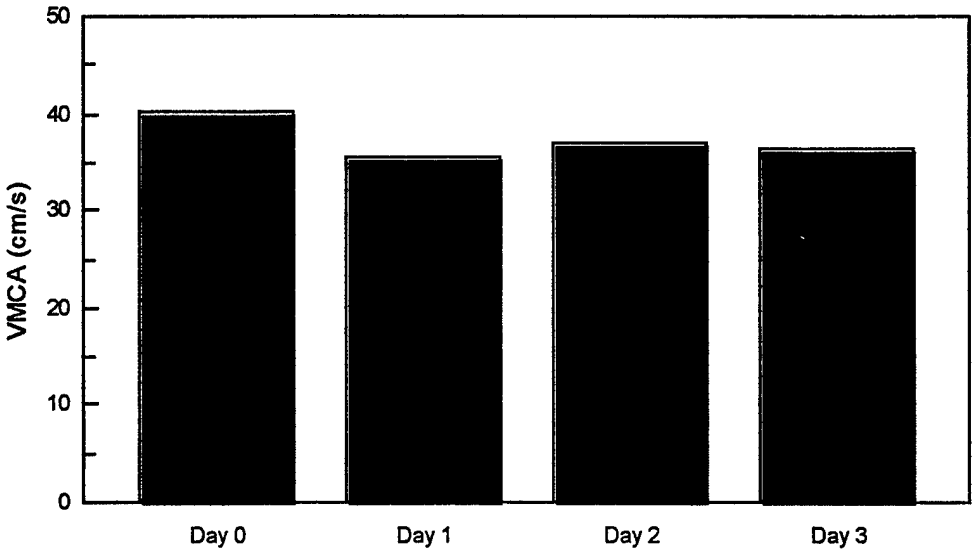


Figure 7. Means of VMCA-Stand

Table 6. Summary of ANOVA for VMCA-Stand

SUBJECT	F	P-VALUE	F-CRITICAL
All	1.1628	0.3386	2.8916
Female	3.3984	0.0456	3.2874
Male	0.3975	0.7567	3.2874

ANOVA with repeated measures was used to compare VMCA-Stand among days of G exposures for all of the subjects (female group and male group). Table 6 demonstrates the significant differences among days of G exposures in the female group.

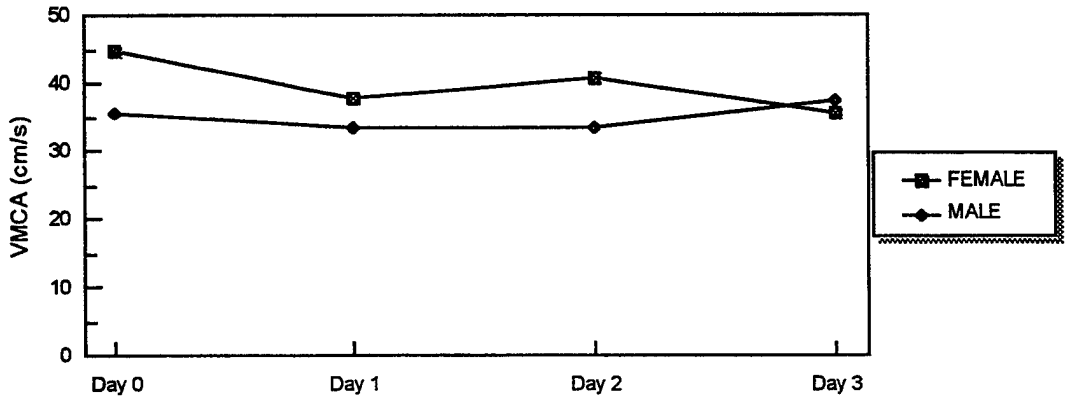


Figure 8. VMCA-Stand of Female Group and Male Group

Figure 8 illustrates VMCA-Stand group averages for males and females at each day of G exposure. The p-values derived from the *t*-test for this gender comparison are 0.4010, 0.4010, 0.2383, and 0.7372.

Percent Change of VMCA

Table 7. Means and Standard Deviations of Percent Change of VMCA

GROUP		DAY 0	DAY 1	DAY 2	DAY 3
All	Mean	-25.55	-24.76	-26.44	-25.91
	SD	12.35	6.36	12.10	11.77
Female	Mean	-20.45	-24.06	-24.24	-26.06
	SD	13.73	8.16	14.49	14.63
Male	Mean	-30.66	-25.45	-27.65	-25.77
	SD	9.19	4.60	10.43	9.53

Table 7 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 9.

