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APPLICATION OF RHEOENCEPHALOGRAPHY TO STUDY PHYSIOLOGICAL RESPONSES UNDER ACCELERATION STRESS

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THE USE OF ELECTRICAL IMPEDANCE PLETHYSMOGRAPHY OF THE HEAD, OR RHEOENCEPHALOGRAPHY (REG), HAS BEEN DEMONSTRATED IN A HIGH ACCELERATION STRESS ENVIRONMENT ON HUMAN VOLUNTEER SUBJECTS. ACCELERATION STRESS WAS PRIMARILY APPLIED IN THE HEAD-TO-FOOT DIRECTION AND IS REFERRED TO AS +Gz. THE REG INSTRUMENT DIVIDES THE CEPHALIC IMPEDANCE WAVEFORM INTO TWO COMPONENTS: 1) A BASELINE IMPEDANCE SIGNAL, Zdc, THAT IS REFERABLE TO THE BULK MOVEMENT OF BLOOD IN AND OUT OF THE HEAD CAUSED BY RESPIRATION AND CHANGES IN POSTURE, AND 2) A PULSATILE IMPEDANCE WAVEFORM THAT IS HEART BEAT COINCIDENT (Zpul). THE REG WAVEFORM CONTAINS INFORMATION ABOUT CEREBROSPINAL FLUID (CSF) VOLUME CHANGES AND SHIFTS RESULTING FROM THE APPLICATION OF ACCELERATION STRESS. BLOOD AND CSF SHIFTS IN AND OUT OF THE CRANIAL AND SPINAL COMPARTMENTS IMPINGE DIRECTLY UPON THE OVERALL FUNCTION OF THE CENTRAL NERVOUS SYSTEM. THE HIGH ACCELERATION ENVIRONMENT PROVIDES AN IDEAL ARENA IN WHICH TO NONINVASIVELY ALTER CEPHALIC FLUID VOLUMES IN ORDER TO OBTAIN BASIC PHYSIOLOGIC KNOWLEDGE OF IMPORTANCE TO BOTH AVIATION AND CLINICAL MEDICINE.

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THIS INFORMATION HAS BEEN OBTAINED IN A NONINVASIVE, SAFE, CONVENIENT, AND UNOBTRUSIVE MANNER ON THE NAVAL AIR DEVELOPMENT CENTER (NADC) HUMAN CENTRIFUGE. USING DATA DERIVED FROM FIVE DIFFERENT SETS OF HUMAN EXPERIMENTS CONDUCTED IN A HIGH +Gz ENVIRONMENT HAVE LED TO THE CHARACTERIZATION OF THE CHANGES IN THE REG WAVEFORM THAT OCCUR WITH INCREASING ACCELERATION LOAD. ANALYSIS OF CHANGES IN Zpul HAVE PROVIDED INDICATIONS OF THE CHANGES IN VASOMOTOR TONE AND SYSTOLIC VOLUME UNDER +Gz-STRESS. ALTERATIONS IN THE Zdc WAVEFORM INDICATE ITS UTILITY AS AN AID IN DETERMINING THE EFFECTIVENESS OF ANTI-G PROTECTIVE DEVICES, SUCH AS RECLINING AIRCRAFT SEATS, AND ANTI-G TECHNIQUES, SUCH AS ANTI-G STRAINING MANEUVERS. THROUGH COMPARISON OF Zdc AND INFRARED PLETHYSMOGRAPHY, EVIDENCE HAS BEEN OBTAINED THAT INDICATES THAT PRESSURE BREATHING FOR G ASSISTS MAINTENANCE OF CEREBRAL BLOOD VOLUME AT THE EXPENSE OF PERIPHERAL CEREBRAL CIRCULATION. Zdc WAVEFORMS ALSO IMPLY THAT CEREBRAL BLOOD VOLUME INCREASES WHEN SUBJECTS PERFORM TRACKING AND COGNITIVE TASKS UNDER +Gz-STRESS.

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INTRODUCTION

Motivation

Current Naval aircraft are capable of generating and sustaining acceleration stresses in the +Gz (head-to-foot) direction which exceed the protected tolerance limits of its aircrew. The physiological reaction to +Gz-stress includes both vascular and neurophysiologic components. As +Gz-stress increases, blood is drawn out of the head towards the dependent regions of the body, e.g. abdomen, legs and feet. Perfusion pressure in the head decreases and heart rate increases. The central nervous system (CNS) is protected (brain and eye) through its intrinsic "functional buffer period," the time the CNS can function without continuous oxygen supplies, as well as an active ability to shift resources to critical areas of the CNS to preserve function and prevent damage. Symptoms associated with +Gz-stress include a reduction in the visual field (LOV) from a loss of peripheral vision, to loss of central vision, to complete visual blackout. If the stress continues, +Gz-induced loss of consciousness (G-LOC) can occur which, in-flight, can lead to loss of life and aircraft.

The Naval Research Advisory Committee's 1990 Summer Study on Aviator Physical Stress stated that "knowledge of the neurophysiological characteristics of reduced cerebral perfusion are a critical part of understanding the adverse effects of rapid onset and high sustain +Gz."

Presently, the major emphasis in dealing with the problem of LOV and G-LOC is the concern for maintaining blood flow in the cerebral circulation. It is vital that such blood flow be maintained in order to preserve the long term homeostasis of the CNS. However, over the relatively short periods of interest in preventing LOV and G-LOC, consideration of cephalic blood volume and cerebrospinal fluid may also be significant. Hemoglobin in the blood is the major oxygen buffer in cephalic neural tissues (24) and PLL and LOC under a +Gz load are caused not only by the critical reduction of blood flow to the head, but also by reduction of the primary reservoir of available oxygen (2, 43). The effects of +Gz on the oxygen availability to neural tissues, as well as benefits of anti-G straining maneuvers, may well be reflected in cephalic blood volume changes.

Rheoencephalography (REG), also known as electrical impedance encephalography, is a subset of electrical impedance plethysmography (EIP). EIP methods have been applied successfully in the aerospace environment to the evaluation of respiration (3), cardiac output (26), and limb engorgement (29). In general, EIP relates changes in physiologic events to changes in electrical impedance. The method depends upon changes of volume and/or conductivity of a body segment subtended by an array of electrodes. Although the exact mechanism of the impedance variations in REG is subject to some controversy, there

is little doubt as to the occurrence of pulsatile variations that are synchronous with the heartbeat (40). It has been shown that these pulsations depend upon integrity of cephalic blood flow (14).

The objective of this effort is to provide a means for noninvasive monitoring of cephalic fluid volume changes under acceleration stress via the use of rheoencephalography. Relative changes in cephalic fluid volume due to pulsatile flow and bulk shifts of blood will be measured. It will be shown that this technique is useful in determining the effectiveness of anti-G protective devices and maneuvers designed to ameliorate the effect of acceleration stress, such as anti-G suits, anti-G straining maneuvers, reclining seat-back-angle and pressure breathing for G.

Effects Of Acceleration Stress

The importance of maintaining adequate blood circulation in the head has been demonstrated in both clinical and aviation environments (10). This is particularly true when flying high onset +Gz aircraft because of the physiological reaction to the acceleration forces involved.

For a normal man at 1 g, the heart must overcome an approximately 30 cm hydrostatic column for blood to reach the CNS. This corresponds to a hydrostatic pressure of approximately 22 mmHg (i.e. 300 mm x 1.055 gm/cm^3 (density of blood) / 13.6 gm/cm^3 (density of mercury)). Therefore in an average man, assuming a systolic arterial pressure of 120 mmHg at heart level (at the third intercostal space), arterial pressures at head and foot levels are 98 and 170 mmHg, respectively. With each 1 g increase in +Gz load, the hydrostatic column effectively increases by another 30 cm until a point is reached in which pressure in the head is critically decreased and blood supply is arrested. Theoretically, arterial pressure at eye level in the average human reaches zero at approximately +5.5 Gz. At this point, assuming that the arterial pressure at heart level had been 120 mmHg at 1g, the arterial pressure at the base of the brain would become zero and pressure at the feet would be 370 mmHg. Therefore, a differential pressure of 250 mmHg would be necessary to return blood from the feet to the heart. This description of changes in blood pressure and redirection of blood flow forms the basis of the "hydrostatic column theory of the human physiological response to applied acceleration stress."

The physiologic symptoms accompanying increasing levels of acceleration stress are particularly detrimental because they can be rapid in onset, their occurrence is somewhat unpredictable, and they limit the most important sensory central nervous inputs to the crew-member. Human physiologic response to a +Gz load depends upon the level and rate of onset of the acceleration.

When acceleration is gradually applied (+0.067 to +0.02 Gz/sec), visual function decreases in stages from grey-out to blackout. However, under very high onset rates (e.g. > +6 Gz/sec) an individual can lose consciousness without recognizable loss of peripheral vision (56). On the other hand, at lower onset rates an individual can experience blackout and still retain normal cortical function (10). Lambert (27) demonstrated that this effect is of retinal origin in an experiment in which vision in one eye was maintained by application of 30-40 mmHg suction to the eyeball while the other unprotected eye "blacked-out." Since the blood pressure at eye level must be less than 20 mmHg for blackout to occur, the arterial pressure in the cerebral cortex must be lower than this during the period prior to LOC. Therefore, such symptoms jeopardize not only the life of the crew, but also the successful completion of a vital mission and an extremely costly aircraft.

Among the many tantalizing observations related to +Gz-tolerance may be found in the following: (a) Straining maneuvers helpful in delaying the onset of LOV and G-LOC in the short term are of a general nature that is detrimental to circulation in the long term; (b) The onset of PLL and LOC (in common with syncope at 1 g) seems rather sudden to be explained by loss of flow alone; (c) Net negative blood velocities, when measured by the doppler ultrasound technique, have been observed in the superior temporal artery for extended periods of time under a +Gz load without significant decrease in pilot performance (25).

Insight into these observations is aided by consideration of some basic physiologic features of neural tissues. These tissues, including the retina and brain, have closely regulated but barely adequate blood circulation to supply nutrients (oxygen, glucose, etc.) and remove metabolites - in contrast with most other organs whose abundant blood supplies reflect their circulatory interface function. Neural tissue comprises only three percent of body weight while it receives about 15% of the cardiac output and consumes about 25% of the oxygen (20). In the retina and in neural grey matter, oxygen consumption can be as high as 12 ml/100gm/min (20). In comparison with cardiac and skeletal muscles (having a similarly high oxygen extraction fraction), neural tissues lack an intrinsic oxygen buffer such as myoglobin. In the brain, oxygen is used only in the "terminal respiratory chain" of enzymes for oxidative phosphorylation in the mitochondria, i.e. ATP synthesis. This process is usually limited by the supply of ADP and inorganic phosphate rather than oxygen tension. Oxygen uptake by mitochondrial suspensions continues until the local partial pressure of oxygen falls to 0.1 mmHg (30). Therefore, when oxygen supply becomes limiting, it is because the volume of oxygen has been exhausted.

Oxygen consumption in the brain is 40 - 50 ml/min (57), or approximately 3 ml O_2/100 gm/min. There is about 2.8 ml of oxygen dissolved in the tissue, or 0.19 ml O_2/100 gm (50). The 75 ml of blood in the cerebral circulation contains about 15 ml

of oxygen (at 100% saturation), mostly combined with hemoglobin (24). (Approximately 1.5% of the oxygen in blood is dissolved). Therefore the hemoglobin in blood is the major oxygen buffer for the neural tissues. Using these figures, if blood flow to the brain was stopped or reversed at neck level, the 17.8 ml of cephalic blood would be consumed in approximately 21 - 27 seconds. This assumes that once arrested, oxygen is consumed at the normal rate and that all of the blood is available for consumption. However, blood in the dural sinuses of the head and arterial and venous blood trapped in the neck is unavailable to neural tissues. Therefore, this rate is not inconsistent with neck occlusion studies reported by Rossen et al (43) in which blood flow to the head was occluded with a cervical cuff. This produced unconsciousness in an average of 5.5 seconds.

Therefore, LOV and G-LOC during +Gz are caused not only by interruption of blood flow to the head, but also by subsequent removal of the major proportion of available oxygen. This view is consistent with observations of the retinal vessels noted during acceleration stress under direct ophthalmoscopic observation using fluorescein as an indicator. During a +Gz load not only is there a total cessation of pulsatile flow but an apparent backward flow of fluorescein dyed arterial blood from distal ophthalmic artery towards the carotid system. At offset of +Gz acceleration, the dye then returns to the ophthalmic artery and then is cleared from the arterial system (28).

The cardiovascular system exhibits a series of reflex responses when exposed to changes in blood pressure. High pressure stretch receptors are located in the carotid sinus and aorta. As pressure drops, the inhibitory action of these receptors is reduced which then causes the brain stem reticular formation to induce vasoconstriction, increased heart rate, and force of contraction. Since arterial pressure changes are most dramatic above the heart, the carotid sinus is the primary sensor for responding to low pressure during +Gz (11).

It has been shown that cerebral blood flow is maintained during acceleration and is not reduced in accordance with simple hydrostatic principles (10, page 597). The stability of the vascular system under acceleration is largely due to the strength of the vessel walls. These walls are relatively thin and have no collagen fibers, except for the capillaries which have a delicate but strong elastic framework. According to Dhenin (6) and Henry et al (19), some of the mechanisms responsible for maintaining blood flow to the brain are:

1) The cerebral vessels and brain are enclosed in the skull and are surrounded by cerebrospinal fluid (CSF). CSF pressure (CSFP) falls due to hydrostatic effects during +Gz in parallel to reductions in arterial pressure so that the pressure differences across the walls of the cerebral vessels remain close to normal (6). Henry et al (19) have shown that the internal and external vertebral venous plexes are protected from collapse by

subatmospheric (20-60 mmHg below ambient) CSFP. Periosteal adhesions of intracranial veins also aid in keeping these vessels patent (4). Therefore, a pathway is provided for return of blood from the brain to the heart.

2) There is active vasodilation of the cerebral arterioles so that resistance to flow is reduced.

Aspects Of The Cerebral Circulation

(Note: Unless otherwise indicated, the primary source of information for this section is based upon Heistad et al (18).)

The cerebral circulation is highly specialized. The brain-blood barrier provides isolation and protection from ionic changes and humoral stimuli. As compared to other vascular beds, large arteries account for a greater percentage of vascular resistance in the brain. Autoregulation in the brain is normally very effective and is responsive to changes in arterial pressure and chemical stimuli.

The brain is supplied primarily by two carotid and two vertebral arteries. It has a high capillary density. It is drained by two systems of veins. Blood to the cerebral and cerebellar cortices flows through vessels on the surface of the brain. Blood emanating from the basal areas flows into the deep venous system, including the straight sinus. Blood exits the skull via the internal jugular and other veins.

The main input variables which determine cerebral blood flow (CBF) are the arterial blood pressure at the base of the skull, jugular venous blood pressure, local autoregulation, and the state of the cranial and caudal veins of the skull. Blood flow rate to the cranial vessels is dependent upon the total hydraulic resistance and is determined by the difference between cephalic arterial and venous pressures. In the closed cranium, CSF and venous pressures balance and the rate of blood outflow is determined by the difference in cranial venous and jugular pressures and upon the vascular resistance of the cerebral venous system (17).

The circle of Willis (CoW) is formed by anastomoses of the major arteries supplying blood to the brain in man. The CoW can provide important collateral circulation when a proximal vessel is occluded. Emanating from the CoW are the anterior, middle, and posterior cerebral arteries. These then traverse the convex surface of the cerebrum. The basilar artery system supplies the brain stem and the cerebellum. Regions bordering the areas supplied by the anterior, middle, and posterior cerebral arteries are the "boundary zones." These areas are particularly vulnerable to reductions in cerebral blood flow. Prolonged

hypotension may produce ischemic necrosis that is most pronounced in these boundary zones.

In addition to the CoW, the pial vessels also have a rather extensive network. This network may compensate for occlusion of arteries distal to the CoW and attenuate the reduction in flow. These vessels account for a large portion of the total cerebral vascular resistance (CVR) and their responses are generally representative of the entire cerebral circulation.

According to Gregg and Huvos (15), total CVR is influenced by intracranial pressure, blood viscosity, and vascular diameter as opposed to direct neural control. The sympathetic fibers innervating the cerebral vessels are apparently physiologically inactive. While CVR becomes elevated in a direct and linear fashion by increased intracranial pressure, CBF remains relatively constant until pressure reaches a very high level (approximately 45 cm of water). CBF increases proportionately to decreased red blood cell concentration. The most important factor affecting CVR, vascular diameter, is determined by structural changes, neurogenic factors, and metabolite concentrations.

The most important factors affecting chemical regulation include O_2, CO_2, and pH. CO_2 and hydrogen ion (H^+) concentration have a pronounced vasodilatory effect on vascular tone. Therefore, changes in CO_2 concentration or in pH strongly influence CBF and CVR. The action of CO_2 may be mediated by the direct effects of H^+ on cerebral arterioles. Hydrogen ion concentration close to the vascular muscle depends on HCO_3^- concentration and on partial pressure of CO_2 (P_{CO2}) of the extracellular fluid in that location. The latter depends on arterial partial pressure of CO_2 (Pa_{CO2}) and on CSF P_{CO2}. When Pa_{CO2} is increased, molecular CO_2 diffuses across the brain-blood barrier, raises the local P_{CO2} of the vascular muscle, and reduces extracellular pH. This produces vasodilation by relaxation of the vascular muscle. There is an indication that the major mechanism of action of CO_2 on cerebral circulation is mediated via changes in CSF pH.

Low O_2 tensions (20-30 mmHg) also causes vasodilatation. Similar responses occur with changes in CSF P_{O2} in the vicinity of the pial vessels. Also during combined occurrences of arterial hypoxia and hypercapnia, cerebral vasodilator effects become additive.

Aspects Of The Cerebrospinal Fluid (CSF) System

The cranio-spinal system is basically an incompressible closed system, i.e. changes in blood volume entering into the head will be accompanied by a shift of venous blood and/or CSF out of the head into the spinal cavity. CSF shifts from cranial

to spinal space periodically with respiration and aperiodically with respect to slow blood volume changes in the skull. Cardiac synchronous volume shifts are compensated for by a redistribution of CSF and venous blood in the cranial space (17). This compensation is produced by direct hydraulic contact of the blood vessels with the spaces containing CSF, extensive connections between cranial and spinal veins, and free communications between CSF cavities in the skull and spinal canal (38).

Changes in CSFP have been used to make relative estimates of blood volume shifts. Since the product of pressure and volume is theoretically constant in an enclosed space, one may calculate from the pulsatile pressure the changes in fluid volume which are responsible for these pressure changes. Here, fluid volume consists of the sum of the average volume of intracranial space, intracranial blood, and intracranial "free space" (i.e. CSF) (17). CSFP is determined by the volume of arterial and venous blood, CSF, and brain tissue, and by the mechanical properties of membranes surrounding the brain and bones of the skull. Hydrostatic pressure accounts for one third of the total CSFP, 10% is attributed to the elasticity of the meninges, the balance depends upon blood pressure, particularly venous pressure, and on the secretion pressure. CSFP is always a few centimeters of water higher than venous pressure (34). CSFP is affected in the following manner. Change in venous pressure causes a change in CSFP of a comparable magnitude and direction. In fact, venous volume is directly determined by the difference between venous and CSF pressures. Change in arterial pressure causes variable alterations in CSFP in magnitude and direction. The rise and fall of CSFP is due to variations in blood volume in the cranio-spinal cavity. Therefore, CSFP is dependent upon the tone of the cerebral vessels (38).

CSFP may increase during such maneuvers as straining, coughing, and vomiting. CSFP may also vary during shifts in posture. These oscillations are balanced by an adaptation or by a reaction of the cerebral blood circulation. Alterations in rheoencephalographic recordings have been observed with various functional tests such as Queckenstadt's maneuver (compression of both jugular veins to block venous outflow), carotid compression, and after withdrawl of CSF (38). As an example, Queckenstadt's maneuver results in an increase in CSFP and upon removal of the compression, CSFP declines relatively faster than the rate at which blood returns to the head. Reaction of CSFP to carotid compression varies depending upon the state of the circulatory system and may increase or decrease (34). External agents which cause a decrease in tone (e.g. CO_2, amyl nitrite) cause an increase in CSFP. External agents causing an increase in tone (e.g. O_2) lead to a fall in CSFP (38). A decrease in CSFP leads to a decline in blood volume as registered by REG (17).

The mechanism of support provided by the CSF system is particularly important in the acceleration environment. The brain is protected from a reduction in systemic blood pressure by

virtue of the fact that it is enclosed in a rigid container, is surrounded by CSF, and such a drop in pressure is often accompanied by a similar decline in CSFP. Therefore, the transmural pressure in cerebral vessels remains almost constant with no tendency for collapse. If, at the same time, venous pressure in the neck falls below atmospheric, blood is sucked through the brain by siphonic action. Cerebral circulation continues as long as the vessels remain patent and until some part of the system empties. Increasing the driving pressure through the siphon can restart the system (10). Akesson (1) found that an increase in CSFP leads to vasodilatation of the pial arteries, which reduces the resistance to flow within them. This and the siphon effect may act to maintain circulation.

Rushmer et al (44) found that CSFP and venous pressure vary simultaneously (and almost equally) over a wide range of negative and positive acceleration loads in cats. They claimed that there is virtually complete protection for veins and small vessels. While the arteries are less fortunately placed, they too receive some compensation from CSF.

Another biophysical aspect of CSF aiding circulation under acceleration is the difference between the specific gravities of the brain and CSF; 1.048 and 1.008, respectively. A 1500 gm brain in such an environment exerts a force of approximately 35 gm on the base of the skull. As an analogy, consider spinning a water filled balloon. As it spins faster and faster, a point will be reached in which the pressure from the centrifugal force will burst the balloon. If, however, the balloon is surrounded by water, the external and internal pressures are balanced and the whirling balloon remains intact.

The level of protection afforded by CSF depends upon the level, rate, and duration of the acceleration stress applied. If the stress acts for less than one second, there is not enough time for compensation flows to occur. If the stress is prolonged (5-7 seconds), effective compensation begins.

Bjorn Magnaes measured the flow of lumbar and ventricular CSF and pressure changes in humans while rapidly sitting up (quick-tilt: sit up in 1 - 2 seconds without Valsalva). He found that there was a caudal shift in CSF (1.5 - 5.6 ml increase in 1 - 3 seconds at about 100 ml/min). There was little changes in filling pressure for a 6 - 8 second period followed by a transient caudal shift of CSF (0 - 3.2 ml increase in 1 - 8 sec). This is a "buffering" volume of CSF - a displacement of CSF to the spinal compartment (33). The magnitude of the flow was about 20 ml/min and the range of pressure rise was from minute to 25 cm H_2O (32). Upon lying down, 37% of patients had immediate pressure drop to pre-tilting level, 56% of patients took 10 - 40 seconds to return to baseline, and 7% had a transient pressure rise immediately after lying down (111 patients total) (31).

In the ventricular CSF measurements Magnaes found that there was a primary pressure fall (hydrostatic) and a second transient pressure rise (filling pressure). The times were very similar to the lumbar measurements (1 ~ 3 sec) but no volumes were listed. Upon lying down, there was a rapid rise in CSFP directly in an overshoot phase to 130 cm H_2O with nearly no time lag (these measurements corresponded to the 56% of patients with longer return to baseline of lumbar CSFP (31).

Of interest to +Gz studies, Magnaes found that blood pressure dropped when patient sat up with a compensatory rise in the sitting position, and a rise upon lying down. The BP fall when sitting up lagged behind the positional CSFP change, while the BP rise on lying down was nearly concomitant with CSFP. The secondary transient CSFP rise started concomitant with the compensatory BP rise when sitting up. (In one strip chart, a 1.5s rise in postural CSFP was followed by a 10s fall to a minimum BP (31).) During the phase of falling BP, the CSF filling pressure remained relatively unchanged, i.e. CBV was more constant during falling BP as compared to the rising phases of BP.

RHEOENCEPHALOGRAPHY (REG)

Background

An inherent property of matter is its exhibition of a resistance to passage of electrical current. This is defined by $\mathbf{r} = E/J$; where $\mathbf{r}$ = resistivity of the material, E = electric field, and J = current density. In the case in which resistance of a body segment, subtended by measurement electrodes, is to be determined the following assumptions are made (36, 40). The segment has a uniform cross sectional area and is filled with a homogeneous conducting material. There is a uniform current density between the electrodes. The length of the segment between the measuring electrodes and the area remain constant while blood enters (exits) the segment. The overall volume is constrained to be a constant. Also, $\mathbf{r}$ is unchanged during measurement. If, for example, a segment in a current field has a hole drilled through it and the external dimensions are fixed, the current lines will experience a high resistance path as they approach the hole (a high resistance area filled with a poor conductor, i.e. air). This will give rise to a non-uniform electrical field and a non-uniform current density distribution. The introduction of the hole does not effect $\mathbf{r}$ (a constant dependent upon the material and temperature). Therefore, this effect at the measuring terminals is seen as a change in resistance (36, page 13). Given the above assumptions, a body segment modeled as a perfect right cylinder exposed to an electric field (defined by $E = V/L$; where V = voltage and L = length of the segment) with a current density given by $J = I/A$ (where I = current and A = cross sectional area), one can solve

for resistance, R, by using Ohm's Law (R = V/I). The measured impedance of the segment is then given by R = rL/A.