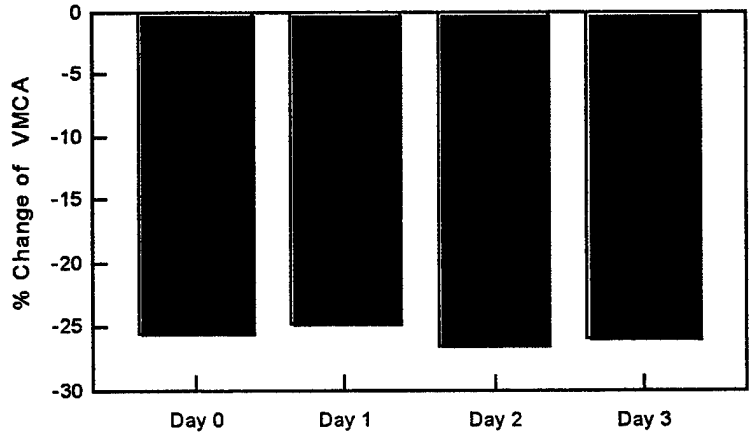


Figure 9. Means of Percent Change of VMCA

Table 8. Summary of ANOVA for Percent Change of VMCA

SUBJECT	F	P-VALUE	F-CRITICAL
All	0.0944	0.9626	2.8916
Female	0.5040	0.6853	3.2874
Male	0.9170	0.4309	4.1028

ANOVA with repeated measures was used to compare percent change of VMCA among days of G exposures for all of the subjects (female group and male group). As seen in Table 8, no significant changes among days of G exposures are noted in all groups.

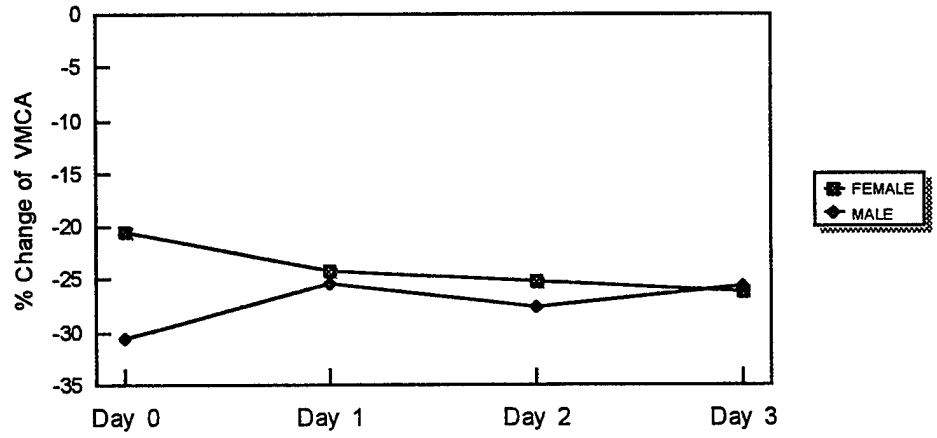


Figure 10. Percent Change of VMCA of Female Group and Male Group

When the two gender groups were compared using *t*-test, the p-values at each day of G exposure are 0.161, 0.724, 0.748, and 0.968.

PI-Squat

Table 9. Means and Standard Deviations of PI-Squat

GROUP		DAY 0	DAY 1	DAY 2	DAY
All	Mean	0.9192	1.2428	1.2086	1.2872
	SD	0.2877	0.6236	0.7782	0.5905
Female	Mean	0.9833	1.4039	1.0928	1.4978
	SD	0.4023	0.8174	0.2243	0.7969
Male	Mean	0.8550	1.0817	1.3244	1.0767
	SD	0.1020	0.3535	1.1179	0.1598

Table 9 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 11.

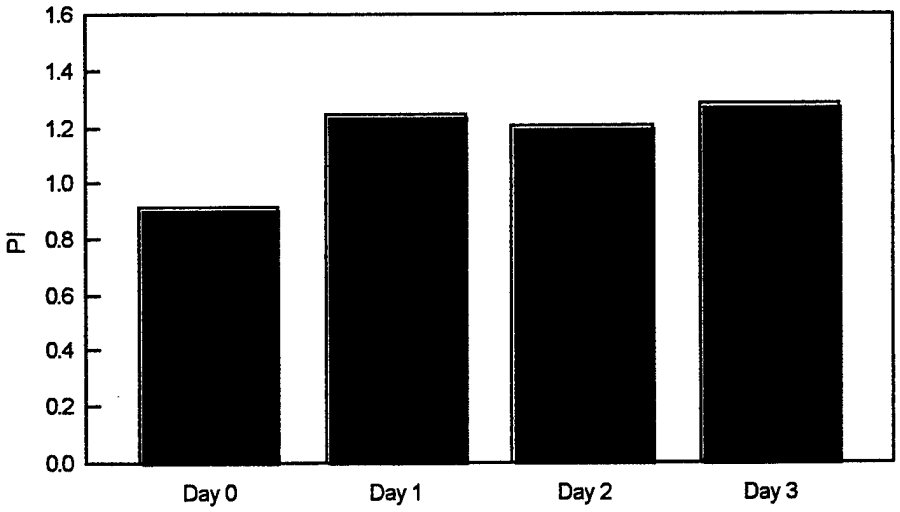


Figure 11. Means of PI-Squat

Table 10. Summary of ANOVA for PI-Squat

SUBJECT	F	P-VALUE	F-CRITICAL
All	0.8911	0.4560	2.8916
Female	0.9207	0.4547	3.2873
Male	0.5801	0.6371	3.2873

ANOVA with repeated measures was used to compare PI-Squat among days of G exposures for all of the subjects. No significant differences are noted in all groups (Table 10).

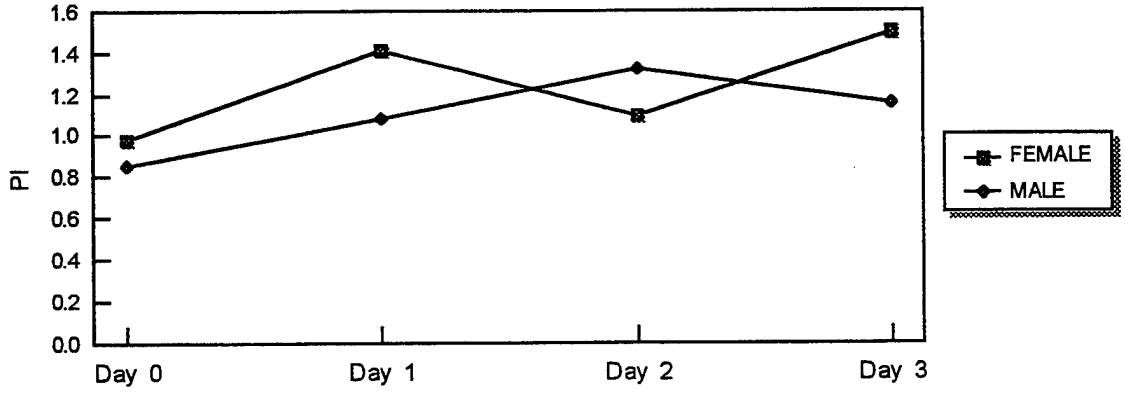


Figure 12. PI-Squat of Female Group and Male Group

Figure 12 illustrates PI-Squat group averages for males and females. For statistical analysis, *t*-test was used. The p-values at each day of G exposure are 0.462, 0.3963, 0.6294, and 0.2331.

PI-Stand

Table 11. Means and Standard Deviations of PI-Stand

GROUP		DAY 0	DAY 1	DAY 2	DAY 3
All	Mean	1.58	1.85	2.21	1.71
	SD	0.44	0.97	1.14	0.35
Female	Mean	1.52	1.98	2.19	1.78
	SD	0.50	1.40	0.88	0.42
Male	Mean	1.63	1.73	2.23	1.64
	SD	0.42	0.26	1.44	0.30

Table 11 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 13.

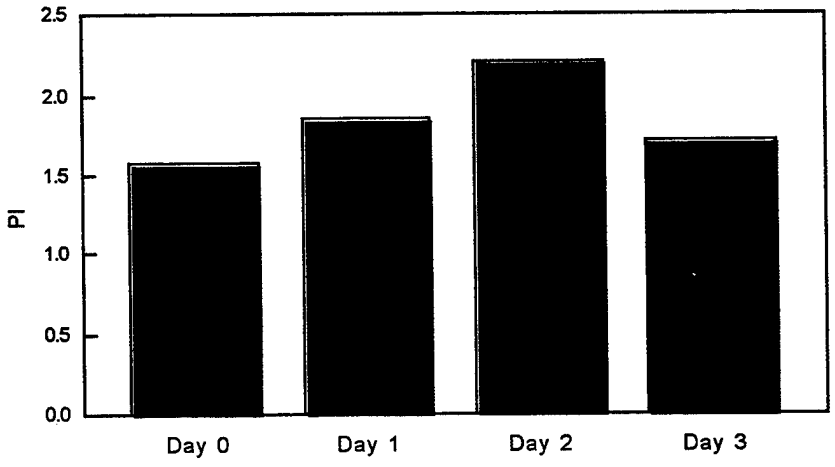


Figure 13. Means of PI-Stand

Table 12. Summary of ANOVA for PI-Stand

SUBJECT	F	P-VALUE	F-CRITICAL
All	1.3778	0.2667	2.8916
Female	0.6456	0.5977	3.2874
Male	0.7508	0.5387	3.2874

ANOVA with repeated measures was used to compare PI-Stand among days of G exposures for all of the subjects (female group and male group) (Table 12). No significant changes among days of G exposures are noted in all groups.