The resistance of biological material is a quantitative measure of the total number of conducting species in a current field. With systole, more conductors appear between electrodes so that total tissue resistance falls in an amount that is quantitatively related to net increase in blood volume (45). Recall that volume (V) for a perfect right cylinder is given as V = LA. In cases in which the length of a body segment is fixed, e.g. the forearm, the change in resistance, dR, can be expressed as a small change in volume as

$$dR = R_1 - R_o = rL/A_1 - rL/A_o \qquad \text{eq. 1}$$

where R_o and A_o are the base resistance and cross sectional area values, respectively, and R_1 and A_1 are the new values of resistance and cross sectional area, respectively. Substituting for base volume, V_o, and new volume, V_1, gives

$$dR = rL\ (\ (L/V_1) - (L/V_o)\ ) \qquad \text{eq. 2}$$

$$= rL^2\ (\ (\ V_o\ - V_1)\ /\ (V_o\ V_1)\ ) \qquad \text{eq. 3}$$

$$= -\ rL^2\ (\ (\ V_1\ - V_o\ )\ /\ (V_o\ V_1)\ ) \qquad \text{eq. 4}$$

If V_1 is not appreciably greater than V_o, then dR can be expressed as

$$dR = -\ (rL^2\ /\ V_o^2)\ dV, \qquad \text{eq. 5}$$

where $dV = V_1 - V_o$.

Electrical impedance plethysmography (EIP) is a noninvasive technique that is used to measure the change in resistance that arises from changes in volume of various biological tissues. Use of equation 5 has been classically applied in EIP to investigate cardiac and respiratory function (42) and vascular changes in body segments, such as the extremities (40), in which the assumption of cylindrical cross sectional area is valid. When investigating the state of cephalic circulation, EIP is called Rheoencephalography. However, this equation does not readily apply to analysis of resistance changes across the head (30). This is due to the shape of the head and the relative rigidity of the structure. Under normal conditions, each systole is accompanied by an influx of 6.5 ml of blood into the head corresponding to an expansion of 0.2 mm (17). There is some dispute over the amount of this volume in that Moskalenko, et al (38) report a influx of 12-15 ml of blood per systole into the head.

Changes in cardiac output are reflected in cerebral hemodynamics and registered by the REG. Changes, particularly of a diffuse or generalized nature in cephalohemodynamics, will be

INSTANTLY reflected in the REG. It is this temporal sensitivity that makes REG so attractive (45).

Contributing to the REG is the circulatory inflow from the internal carotid, vertebral, and external carotid arteries and the CSF (r for CSF is about 65 ohm-cm (8)). The REG is a function of pulsatile flow. The pulse wave causes a drop in overall impedance with its influx of electrical carriers (39). The blood contains about 45% highly resistive blood cells and about 55% highly conductive plasma (r for whole blood is about 154 ohm-cm (8)). Note that in equation 5, r is a constant throughout the cardiac cycle. Lifshitz (30) theorized that the blood entering the head with systole, which is distributed through the arterial network, would have an electrical shunting effect greater than the large mass of blood in the venous sinuses. The overall effect would be a transitory decrease in r with systole of approximately 0.1 percent. Other important resistivities are: r for brain is 250 - 300 ohm-cm, r for skin is 300 ohm-cm, and r for excised bone is 4000 ohm-cm (8). For in vivo bone, r is 300 ohm-cm, due to the blood forming elements it contains (30).

The REG also contains a slowly varying "baseline" or dc component (47). Changes in the bulk volume movement of fluid in and out of the head with respiration and changes in posture will change this value.

The REG contains an extracranial component. In general, the extracranial-intracranial ratio is strongly dependent on electrode placement and size (46). Small electrodes favor registration of superficial impedance changes (30, 46). The amount of extracranial component in the REG is one of the criticisms raised in clinical applications of this technique.

To summarize, interpretation of REG is more complex than other plethysmographic studies. The vessels of the brain are surrounded by CSF and housed within a rigid container, the skull. The REG has two main driving sources: heart rate and changes in intrathoracic pressure. REG signals must be considered as a composite of the pulsatile changes in volume (heart rate), the redistribution of blood and CSF to compensate for the increased volume, the tidal flow of blood and CSF to and from the head through changes in chest pressure action on the heart and spinal CSF space and, marginally, the velocity of blood flow (17). These changes depend on the vascular resistance of cranial vessels. Therefore, the impedance changes and the REG reflect changes in cerebral vascular resistance (16). The effect of acceleration stress on the system further complicates matters due to the bulk shifts of fluid.

REG Configurations

The basic design of the bipolar (two electrode) REG is, conceptually, very simple (see Figure 1). The body segment to be examined is connected to a resistance bridge. The excitation source of the bridge is generally sinusoidal in the frequency range of 15 to 150 kHz. Currents in this frequency range will not effectively stimulate the heart or skeletal muscle. According to Nyboer (40, page 24), when excited at frequencies between 100 kHz and 1 Mhz, a biological segment becomes a pure resistance and reactance of the tissue approaches zero. Therefore, changes in volume are directly related to conductance. The phase angle as measured between the excitation source (Figure 1, points b-d) and the bridge output (Figure 1, points a-c) does increase at frequencies greater than 1 MHz, though its sign is the same as at low frequencies. The output of the bridge is amplified and demodulated (40). The major disadvantage to the classical design is that over time the bridge must be rebalanced and care must be taken that the impedance of the arm adjacent to the subject (Figure 1, points c-d) is much greater than the impedance between the electrodes. If the latter point is not addressed then the impedance change recorded will be due in some unknown amount to the undesirable interelectrode impedance. Advantages of this configuration include the ability to detect a wide range of impedances and great sensitivity to low level impedance changes (9).

In bipolar systems, it is desirable to place the electrodes as closely as possible on a straight line joining opposite ends of the head. In this way the current flow through the interior of the head will be maximized. The longer undesirable current pathway around the head through the scalp and subcutaneous tissues will then be minimized. As the electrodes are brought closer together an increasing percentage of the superficial tissues will contribute to the overall REG signal (30) along with field effects from the electrodes themselves (i.e. nonuniform current lines). Seipel (46) conducted a series of experiments in which he varied electrode size and composition and he determined that increasing the size of the electrodes minimizes the extracranial contribution to the REG waveform. This investigation found that Sentry Silver Sircuit Pediatric Electrodes (Catalog No. 1071, Sentry Medical Products, 2615 S. Orange Ave., Santa Ana, CA 92707) provided excellent results in terms of signal quality and subject comfort.

In an effort to avoid the necessity of rebalancing and to minimize the measurement of superficial changes, a four electrode, or tetrapolar, configuration was developed (this is sometimes referred to as Rheoencephalography II). In this design two outer electrodes inject a current and two inner electrodes detect voltage changes when the signal is passed into a high input impedance amplifier (see Figure 2). Ideally, no current flows through the pickup electrodes. Therefore, the high

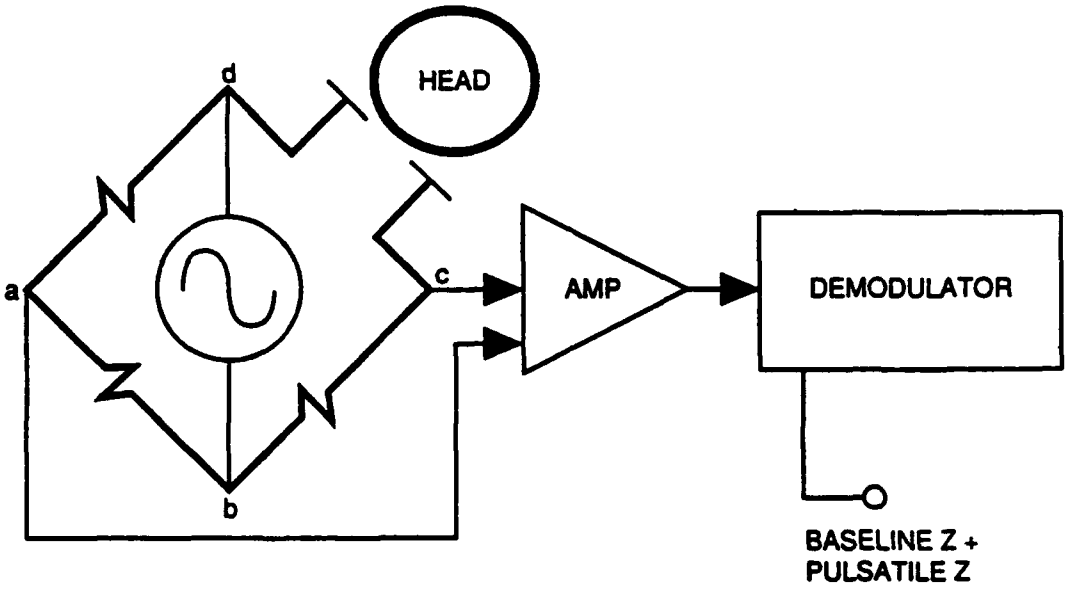


Figure 1. Basic two electrode rheoencephalograph (REG I).

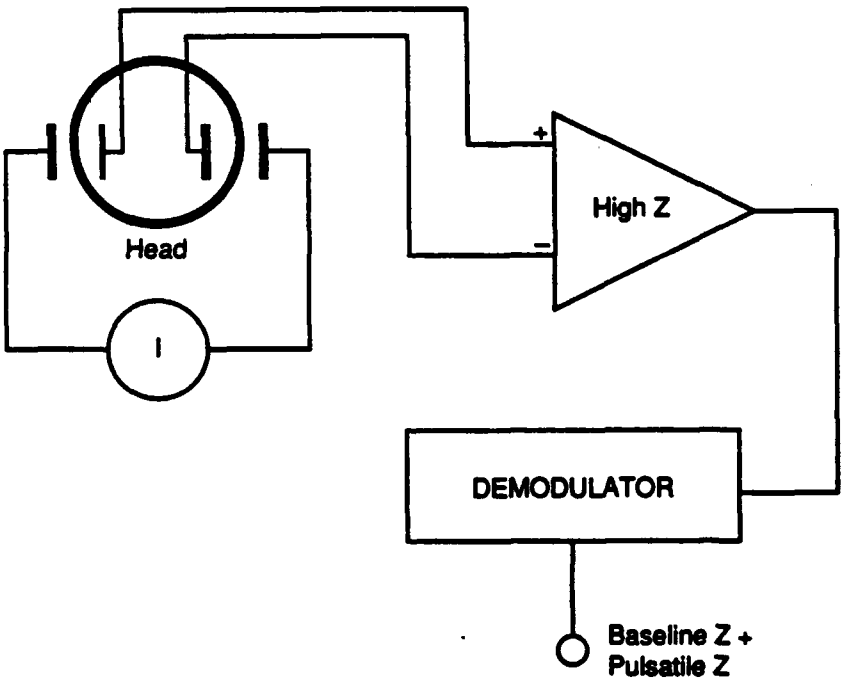


Figure 2. Basic four electrode rheoencephalograph (REG II).

impedance amplifier isolates the head and changes in voltages are directly due to changes in impedance by Ohm's Law. This occurs without introducing the effect of an impedance drop caused by current flow to the electrodes through more superficial tissues. However, events close to the detectors will distort potential current lines more than distant ones. Therefore, the current supplying electrodes and their voltage pickup counterparts should be spaced as far away as possible from their respective mates in tetrapolar systems, i.e. no closer than 3 cm (30).

The four electrodes should also be placed in a linear array. This is particularly important when the electrodes are placed on an irregularly shaped object, such as the head. For simplicity, consider a spherical head of homogeneous content and uniform r. If we placed the electrodes on either side of the head, the bulk of the current density would go directly through it. This would minimize the contribution of superficial tissues to overall impedance measurements.

The following are some possible electrode placements (these apply for both bipolar and tetrapolar configurations):

1) Fronto-mastoid - this presents a symmetrical view of the right and left cerebral hemispheres.

2) Bi-temporal - this arrangement is considered to indicate primarily vascular changes in the internal carotids.

3) Bi-occipital - this primarily indicates vascular changes in the vertebral artery area.

4) Fronto-occipital or fronto-mastoid, with the two homologous electrodes tied together - may be considered to give an average representation of the entire cerebral circulation (30).

While the tetrapolar design does eliminate the need for balancing the bridge, its use on the head is complicated by the shape of the skull. It is difficult to obtain the proper linear arrangement of electrodes to provide essentially intracranial measurements. Bipolar configurations are more sensitive to small variations in resistance than the tetrapolar and it is easier to apply on the head given the geometric constraints.