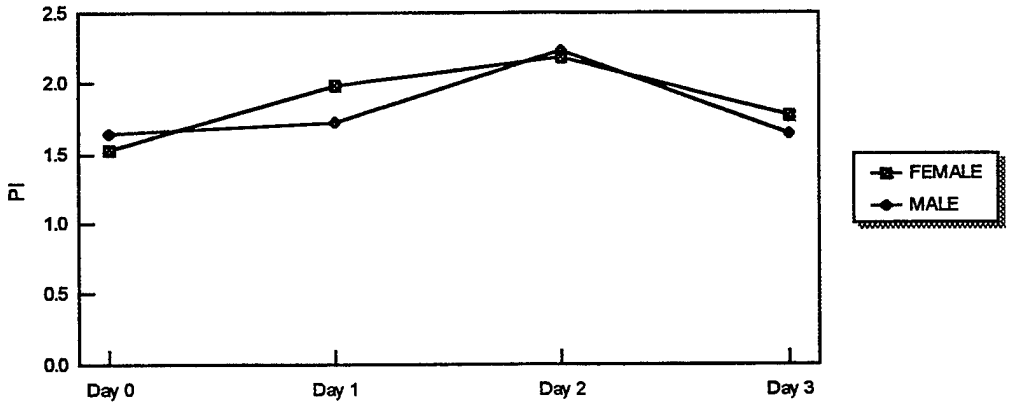


Figure 14. PI-Stand of Female Group and Male Group

PI-Stand group averages for males and females at each day of G exposure are illustrated in Figure 14. The p-values derived for this gender comparison are 0.6723, 0.6723, 0.9486, and 0.5325.

Percent Change of PI

Table 13. Means and Standard Deviations of Percent Change of PI

GROUP		DAY 0	DAY 1	DAY 2	DAY 3
All	Mean	76.81	52.84	93.42	58.75
	SD	44.18	34.40	60.76	65.46
Female	Mean	61.19	37.83	104.91	44.71
	SD	38.59	24.63	80.20	68.06
Male	Mean	92.42	67.85	81.93	72.79

Table 13 shows group averages and standard deviations for all of the subjects (female group and male group). These group averages are illustrated in Figure 15.

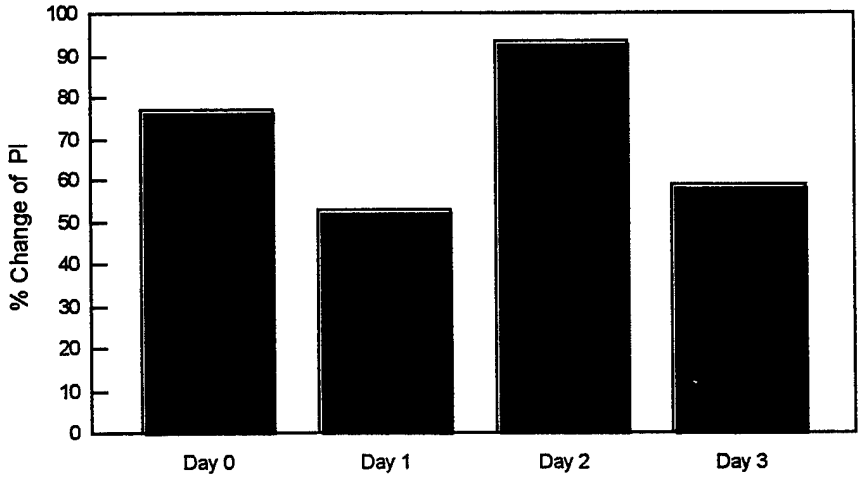


Figure 15. Means of Percent Change of PI

Table 14. Summary of ANOVA for Percent Change of PI

SUBJECT	F	P-VALUE	F-CRITICAL
All	1.6594	0.1947	2.8916
Female	1.6655	0.2169	3.2874
Male	0.4151	0.7447	3.2874

ANOVA with repeated measures was used to compare percent change of PI among days of G exposures for all of the subjects (female group and male group). Table 14 shows that there are no significant differences among days of G exposure in all groups.

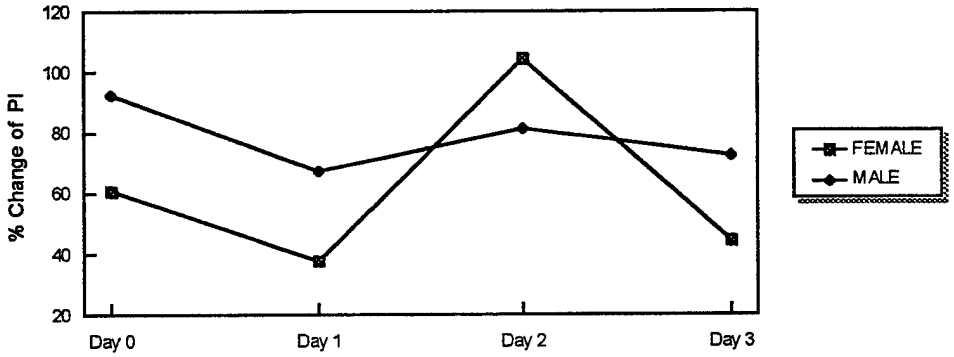


Figure 16. Percent Change of PI of Female Group and Male Group

When the "between-gender" comparison was analyzed by using a *t*-test, the p-values at each day of G exposure are 0.2378, 0.1366, 0.5383, and 0.4840.

DISCUSSION

To quantify the accumulative physiological effects of G training on cerebral hemodynamic, this investigation measured changes in middle cerebral blood flow velocities during the squat-stand orthostatic test after centrifuge exposure. Convertino and Tripp (13) studied the effects of G on cardiovascular function and also used the squat-stand test. They found that orthostatic performance, compliance, cardiac function, and baroreflex function were increased after high G training. If the high G training is able to enhance baroreflex and orthostatic functions, it seems that cerebrovascular hemodynamics should be enhanced, too. No significant adaptations in cerebral blood flow velocities were found after three days of G exposure (total of 5.3 minutes >1

G) in this research. It is possible that the cerebrovascular adaptation to G is different from that of the cardiovascular system. Other factors that should be considered include the number of G exposure days and a wide individual variation in subjects in this study.

In the female and male comparison, females had higher VMCA than males in both squatting and standing postures before G exposure (Day 0) and after G exposure (Day 1 and Day 2). However, female VMCA tended to decrease and become lower than the males' VMCA in Day 3. Males' VMCAs in Days 1 and 2 were slightly lower than in Day 0 and tended to increase in Day 3. None of these changes was significant.

The percent change of VMCA during changing posture from squatting to standing represents the orthostatic tolerance of the cerebrovascular function. This investigation found that before exposure to G, females had a higher VMCA than males. It also demonstrated that after exposure to G, females' percent VMCA tended to increase as males decreased. Seemingly, male cerebrovascular function might have an adaptation to the orthostasis after G exposure. Nevertheless, these results are not statistically significant. The literature shows that there is a reason to suspect that males and females have lower tolerance to various orthostatic challenges (13).

Frey et al. (22) found that females experienced greater absolute increases in thoracic impedance (indicating greater decreases in thoracic fluid volume) with postural change than males. This agrees with reported data from lower-body negative pressure (LBNP) tests (21) and may indicate that females experience greater lower-body pooling, especially in non-leg regions, such as the organs of the abdomen and pelvic region, than the males during orthostatic stress. In two other studies, one in response to 55 mmHg LBNP (21) and the other in response to the stand test (27), total peripheral resistance of the males increased more than that of the females. This indicates that females may have more difficulty adapting to the cardiovascular challenge of high G stress. Fischer and Weigman (18) showed that females demonstrated lower G tolerance on a centrifuge; however, they concluded that their results were confounded by the lack of good fitting anti-G suits for the female subjects. In the study of gender differences in cardiovascular reactivity after exposure to high G, Convertino and Tripp (13) found that females had lower levels of orthostatic performance and cardiac function than males. Males may have better cardiovascular and cerebrovascular adaptation capability than females. Savul (46) studied gender differences in cerebral and arterial oxygenation after exposure to high G. No physiologically significant differences were noted between the two genders. Although the orthostatic challenge tests such as squat-stand, passive head-up tilt, and LBNP and +Gz acceleration exposure, represent effective techniques for inducing orthostasis, each has distinct characteristics that provide different information about the cardiovascular system and its reflex mechanisms.

Pulsatility index (PI) was also analyzed in this study. PI, as utilized in transcranial ultrasonography, is an indicator of vascular resistance. PI increases with arteriolar vasoconstriction or vasodilation (29, 45). Males had a higher level of percent change of PI than females, but this difference was not significant, nor were the differences between pre- and post-training.

Physiological changes during the orthostatic challenge test can be explained as follows. Gravitational forces create a head-to-foot hydrostatic pressure gradient within the cardiovascular system. This hydrostatic gradient causes a redistribution of blood into the compliant veins of the lower extremities. The subsequent pooling of venous blood results in a cascade of events that include reduction in central venous pressure which includes sequential reduction in central venous pressure, end-diastolic volume, stroke volume, and cardiac output (1, 7, 24, 38, 39). Since blood pressure varies as the product of cardiac output and systemic peripheral resistance, orthostatically-induced changes in cardiac output at a given peripheral resistance tend to decrease arterial pressure. Subsequently, this induces a reduction in cerebral perfusion pressure (CPP) defined as arterial blood pressure minus intracranial pressure, causing the subject's response to move to the left along the autoregulation curve. Adequate cerebral blood flow is maintained as long as CPP does not drop below the lower threshold of autoregulation. The sudden drop that occurs in blood pressure during changing posture from squatting to standing is reflective of falling below the lower threshold of cerebral autoregulation. Regardless of the cause of diminished blood flow to the brain, the physiologic response is to preserve basic functions, such as circulation and respiration (8). Cerebral perfusion must be optimized in critical areas of the central nervous system (CNS), such as areas controlling brain stem reflexes. Falling left ventricular output and blood volume available to the CNS triggers in the brain to provide optional shunting of blood away from non-life-threatening areas of metabolism to those involved with reflexes established to ensure the integrity of the body. By reducing blood flow through the cerebral cortex below threshold, but not through the brain stem, the body is able to optimize reduced blood volume to the brain stem to sustain life until the hypovolemic state has subsided. It was evident that behavior of individuals' autoregulation systems varied widely.