Clinical Problems With REG

In the late 1960's and early 1970's, the use of Rheoencephalography held high promise in clinical neurology. The method is noninvasive, convenient, and adaptable to both patient monitoring and diagnosis of cerebral vascular disorders. It is non-intrusive and objective. Some problems attributed to the clinical use of REG include a relative lack of anatomic selectivity and rather major signal "artifacts" upon changes in posture (particularly in the cranio-caudal axis) and respiratory efforts, such as the Valsalva maneuver. Its use was discontinued clinically in the USA with the advent of CAT and MRI scanning

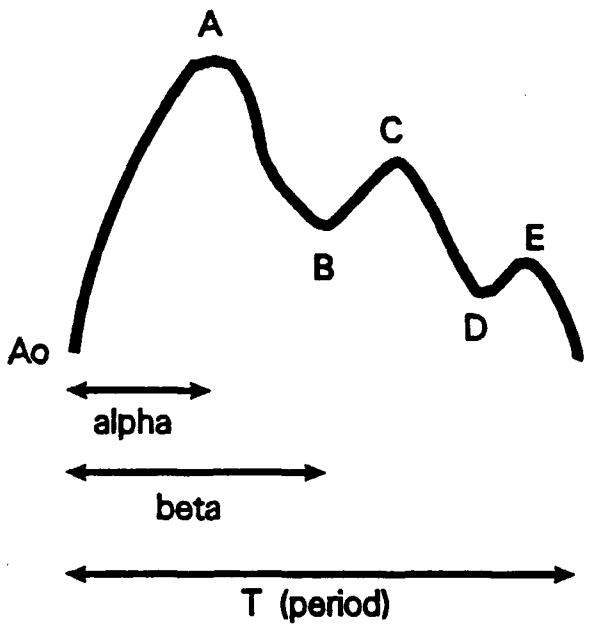
devices. The use of REG for the evaluation of cephalic circulation under conditions of acceleration stress is warranted because the very same "artifact" which apparently interferes with the use of REG in clinical neurology is of critical interest in acceleration studies; namely, the bulk movement of blood between the head and the rest of the body with postural (gravitational field orientation) changes and respiratory maneuvers. Also, in acceleration studies, it is of interest to monitor the total cephalic circulation not just the intracranial component.

Interpretation Of Pulsatile REG (Zpul) Waveform

The form of the pulsatile REG waveform, or Zpul, is quite variable and is subject to change depending on the state of the cephalic vasculature, CSF and intrathoracic pressures, size and placement of the electrodes, and preparation of the electrode site. It has a few prominent features, the size and timing of each can give an indication of the ebb and flow of the cephalic circulation (see Figure 3).

There is an initial large peak, usually a global maximum, called an "**A**" wavelet. This occurs with the systolic phase of the cardiac cycle and the peak of the **A** wavelet follows the R wave of the ECG (under normal conditions) by an average of 300 msec. Under certain conditions (see below) a "pre-systolic wave" occurs during the rise of the **A** wavelet. A downward inflection, the "B" wavelet, follows the **A** wavelet and is similar in appearance to the dichrotic notch seen in arterial pressure waveforms. Following the **B** wavelet is another rising peak, usually smaller in magnitude than the **A** wavelet, called the "**C**" wavelet. Following this peak there can be a number of smaller inflections before the end of the period of the waveform. The period, "T", is the same length as the ECG R-R interval. The time from the initial rise of the **A** wavelet to the peak is called the REG peak time (**a**) and the ratio **a**/T is called the "rheographic time." Some authors also measure the angle of inclination of the rising **A** wavelet and use it to determine the "expansion rate" of cerebral vessels, expressed as the tangent of that angle (41). It is important to realize that the REG in its present state ONLY provides information on the RELATIVE state of the cephalic circulation. Therefore, the REG contains valuable information as expressed by changes in rheographic indices that result when comparing unstressed waveforms to those measured during acceleration stress or functional testing.

Clinical investigators have used these features and along with the results of functional tests, e.g. orthostatic tests, inhalation of CO_2, performance of straining maneuvers, etc., and correlative measurements (5,16,23,39) have proposed a number of indices to evaluate Zpul as follows:



A = Peak systole
C = Overall venous pressure & impeded venous outflow
B/A = Arteriolar tone
C/A = Venous tone
alpha/T = large & intermediate vessel tone
alpha = steeper slope means reduced tone
T = ECG R-R interval

Figure 3. REG indices and a list of clinically derived interpretations of their physiological significance.

1. **A** wavelet: this is referable to the peak of the systolic inflow of blood into the cephalic circulation. This observation is based on studies employing vasodilators, such as CO_2 (39);

2. **C** wavelet: this is associated with overall venous pressure and the relative amount of impedance to venous outflow, based upon studies using intravenous injection of nicotinic acid (17);

3. **a/T**: this gives information as to the elasticity and tone of large and intermediate size vessels, i.e. CVR (23,38). Correlative studies by Hadjiev (16) and Jacquy et al (23), using radioisotopic clearance measurements, have been conducted to support this claim;

4. B/A: this ratio gives an indication of arteriolar tone (23,37,38), based on experiments in which chemical agents affecting vascular tone altered the timing and amplitude of the REG "dichrotic notch";

5. C/A: changes in this ratio indicate alterations in blood outflow and venous tone. This observation is based on the effects of functional testing, such as anti-orthostatic tests which promote venous congestion (37,38);

6. **a**: a shorter **a**, and therefore a steeper **A** wavelet, is an indication of decreased vascular tone (23);

7. Pulse wave delay: this is the time from the peak of the R wave of the ECG to the peak of the Zpul **A** wavelet. McHenry (35) noted that this delay was prolonged with increased CSFP. He attributed this change to an increase in pulse propagation time or to an increase in venous pressure. This explanation may be inadequate in the case of an increase in pulse wave delay under a +Gz load (22);

8. Pre-systolic wave: Hadjiev (17) noted that there was no direct association with this wave and overall venous pressure or changes in CSFP. He attributes this to regional fluctuations in the filling of cerebral veins.

Most of these measures will reflect changes in CVR. Pathologic deviations or exposure to a high +Gz field will be manifested by signs of dilated or constricted vascular lumen. Therefore, changes in the shape of Zpul and the indices may give information on the existence of vascular dystonia and alterations in cephalic venous outflow.

To summarize, these are the alterations in Zpul that accompany changes in CVR, according to Hadjiev (17):

1. Reduced vascular tone:

a. steep rise of ascending portion of the **A** wavelet (decreased **a**);

b. increased blood filling (decreased impedance as reflected in the **A** wavelet);

c. sharp peak of **A** wavelet;

d. overt incisure (**B** wavelet) located in the lower third of the descending portion of the curve or very close to the baseline.

2. Increased vascular tone:

a. slower rise of ascending portion of the **A** wavelet (impedance is altered more slowly due to impeded blood inflow);

b. decreased blood filling (increased impedance as reflected in the **A** wavelet);

c. rounded peak of **A** wavelet;

d. poorly defined incisure (**B** wavelet) located in the upper third of the descending portion of the curve.

Factors other than those affecting CVR contribute to the overall state of the cephalic circulation and therefore indirectly affect Zpul. The skull limits the amount of expansion of the brain to compensate for increased blood volume which leads to blood and CSF redistribution. The CSF acts to keep the venous circulation patent by following changes in venous pressure with similar changes in CSFP. Finally, the lumen and tone of the cerebral vessels are influenced by arterial and venous pressure, heart rate, and some metabolic factors, e.g. P_{CO2} and arterial pH.

Many laboratories have used different REG instruments or have taken standard EIP devices not designed for use on the head to perform rheoencephalographic measurements. The REG device that was developed in the course of this project is unique, particularly since it treats the baseline of dc REG (Zdc) as a source of useful information, not as an unwanted artifact. This device was designed to be operated in the high +Gz-stress environment for use on both human and animal subjects. A block diagram of the device is shown in Figure 4. Details of the construction of the device can be found in chapter three of NADC Technical Report NADC-89042-60 (50).

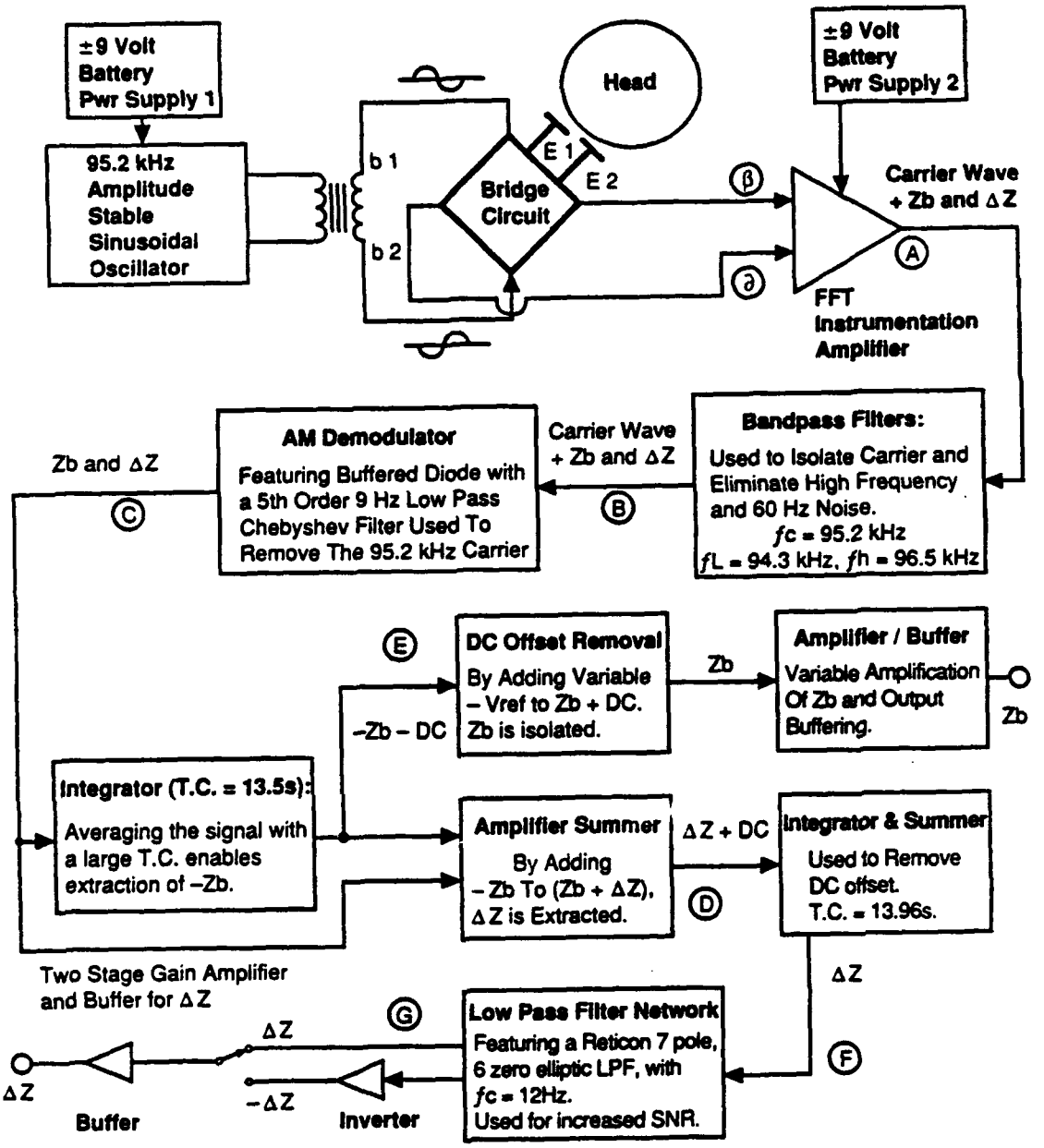


Figure 4. Block diagram of circuit used to detect impedance changes due to pulsatile changes in blood volume, cephalic baseline impedance shifts due to respiration and M1/L1 maneuvers, and bulk movement of cerebrospinal fluid in and out of the skull (REG).

KEY

E1-2 : Electrode connections from the bridge circuit to the subject's head.
Zb : Baseline impedance reflecting bulk movement of blood in and out of head. (Zdc)
ΔZ : Pulsatile impedance change (≈ 20 – 200 mΩ). (Zpul)

METHODS

Human Centrifuge Experiments

All experiments using the REG were performed on volunteer subjects under the NADC Advisory Committee for the Protection of Human Subjects Protocol No. ACPHS 190, along with separately approved test plans for each study. A total of 58 subjects participated under this protocol. The following are brief descriptions of the studies. Results from a selection of these investigations are presented in Section 4.0. Study results not presented in this report will appear in a subsequent document.