Factors of G exposure that may influence the physiological adaptation to G training include the level of G, the number of G exposures, and the time between each day of G exposure. Several animal studies have indicated that there is an adaptation to G stress with frequent exposures to acceleration forces (11, 12, 14, 19, 50). Vartbaranov et al. (51) showed that it was possible to achieve a rapid increase in +Gz stress tolerance within a month of initiating an intensive G exposure schedule. Frazier et al. (20) noted that centrifuge riders felt that they could tolerate G stress better when they were frequently exposed to G. This was borne out by the heart rate data of the subjects that suggested there was an adaptation to G stress over a one-week period. Epperson et al. (17) also noted that the G tolerance increased after multiple exposure to Simulated Aerial Combat Maneuvers on the human centrifuge over several days. The control subjects for his experiment also showed improvement, simply due to exposure to repeated G stress. Gillingham reported from his experience with training centrifuge subjects and from what pilots know from their experience in high performance aircraft, that pulling G's three times a week results in higher G tolerance than does once-a-week exposure, and once-a-week exposure provides better tolerance than does once-a-month (23). All this evidence implies that there is an improvement of G tolerance capabilities with repeated exposures to G stress. In this study, the subjects experienced 5.3 minutes of 2 to 5 G over three days of centrifuge training. No significant differences in VMCA were found. Mostly likely, the level and number of G exposures used in this study were not high and long enough to affect the adaptation of cerebrovascular system. Convertino and Tripp (13) investigated four days of high G exposure (6, 7, 8, 9 +Gz) and found significant differences in cardiovascular function between before and after training.

The orthostatic challenge test and the data collection were performed within seven days after each day of G exposure. It has been reported that loss of G adaptation begins to occur within a two- to four-week time frame from the last exposure (32, 51). Toth et al. (49) noted that trained centrifuge subjects began to show signs of deconditioning (increased heart rate) after a 14-day period of layoff from G stress.

The squat-stand test used in this study was developed by Tripp (13) as a provocative orthostatic challenge test for normotensive subjects. The test involves having the subject assume a squatting position for four minutes followed by rapid standing assuming an erect posture. This test may elicit several cardiovascular mechanisms including venous pooling during the squatting phase (as venous return is somewhat attenuated by the articulation of the vasculature). The immediate compensatory responses due to acceleration forces in the +Gz direction and footward shift of blood upon standing involves: (1) the rapid adaptation of the smooth muscle of the arterial and venous vessels above and below the diaphragm to the charged vascular diameter; (2) autonomic reflexes, particular arterial baroceptors, which provide the indispensable increase in general vasoconstrictor tone and improved cardiac function; (3) the skeletal muscle pump of the lower body; (4) neurohormones; and (5) ischemia of the leg muscles. The squat-stand test induces a higher degree of orthostatic stress than does the stand test because of an additional +Gz load during posture change from squatting to standing upright and because of an increased venous pooling to lower extremities due to vasodilation after the effect of muscular ischemia during squatting. Unlike LBNP, this test does not require complicated instrumentation. Because of its short testing time and simplicity, the squat-stand test may be a new technique to evaluate the orthostatic tolerance in G training, G layoff, and even the effect of microgravity.

CONCLUSION

This study establishes a foundation for learning more about the effect of +Gz on the cerebrovascular system. Even though no significant changes in middle cerebral blood flow velocity after exposure to repeated G were found, male-female adaptation differences may exist and should be studied. The data are only suggestive because of the low subject number and minimal exposure to G >1 (5.3 minutes). Further studies with more subjects, higher G levels, and more repeated G exposure durations are suggested. Finally, the use of the squat-stand test and TCD Doppler to measure cerebral blood flow velocity may indeed have promise as an evaluation tool for G training.

REFERENCES

1. Abboud, F.M., Eckberg, D.L., Johnnsen, U.I., Mark, A.L. Carotid and cardiopulmonary baroreceptor control of splanchnic and forearm vascular resistance during venous pooling in man. J. Physiol. 1979; 286:173-184.

2. Aaslid, R., Huber, P., Nornes, H.. Evaluation of cerebrovascular spasm with transcranial doppler ultrasound. J. Neurosurg. 1984; 60:37-41.

3. Aaslid, R., Markwalder, T.M., Nornes, H. Noninvasive transcranial doppler ultrasound recording of flow velocity in basal cerebral arteries. J. Neurosurg. 1982; 57:769-774.

4. Adam, R.J., Nichols, F.T., Stephens, S., et al. Transcranial doppler: The influence of age and hematocrit in normal children. J. Cardiovasc. Ultrosonogr. 1988; 7:201-205.