The first human centrifuge experiment (CE1) was performed on a single day (April 30, 1987) in conjunction with another experiment in which an inertia reel was tested. Acceleration runs were performed on six male adult subjects riding on the human centrifuge at NADC (48). These were "familiarization" runs in which LOV was not seen nor expected. The subjects were exposed to gradual onset +Gz-stress (at a rate of 0.3 Gz/sec) from +1 to a maximum of +3 Gz. They were maintained at +3 Gz for 25 second plateau and then returned to +1.03 Gz at a rate of 0.1 Gz/sec. During each insertion, two rapid onset runs, ROR, were also performed. In these maneuvers, +Gz-stress was altered in the following manner: +Gz was decreased from +1.8 to +1 Gz in two seconds, maintained at +1 Gz for ten seconds, then increased to +1.8 Gz in two seconds. At the same time -Gx (acceleration from chest-to-spine) was changed from 0 to -1.5 Gx and back to 0 Gx, mimicking the change in +Gz.

The following data were recorded onto strip chart and FM tape for each experiment:

1. EKG (orthogonal lead configuration);
2. pulsatile impedance, Zpul, recorded off of the forehead;
3. "baseline" impedance, Zdc ;
4. superficial temporal artery infrared plethysmograph (IRP);
5. acceleration in the +Gz and -Gx planes.

The purpose of this first series of runs was to demonstrate the ability of an early version of the REG device to perform under acceleration stress on humans. After successful completion of this task, data was examined and processed in a preliminary attempt to characterize acceleration induced changes in REG indices. Based on these results, the REG device underwent a few refinements, particularly in the area of control of the output waveforms, i.e. Zpul baseline wander control and improved Zdc quality.

The second experiment (CE2) was conducted in November of 1987 in conjunction with a study in which automatically reclining aircraft seats were evaluated. These included a tilt-back and

PALE (pelvis and legs elevating) seats. The tilt-back seat design was based on the principle of counterbalancing of moments about an acceleration sensitive pivot point. Of most interest were the results obtained from the runs using the PALE seat, which in this experiment served as the control. These runs afforded an opportunity to not only test the REG instrument at higher onset rates and acceleration levels, but to determine the effects of anti-G protective devices on the impedance waveforms.

Five Navy corpsmen wore MA-2 harnesses and standard Navy anti-G suits (AGS), which were inflated according to the equation:

$$((\cos(SBA)\ (Gz))\ -1)(1.5). \qquad \text{eq. 6}$$

The maximum +Gz allowed was +7 Gz and maximum inflation pressure was 5.25 psi. The subjects were exposed to a series of ramp type profiles in which the onset/offset rates were 0.1 Gz/sec, 0.5 Gz/sec, and 2.3 Gz/sec. These profiles included a +7 Gz plateau that was maintained for five seconds. Subjects were also exposed to a series of low level simulated aerial combat maneuvers (SACM) that were used to test the ability of the tilt-back seat to rapidly and comfortably follow the +Gz load about the acceleration sensitive pivot point. This was in contrast to earlier experiments in which a reclining seat was simply set at larger than usual angle from the vertical, e.g. 60° (21). The tilt-back seat was set at an initial SBA of 30° and reclined to a maximum of 70° at approximately +3.0 Gz. The PALE seat was initially set at 25° and reclined to 65° at approximately +6 Gz +/- 0.5 Gz, depending upon the onset rate. Physiological data (ECG, Zpul, Zdc, and respiration) and mechanical data (SBA, AGS pressure, and Gz) were recorded.

During these experiments two different electrode types were employed. One was a commercially produced 25 x 38 oval flexible, self adhesive, silver-silver chloride pediatric long-term monitoring type (Sentry Medical Products, #1071, 2615 So. Orange Ave., Santa Ana, CA 92707). The other was the author's own design consisting of a 20 mm diameter hypoallergenic stainless steel reusable disk. Use of either design produced useable results though the former design proved to be more convenient to use.

The third experiment (CE3), held in February, 1988, was performed along with a study conducted by the Naval Aerospace Medical Research Laboratory (NAMRL) in which the effects of exercise on +Gz-tolerance was investigated. These trials were held over two weeks and involved 20 volunteer subjects, 18 of which were aviators. Subjects were placed in a 15° SBA ESCAPAC seat, wore a MA-2 flight harness and no helmet, and performed a tracking task. There were two phases of each subject's high +Gz exposure. Relaxed tolerance, using an inflated AGS without performing AGSM, to 15 second plateau, two second onset/offset rate ROR profiles was determined. These runs started at +2.5 Gz

and increased in 0.5 Gz increments until the highest level in which the subject could maintain peripheral vision (defined as a 60^{o} forward visual cone) for the full 15 second plateau. This was the relaxed tolerance limit, or G_{15} level. Following these runs, two straining runs to G_{15} +1 Gz and G_{15} +2 Gz plateaus were conducted. After these runs, relaxed +Gz-tolerance determination was repeated. The next insertion, usually one to two days later, was a two part SACM in which a relatively equal amount of workload was imposed on each individual based on their G_{15} level. The first part consisted of a 15 second warm-up plateau of 1.75 Gz, then a two second rise to the G_{15} level for ten seconds, then alternating one second rise to G_{15} + 2 Gz for ten seconds and back down to G_{15} for ten seconds until the subject decided he was too fatigued to continue. After a one minute rest period, the second part of the SACM runs took place. These runs were an alternation from 1.75 Gz for ten seconds to G_{15} + 2 Gz for ten seconds and back to 1.75 Gz until the subject stopped the run. The latter SACM was run to ensure that the metabolism of motivated subjects would be functioning anaerobically.

Physiological data (ECG, Zpul, Zdc, IRP, doppler blood velocity at the superficial temporal artery, upper arm blood pressure recorded automatically each minute, before and after SACM blood lactate levels, and respiration) and mechanical data (AGS pressure, light bar tracking, and Gz) were recorded. The IRP was placed on the right temple over the superficial temporal artery, the doppler ultrasound velocimeter was placed over the left temple and the REG electrodes (Sentry Medical Products) were placed bi-occipitally. Respiration was measured as thoracic and abdominal excursions as measured by a strain gauge type device, a Respitrace™.

For these trials further improvements in the REG device were made including changes to both the Zpul and Zdc processing circuitry. These runs afforded an opportunity to test the REG on large numbers of individuals under conditions in which comparisons could be made in terms of the response of the REG device to relaxed vs stressed environments. Determination of the effects of anti-G protective maneuvers on the impedance waveforms was now also possible.

The fourth procedure (CE4), from November, 1988 to January 1989, was performed in conjunction with training the first thirteen volunteers for the NADC Human Acceleration Subject Panel. The purpose of these exposures was to familiarize the subjects with the centrifuge gondola, experimental procedures, vision tracking, anti-G straining maneuvers (AGSM), and to determine the +Gz-tolerance of these subjects to a variety of anti-G protective modalities. These included no protection ("relaxed" tolerance), Navy AGS alone, AGSM alone, or a combination of AGS with AGSM during either gradual onset (GOR at 0.1 G/sec), rapid onset (2 second onset/offset, 15 second plateau haversine) exposures or AGSM (as described in CE3, above).

Endpoints were loss of peripheral vision down to a forward 60° cone.

Physiological data (ECG, Zpul, Zdc, IRP, doppler blood velocity at the superficial temporal artery, and oxygen saturation measured over the bridge of the nose (SaO_2) and mechanical data (AGS pressure, light bar tracking, and Gz) were recorded. The IRP was placed on the right temple over the superficial temporal artery, the doppler ultrasound velocimeter was placed over the left temple and the REG electrodes were placed bi-occipitally.

The fifth procedure (CE5), April - June 1990 was a continuation of the reclining seat study in which both seats were again tested. During this series, besides measures of +Gz-tolerance with the PALE and tilt seat, cognitive tests were performed. The PALE seat began to elevate at 2.5 G radial and rose at a rate of 20°/sec. The higher Gx loads required that additional respiratory support be given so pressure breathing for G using a standard PBG mask and helmet and a counter pressure jerkin was employed. PBG began at 4 Gr and increased at 12 mmHg/Gr up to a max of 60 mmHg at 9 Gr. 5 mmHg safety pressure used by PBG regulator. Four subjects participated in both phases of the experiment, in which they were exposed to as many as 150 haversine G runs.

The experiment was divided into two phases, each using either the PALE or tilt seat. Phase I consisted of a determination of G tolerance based on the amount of anti-G protection provided. These runs started at 2.5 G for 15 seconds and the G level was incremented in 0.5G steps until 60° peripheral light loss was noted. No anti-G straining maneuvers were used. The conditions included:

1. No operating anti-G suit (AGS);
2. No operating AGS with PBG activated;
3. Operational AGS;
4. Operational AGS with PBG activated;

Each of these four conditions occurred both Upright (27° SBA) and Supine (67° SBA) using either seat. The PALE seat began supination at 2.5G at a rate of 20° per second to maximum of 67°.

During the second phase of the experiment, subjects were protected by operational AGS and PBG gear, upright and supine, while performing a variety of cognitive tasks. These included:

1. Cross hair tracking
2. Cognitive A: determine whether a sequence of symbols represented an even or odd number;
3. Cognitive B: same as A with the additional determination of whether the sum of the symbols was greater than a presented target value;
4. Cognitive A or B along with cross hair tracking.

Cognitive task runs started at 3.0G increased in 0.5G steps to the highest G level attained for 15 seconds during Phase 1 (G-tolerance level).

Physiological data (ECG, Zpul, Zdc, pulsatile and dc infrared plethysmograph (IRP), pneumotach, and heart rate) and mechanical data (AGS pressure, peripheral vision indicators, mask pressure, breathing regulator, head Gx, head Gy, head Gz and Gz) were recorded. The IRP was placed on the ear and the REG electrodes (Sentry Medical Products) were placed bi-occipitally. The IRP was modified to output both pulsatile and dc output signals. Changes in the dc IRP reflect bulk shifts of blood in similar to the dc REG.

The sixth procedure (CE6), September 1990, was performed along with a study conducted by the Biomedical Engineering and Science Institute of Drexel University in which the effects of a pulsating anti-G suit (PAGS) on +Gz-tolerance was investigated. Twelve subjects participated. The PAGS consists of three sets of valves, a pressure reservoir, safety valve, pressurized air supply, computer and hardware interface. A standard Navy AGS was specially modified such that the 2 calf, 2 thigh and the abdomen bladders could be inflated separately. Different inflation schemes were tested which synchronized the inflations to heart rate (except when the PAGS was operated in the standard mode) such that all bladders were pulsed simultaneously or sequentially from calf to thigh to abdomen. The pressures were superimposed on the standard inflation regime (eq. 6) were +/- 1.5 psi. Rapid onset and gradual onset runs were performed as described in CE3 except that the ROR plateaus were 25 seconds long. A maximum inflation of 11 psi was used which corresponded to a +7.1 Gz maximum. Endpoints were loss of peripheral vision down to a forward 60^{o} cone.

Physiological data (ECG, Zpul, Zdc, photoplethysmograph (IRP), doppler blood velocity at the superficial temporal artery, and heart rate) and mechanical data (AGS pressure at calf, thigh and abdomen, peripheral vision indicators, and Gz) were recorded. The IRP was placed on the right temple over the superficial temporal artery, the doppler ultrasound velocimeter was placed over the left temple and the REG electrodes (Sentry Medical Products) were placed bi-occipitally.

RESULTS AND DISCUSSION

Data Analysis

The REG has been constructed and has undergone testing at both 1g and under acceleration stress in the NADC human centrifuge. The REG has withstood stresses of at least +14 Gz. Measurements on human subjects have been taken at extremes of +10 Gz and -1.5 Gx. One of the most notable features of the Zpul

waveform is its highly variable nature. There was also great variability in response both intra- and inter-subjects and individual subjects served as their own controls, using pre-stress data. As such, data were calculated and analyzed based on the relative change before and during G-stress.

In order to orient the reader, a modified "Wiggers" diagram in which the timing of Zpul with respect to other cardiovascular events (ECG, venous pulse, ventricular volume, aortic blood flow, and various pressures) is presented in Figure 5. The Zpul waveform is an average of six waveforms obtained from one subject at 1 g.

To account for random noise sources, groups of five to eight REG waveforms were averaged for analysis. According to the hydrostatic column theory of +Gz-stress, cardiovascular system (CV) reflexes should be active after about 10 seconds, depending upon the rate of application, level and duration of the stress. To attempt to follow these reflexes during rapid onset runs, REG samples were taken within 20 seconds prior to G onset, between 0-5, 5-10, and 10-15 seconds during plateau and 5-10 and 15-20 seconds after G offset. Samples were calculated during 0.5 G intervals during gradual onset runs.