5. Bagian, J.P., Hackett, P. Cerebral blood flow: comparison of ground-based and space flight data and correlation with space adaptation syndrome. J. Clin. Pharmacol. 1991; 31:1036-1040.

6. Berne, R.M., Winn, H.R., Rubio, R. The local regulation of cerebral blood flow. Prog. Cardiovasc. Dis. 1981; 24:243-260.

7. Blomqvist, C.G. and Stond, H.L. Cardiovascular adjustment to gravitational stress. Handbook of Physiology, Vol III: Peripheral circulation and organ blood flow. Part 2. Besthesda, MD.: American Physiological Society, 1982; 1025-1063.

8. Bonder, R.L., Kassam, M.S., Stein, F., et al. Simultaneous transcranial doppler and arterial blood pressure response to lower body negative pressure. J. Clin. Pharmacol. 1994; 34:584-589.

9. Bondar, R., Stein, F., Kassam, M.S., Dunphy, P.T., Bennett, B.S., Johnston, K.W. Cerebral blood flow velocities by transcranial doppler during parabolic flight. J. Clin. Pharmacol. 1991; 31:915919.

10. Brouwers, P., Vriens, E.M., Musbach, M., et al. Transcranial pulsed doppler measurements of blood flow velocity in the middle cerebral artery: Reference values at rest and during hyperventilation in healthy children and adolescents in relation to age and sex. Ultrasound Med. Biol. 1990; 16:1-8.

11. Burns, J.W., Laughlin, M.H., Witt, W.M., Young, J.T., Ellis, V.P. Pathophysiologic effects of acceleration stress in the miniature swine. Aviat. Space Environ. Med. 1983; 54:881-893.

12. Burton, R.R. and Smith, A.H. Stress and adaptation responses to repeated acute acceleration. J. Appl. Physiol. 1972; 222:1505-1509.

13. Convertino, V.A. and Tripp, L.D., Jr. Female performance at high G: Changes in measures of cardiovascular reactivity. 67 th Annual Scientific Meeting of the Aerospace Medicine Association, Atlanta, Georgia, May 5-9, 1996.

14. Duling, B.R. Effects of chronic acceleration at 3 G on cardiovascular reflexes of the rat. Am. J. Physio. 1967; 213:466-472.

15. Edvinsson, L., MacKenxie, E.T., McCulloch, J. Cerebral blood flow and metabolism. Reven Press. New York 1993.

16. Effenhauser, R.K. and Tripp, L.D., Jr. Pulse waveform and transcranial doppler analysis during lower body negative pressure. Interim report for the period January 1992 to October 1992, AL/CF-TR-1993-0097, Armstrong Laboratory, Wright-Patterson Air Force Base, Ohio, Apr 1993.

17. Epperson, W.L. and Burton, R.R. The influence of differential physical condition regimens on simulated aerial combat maneuvering tolerance. Aviat. Space. Environ. Med. 1982; 53:1091-1097.

18. Fischer, M.D., Wiegman, J.F., Bauer, D.H. Female tolerance to sustained acceleration--a retrospective study. SAFE Proc. 1992; 22:31-35.

19. Frazier, J.W. and Reeves, E. Adaptation to possitive acceleration. Report Number NADC-MA-5818, Aviation Medical Acceleration Laboratory, US Naval Air Development Center, Johnsville, Pennsylvania, 1958.

20. Frazier, J.W., Repperger, D.W., Toth, D.N., Skowronski, V.D. Human tracking performance changes during combined +Gz and $\pm$Gy stress. Aviat. Space Environ. Med., 1982; 53: 435-439.

21. Frey, M.A.B. and Hoffler, G.W. Association of sex and age with responses to lower body negative pressure. J. Appl. Physiol., 1988; 65:1752-6.

22. Frey, M.A.B., Tomaselli, C.M., Hoffler, W.G. Cardiovascular responses to postural changes: Differences with age for women and men. J. Clin. Pharmacol., 1994; 34:394-402.

23. Gillingham, K.K. High G stress and orientational stress: Physiologic effects of aerial maneuvering. Aviat. Space Environ. Med., 1988; 59:A10-20.

24. Goldsmith, S.R. and Francis, A.W. Response of vasopressin and norepinephrine to lower body negative pressure in humans. Am. J. Physiol., 1982; 243:973-970.

25. Gosling, R.G., Dunbar, G., King, D.H., et al. The quantitative analysis of occlusive peripheral arterial disease by a noninvasive ultrasonic technique. Angiology, 1971; 22:52-55.

26. Gosling, R.G. and King, D.H. Arterial assessment by doppler shift ultrasound. Proc. R. Soc. Med., 1974; 67:447-449.

27. Gotshall, R.W., Tsai, P.F., Frey, M.A.B. Gender based differences in the cardiovascular response to standing. Aviat. Space Environ. Med., 1991; 62:855-9.