Data were analyzed in both the time and frequency domains. Time domain analyses included calculation of the REG indices, including the magnitude of the A (systolic volume), B, C (venous pressure) peaks, the ratios B/A (arteriolar tone) and C/A (venous tone) and the period T. Timing parameters included the rise time of the slope (a, where a decrease in a means reduced tone or larger vessel diameter), the ratio a/T (large and intermediate vessel tone), the time until the B peak (beta) and the time until the C peak (gamma). Power spectral densities were performed on Zpul and electrocardiograms. It was found that under stress, the frequency content of Zpul changes, possibly reflecting greater respiratory influence.

Due to its highly variable nature, automatic data processing of Zpul must be used very carefully in order to trust its evaluations. A discussion of the difficulties in automatic REG processing is found in (50). As such, data processing was done by hand using strip charts directly or through the use of DaDISP (Data Analysis and Digital Signal Processing Software, DSP Development Corp, One Kendall Square, Cambridge, MA 02139) after the data was digitized using sign extended 12 bit A/D hardware and software (Data Translation DT2821-G-16SE and ATLAB (SP0143, V01.11), respectively - Data Translation, Inc. 100 Locke Drive, Marlboro, MA 01752-1192). Statistical analyses included one-way and two-way ANOVA and paired t-tests using the Number Crucher Statistical System, Version 5.0 (NCSS, c/o Dr. Jerry L. Hintze, 865 East 400 North, Kaysville, Utah 84037). It is important to point out at the onset of this discussion that demonstration of statistical significance does not imply clinical or experimental

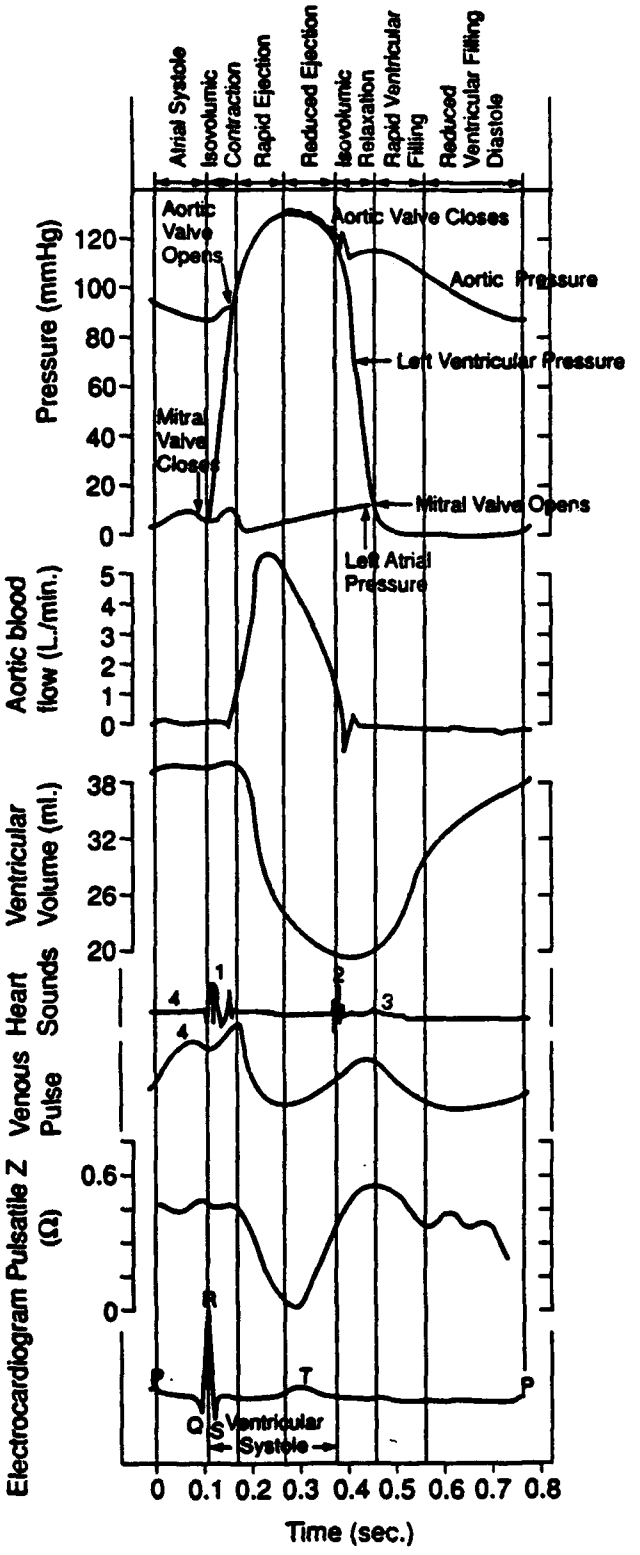


Figure 5. Modified Wigger's diagram including pulsatile REG (Z).

significance. Statistical significance can merely determine whether or not events occur due to chance alone.

Effects of G-stress and modes of anti-G protection

Experiment CE1

During CE1, the earliest version of the device was used which had no calibration switch, small surface area electrode were used (10mm gold or silver-silver chloride Grass ECG cup electrodes), and there was much noise in the signal. These measurements were taken at low G levels on a single day. The purpose was to demonstrate ability of device to survive in a G environment and to output signals over the slip ring assembly.

The analysis of the data obtained during CE1 was centered on the best available data, i.e. from subjects S1 and S5. For this analysis, data used were from gradual onset runs (GOR) and rapid onset runs (ROR). For S1, these started at +1.03 Gz and for S5, these started at +1.8 Gz.

Zdc contained a rather large dc offset that obscured the low level changes in Zdc seen in subsequent experiments. However, upon careful examination of the strip charts, Zdc changed in magnitude and followed the +Gz trend, indicating a shift of blood out of the head. Unfortunately, the magnitude of these changes with respect to those at 1 g was insignificant.

One expects that under a +Gz-load, cephalic fluid volume should be reduced causing the number of electrical conductors to decrease, leading to an increase in impedance which would be reflected by an increase in the amplitude of the A wavelet. Comparison of the effects of acceleration during GOR exposures to S1 and S5 on A wavelet amplitude were inconclusive. For both individuals the A wavelet initially decreased as acceleration approached +1.8 Gz. "A" wavelet amplitude for S1 then increased until the acceleration was offloaded (see Figure 6). In the case of S5, however, A wavelet amplitude oscillated (see Figure 7). There was certainly enough time for compensation to occur though it is difficult to conclusively state that from A wavelet analysis alone.

As was found by Hrebien in doppler ultrasound studies of the superficial temporal artery under +Gz-stress in humans (22), there was a similar relationship between the time of the occurrence of the ECG R wave and the subsequent peak of the A wavelet and the imposition of a high +Gz load (the "delta delay", DD). As +Gz increased, the delay also increased linearly. The peak of the A wavelet occurred approximately 320 msec after the "R" wave at +1 Gz and about 360 msec after the "R" wave at +3 Gz. These values were somewhat higher than those reported by Hrebien but the acceleration profiles were also quite different. These trends are found for S1 and S5 in Figures 8 and 9.

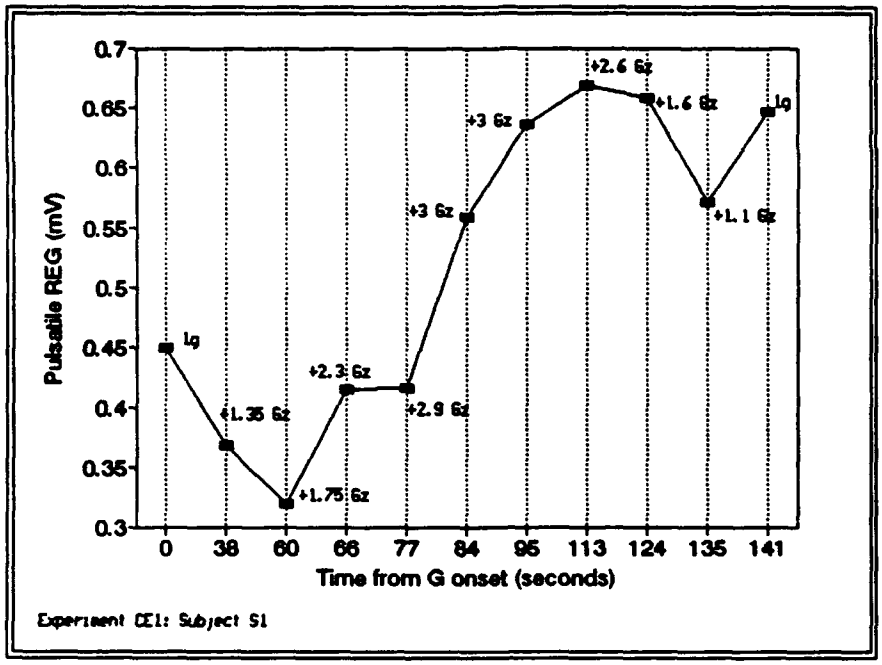


Figure 6. Effects of increasing +Gz-stress during GOR on amplitude of averaged A wavelet.

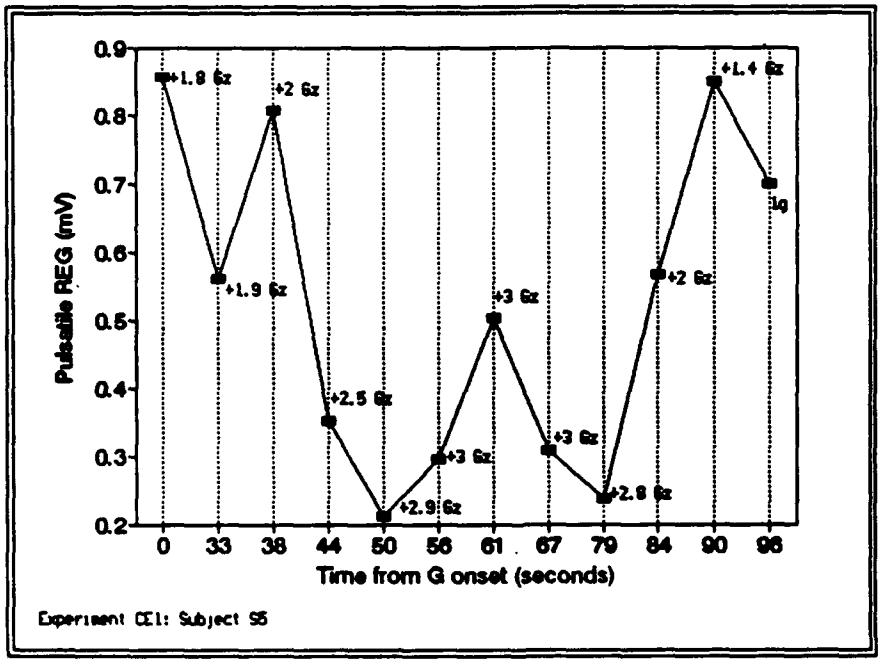


Figure 7. Effects of increasing +Gz-stress during GOR on amplitude of averaged A wavelet.

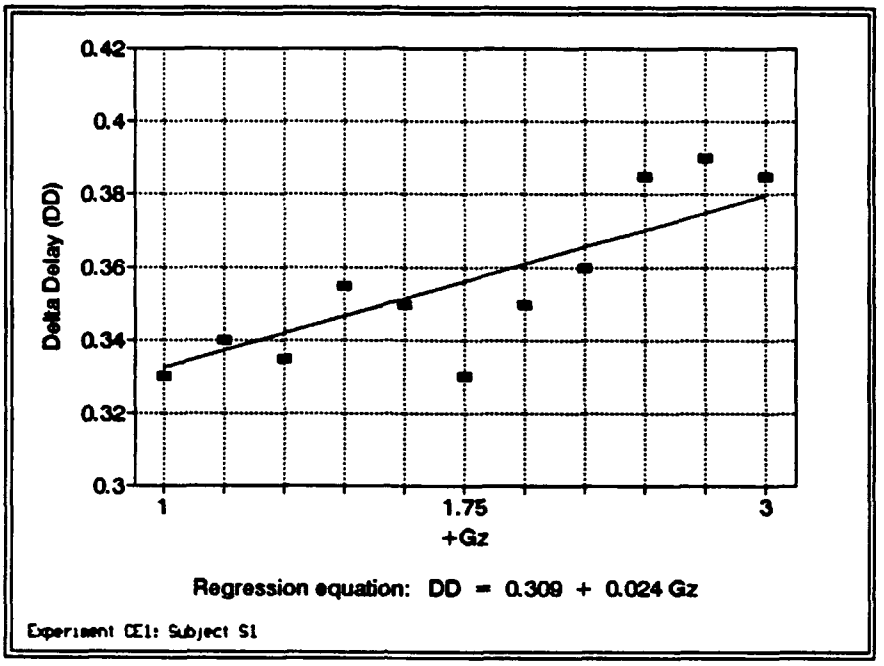


Figure 8. Pulse wave (delta) delay (DD) during experiment CE1; Subject S1.

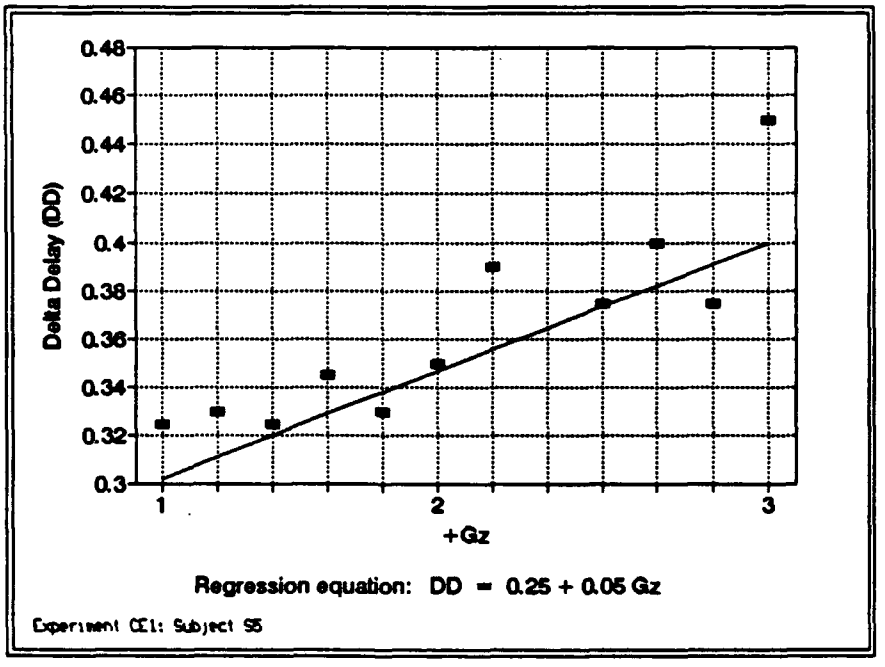


Figure 9. Pulse wave (delta) delay (DD) during experiment CE1; Subject S5.

The linear regression equations are:

S1: DD = 0.309 + 0.024 Gz; R^2 = 0.89 , eq. 7

S5: DD = 0.25 + 0.05 Gz; R^2 = 0.80 . eq. 8

In the course of examining the frequency content of the signals, several interesting features became apparent. The frequency content for GORs is shown in Tables 1 and 2. Under +Gz-stress the frequency content of Zpul changed whereas the frequency content of both the ECG and the IRP remained the same. Waterfall plots of the effect of increasing acceleration stress on frequency content are shown for Zpul in Figure 10 and for the IRP in Figure 11. This changes occurred even though heart rate only rose during the onset to plateau periods, from 88.9 to 108 bpm (S1) and from 86.3 to 101.7 bpm (S5). The most notable change seen under a +Gz load included an increase in frequency content of the primary lobe at +3 Gz (from about 2 Hz to 4 Hz, for S1, to 5.8 for S5) and a reversal from minima to maxima at +3 Gz at about 9.5 Hz. There was another change from an unstressed frequency maxima to a stressed frequency minima, though these occurred at different frequencies (S1: 6.4-6.8 Hz and S5: 8.6 Hz).

+Gz	FREQUENCY (Hz)	MAGNITUDE(dB)	MAXIMA or MINIMA
any	2 to 2.6	0 to -1	maxima
3	**2 to 4**	**0**	**maxima**
any	4 to 4.5	0 to -5	maxima
any	7.2 to 8.2	-11 to -20	maxima
any	10.6 to 11.6	-20 to -31	maxima
any	5.4 to 7	-12.5 to -34	minima
any	9 to 10.6	-22 to -34	minima
< 3	6.2 to 6.4	-12.25	maxima
3	**6.4 to 6.8**	**-21.5**	**minima**
< 3	9.4 to 10	-30.1	minima
3	**9.6**	**-14.5**	**maxima**

Table 1. Subject S1: Zpul frequency content changes with increased +Gz load. Reversals from maxima to minima and vice versa at +3 Gz are shown in bold face. Runs were gradual onset.

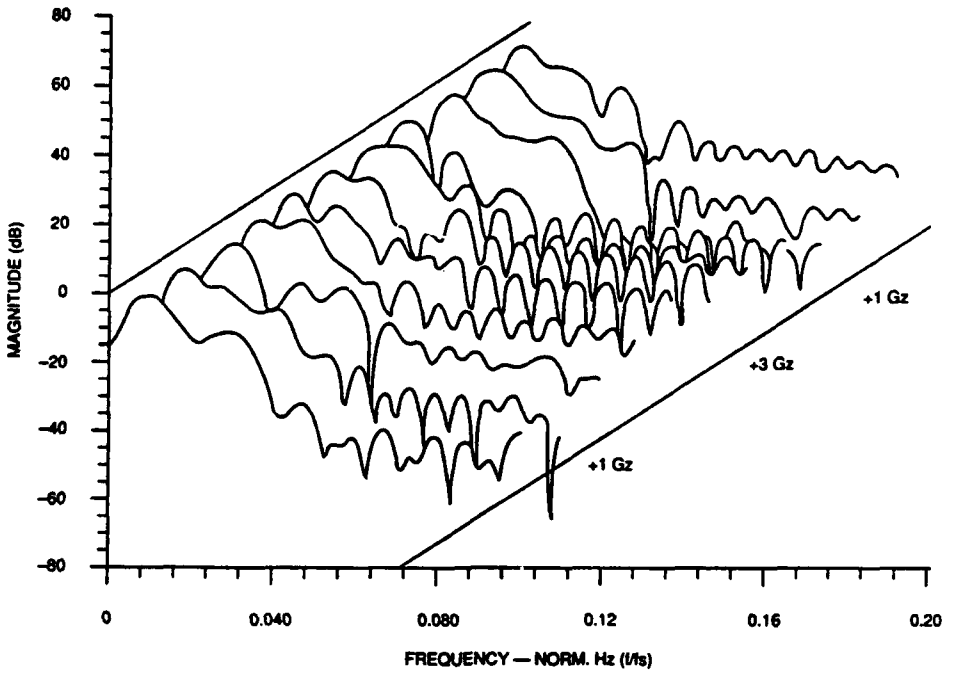


Figure 10. Power spectral density of Zpul as acceleration load varies from +1 to +3 to +1 Gz.

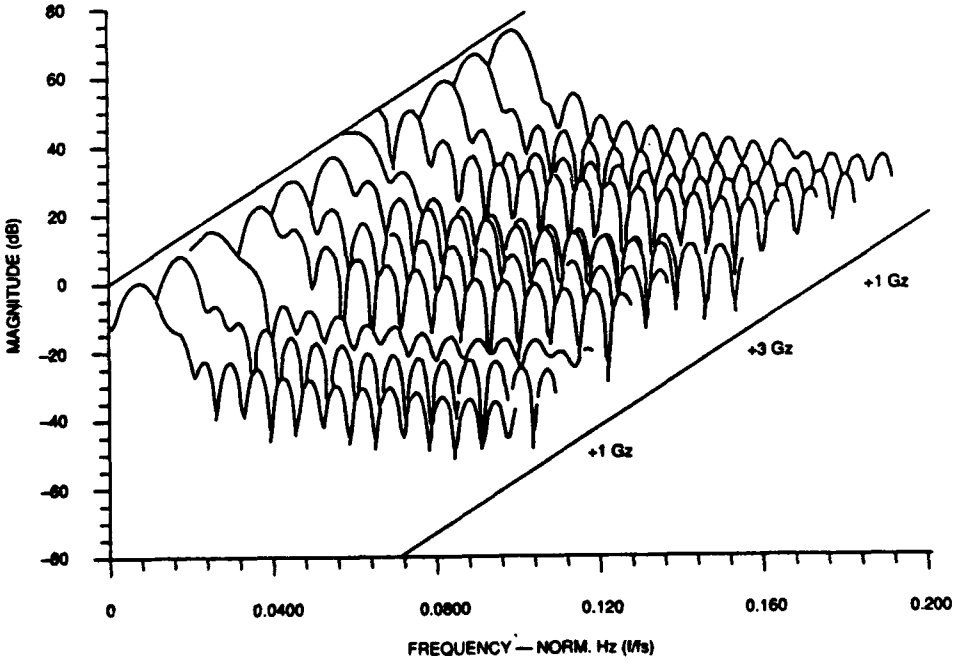


Figure 11. PSD of infrared plethysmograph on superficial temporal artery as +Gz-load varies from +1 to +3 to +1 Gz.

+Gz	FREQUENCY (Hz)	MAGNITUDE(dB)	MAXIMA or MINIMA
any	1.8 to 2.4	0	maxima
< 3	4 to 5.4	-15.5	minima
3	1.8 to 5.8	0	maxima
any	5.4 to 6.2	-7.75	maxima
any	10.6 to 11.4	-17.5	maxima
any	6.4 to 6.8	-19.25	minima
3	9.4 to 9.8	-16.5	maxima
< 3	9.4 to 9.8	-30.4	minima
3	8.6 to 9.2	-25.9	minima
< 3	8.6 to 9.2	-18	maxima

Table 2. Subject S5: Zpul frequency content changes with increased +Gz load. Reversals from maxima to minima and vice versa at +3 Gz are shown in bold face. Runs were gradual onset.

Experiment CE2

In this study, the effects on REG waveforms of a common technique to increase +Gz-tolerance, i.e., reclining the seat back from the vertical was investigated. Of most interest in this study was the effects of changing seat-back-angle (SBA) under acceleration on Zdc while the subjects were seated in a PALE (pelvis and legs elevated) seat. Results from this experiment were presented at the 1988 Annual Scientific Meeting of the Aerospace Medical Association (see 49 for the abstract).

As a +Gz-load is applied to a subject, there is a fluid shift out of the head down towards the abdomen and large capacitance veins of the legs. If Zdc does indeed reflect the bulk movement of blood in and out of the head, then one should see a change in inflection in the waveform in conjunction with applied stress. Under 1 g conditions, Zdc remains fairly stable without much change in the overall signal level. With the application of stress, Zdc decreases along with the increasing +Gz load during a "relaxed" run (see Figure 12). A relaxed acceleration exposure usually consists of a subject wearing a standard anti-G suit, which may or may not be inflated, a flight harness, and the subject does not perform an anti-G straining maneuver. In fact, as acceleration increases so does the magnitude of change in Zdc. As the +Gz load is lifted, Zdc returns back to a consistent level that is approximately the same as the prestress levels. Prior to attaining this level, there is an overshoot in the waveform. This overshoot is consistent with the onrush of blood back into the head and increased blood pressure (10, page 622) that occurs to compensate for the temporary acceleration induced loss in volume. Signal overshoot