28. Grolimund, P. and Seiler, R.W. Age dependence of the flow velocity in the basal cerebral arteries - a transcranial doppler ultrasound study. Ultrasound Med. Biol., 1988; 14:191-198.

29. Grubb, B.P., Gerard, G., Roush, K., Temesy-Armos, P., Monstford, P., Elliott, L., Hahn, H., Brewster, P. Cerebral vasoconstriction during head-upright tilt-induced vasovagal syncope. Circulation 1991; 84:1157-1164.

30. Gur, R.C., Gur, R.E., Brist, W.D., Skolnick, B.E. Age and regional cerebral blood flow at rest and during cognitive activity. Arch. Gen. Psychiatry, 1987; 44:617-612.

31. Hess, D.C., Adams, R.J., Nichols, F.T., et al. Transcranial doppler: Analysis of pulsatility index in patients with cerebrovascular disease. Neurology, 1989; 39 (suppl 1):186.

32. High G physiological protection training. Aerospace Medical Panel (AMP) working group 14, AGARDograph AGARD-AG-322, Dec 1990.

33. Johnston, S.L. An investigation of middle cerebral artery blood flow velocity and arterial oxygen satuation under sustain positive Gz. Thesis for the degree of Master of Science. Wright State University, 1992.

34. Ketty, S.S. The physiology of the human cerebral circulation. Anesthesiology, 1949; 10:610-613.

35. Lassen, N.A. Cerebral blood flow and oxygen consumption in man. Physio. Rev., 1959 39:183-238.

36. Lundar, T., Lindegaard, K.F., Froysaker, T., Aaslid, R., Wiberg, J., Nornes, H. Cerebral perfusion during nonpulsatile cardiopulmonary bypass. Ann. Thorac. Surg., 1985; 40:144-150.

37. Macdonald, D.A. Blood flow in arteries. London : Arnold 1974.

38. Mangseth, G.R. and Bernaucer, E.M. Cardiovascular response to tilt in endurance trained subjects exhibiting syncopal reactions (abstract). Med. Sci. Sports. Exerc., 1980; 12:140.

39. Montgomery, L.D., Kirk, P.J., William, B.A. Cardiovascular responses of men and women to lower body negative pressure. Aviat. Space Environ. Med., 1977; 48:138-145.

40. Newell, D.W. and Aaslid, R. Transcranial doppler. Raven Press. New York 1992.

41. Nornes, H. Hemodynamic aspects in the management of carotid cavernous fistula. J. Neurosug., 1972; 37:687-694.

42. Normes, H., Knutzen, H.B., Wikeby, P. Cerebral arterial blood flow and aneurysm surgery. Part 2: Induced hypotension and autoregulatory capacity. J. Neurosurg., 1977; 47:819-827.

43. Normes, H. and Wikeby, P. Cerebral arterial blood flow and aneurysm surgery. Part 1: Local arterial flow dynamics. J. Neurosurg., 1977; 47:810-818.

44. Padayachee, T.S., Gosling, R.G., Bishop, C.C., Burnand, D., Browse, N.L. Monitoring middle cerebral artery blood velocity during carotid endarterectomy. Br. J. Surg., 1986; 73:98-100.

45. Petty, G.W., Wieber, D.O., Meissner, I. Transcranial doppler ultrasonography: Clinical Applications in Cerebrovascular Disease. Mayo Clin. Proc., 1990; 65:1350-1364.

46. Savul, S.A. Gender differences in cerebral and arterial oxygenation after exposure to high Gz forces. Thesis for Master of Science. Wright State University, 1996.

47. Sortgberg, W., Langmoen, I.A., Lindegaard, K.F., Nornes, H. Side to side differences and day to day variations of transcranial doppler parameters in normal subjects. J. Ultrasound Med., 1990; 9:403-409.

48. Thomas, D.J., Marchall, J., Russel, R.W., et al. Effect of hematocrit on cerebral blood flow in man. Lancet, 1987; 2:941-943.

49. Toth, D.N., Repperger, D.W., Frazier, J.W. The effects of test and training intervals on performance evaluations in acceleration stress. 71st Annual Scientific Meeting of the Aerospace Medical Association, Anaheim, California. May 1980.

50. Tripp, L.D., Jr. and Chelette, T.L. Cerebral blood flow during +Gz acceleration as measured by transcranial doppler. J. Clin. Pharmacol., 1991; 31: 911-914.

51. Vartbaranov, R.A., Glod, G.D., et al. Adaptibe and cumulative effects on dogs of regular exposure to +Gz accelerations. JPRS Report, JPRS-USB-87-004 USSR. Space Biol. Aerospace Med., 1987.

52. Vriens, J.M., Kraaier, V., Musbach, M. Transcranial pulsed doppler measurements of blood velocity in the middle cerebral artery: reference values at rest and during hyperventilation in healthy volunteers in relation to age and sex. Ultrasound Med. Biol., 1989; 15: 1-8.