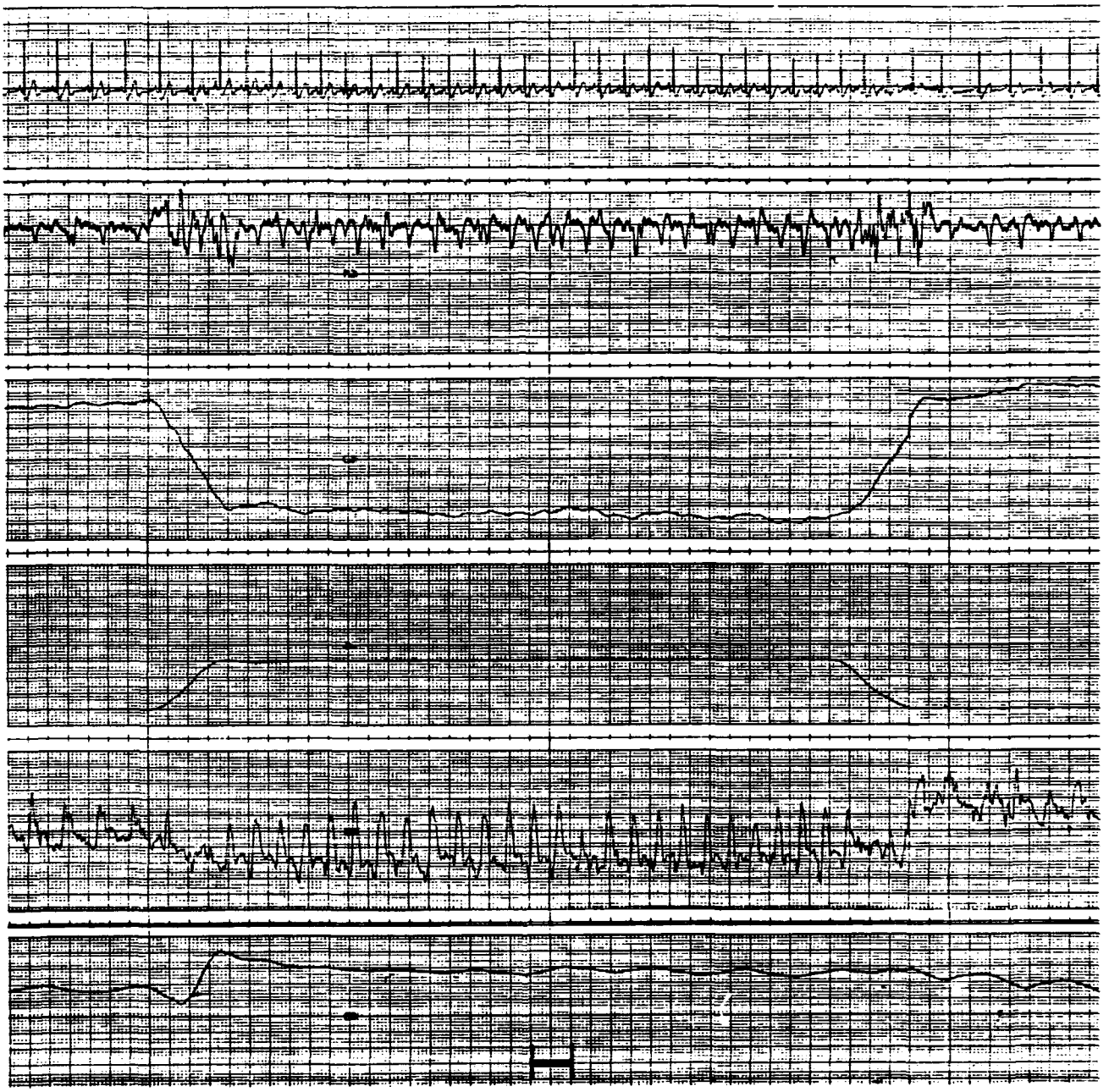


Figure 12. Effect of +Gz-load on Zdc. This example was taken during a +4 Gz ROR exposure. From top to bottom: ECG, Zpul, Zdc, +Gz, ultrasound doppler of superficial temporal artery, thoracic breathing excursions. Note change in REG period during plateau and overshoot in Zdc above prestress level as +Gz is off-loaded. Horizontal bar denotes one second.

has also been seen in doppler ultrasound velocimetry recordings under a +Gz load performed in the human centrifuge at NADC.

In experiment CE2, during relaxed +Gz exposures, as the +Gz-load is applied the magnitude of Zdc changed along with the applied stress. However, as the seat approached a 40° to 50° SBA, the decline in Zdc reversed and Zdc either started a slow rise or maintained a constant level higher than under relaxed conditions but lower than unstressed values. An sample strip chart recording of a +1.0 Gz/second onset rise to a +7 Gz, 5 second plateau run is shown in Figure 13. This change in inflection (marked with an arrow in the figure) occurred at this range of angles regardless of onset rate and corresponding +Gz level. For clarity, plots of percent change in Zdc, {%Zdc ((|Zdc at +1.03 Gz| - |Zdc at Gz > +1.03|) / |Zdc at +1.03 Gz|)} versus run time, SBA, and +Gz level for two subjects (MB and ES) during a GOR (+0.5 Gz/second) are shown in Figure 14. This indication of increased cephalic circulation and therefore ability to withstand higher acceleration stress occurs at an angle which is consistent with the studies done by Harald von Beckh at NADC in the 1970's (58). In that study he reported an increase in +Gz-tolerance at a SBA of 45°. During experiment CE2, the average SBA in which there was an indication of the reversal of outward blood flow from the head was 49.25°. In Table 3, a summary of the SBA, Gz level and onset rate for ramp-type centrifuge runs at the point of inflection of Zdc is presented. Upon offloading of the stress, the Zdc waveform demonstrates a similar overshoot and subsequent return to prestress levels as seen in relaxed runs. These changes in Zdc indicate the utility of the REG to aid in determining the efficiency of anti-G protective devices.

ONSET RATE	+Gz at Zdc INFLECTION	SBA
+2.3 Gz/sec	6.8	50°
+2.3 Gz/sec	6.8	48°
+0.5 Gz/sec	5.5	54°
+0.5 Gz/sec	4.7	48°
+0.5 Gz/sec	4.6	48°
+0.1 Gz/sec	4.8	51°
+0.1 Gz/sec	4.6	49°
+0.1 Gz/sec	4.4	46°

Table 3. +Gz and seat-back-angle (SBA) at which there is a change in inflection of Zdc during ramp-type acceleration exposures in experiment CE2.

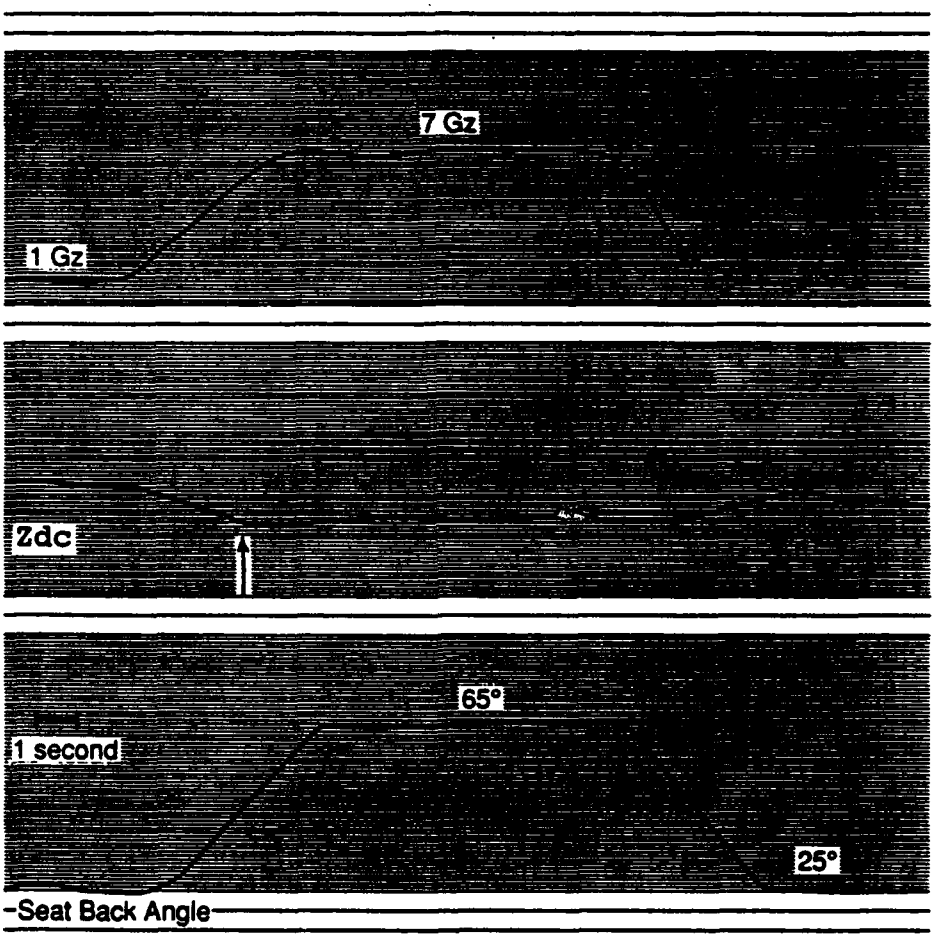


Figure 13. Strip chart recording of the effects of reclining seat-back-angle on Zdc. From top to bottom: Gz (+7 Gz plateau), Zdc, SBA (65° maximum). Point of inflection denoted by arrow.

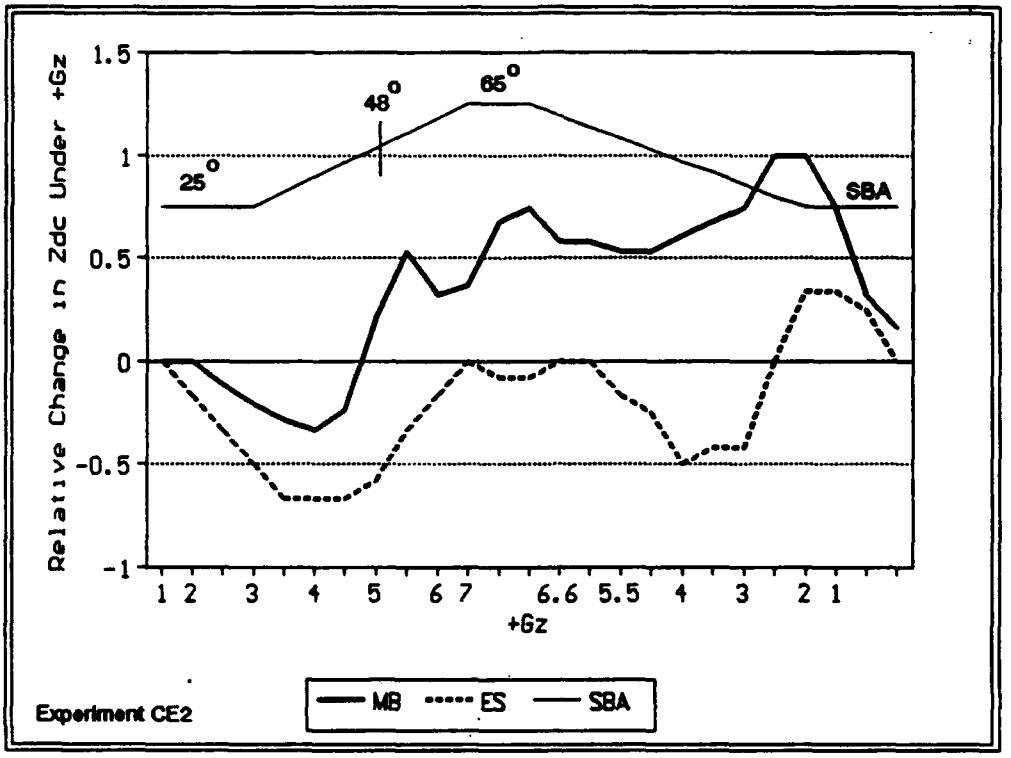


Figure 14. Plot of the effects of increasing seat-back-angle (SBA) on Zdc for subjects MB and ES during a 0.5 Gz/sec rapid onset run. X-axis shows where +Gz-level changed during onset and offset. Upper trace shows change in SBA.

Experiment CE3

Prior to running CE3, circuitry and electrode improvements in the REG device were made which permitted the collection of better Zpul and Zdc data than in CE1 and CE2. Specifically, analysis of the changes in magnitude and timing information contained in Zpul under acceleration stress during relaxed and straining conditions was performed.

Baseline REG, Zdc

In the REG device, Zdc is derived from a analog hardware combination of subtraction from and a slow (i.e. a long time constant) integration of Zpul. Measurements are expressed as a percentage change in baseline from unstressed (i.e. resting centrifuge plateau) to a high +Gz load environment.

As mentioned previously, as +Gz-load increases, so does the magnitude of the change in Zdc. Zdc data from four of the subjects was used to describe the change in Zdc with respect to unstressed (+1.03 Gz) values taken five seconds prior to +Gz onset. These values were expressed as a percent change (%Zdc), with the unstressed levels arbitrarily set to zero (where 1.0 = 100% increase). The average values of %Zdc at +2.5 to +4.5 Gz for four relaxed subjects are presented in Table 4. According to the hydrostatic column theory, CV compensation can occur after about ten seconds of acceleration exposure, assuming that the onset rate was not so great as to overwhelm the CV system, which leads to loss of consciousness. Therefore, readings were taken five seconds prior to acceleration onset, during the two second onset, during the first, second, and third five second periods at plateau, during the two second acceleration offset, at the peak of the overshoot ("peak"), and at the point of baseline recovery ("settle"). Also in Table 4 are values for runs that were stopped because the subjects' peripheral vision closed down to a 60° forward visual cone (labelled PLL - peripheral light loss - in the table). This endpoint occurred at an average level of +5.17 Gz after approximately ten seconds at plateau. The last line in the table, labelled AGSM, are the values of %Zdc obtained while the subjects performed a "HOOK maneuver" (59). These values are taken during the forced exhalation period of the straining maneuver. A plot of %Zdc with respect to run time and acceleration level is presented in Figure 15.

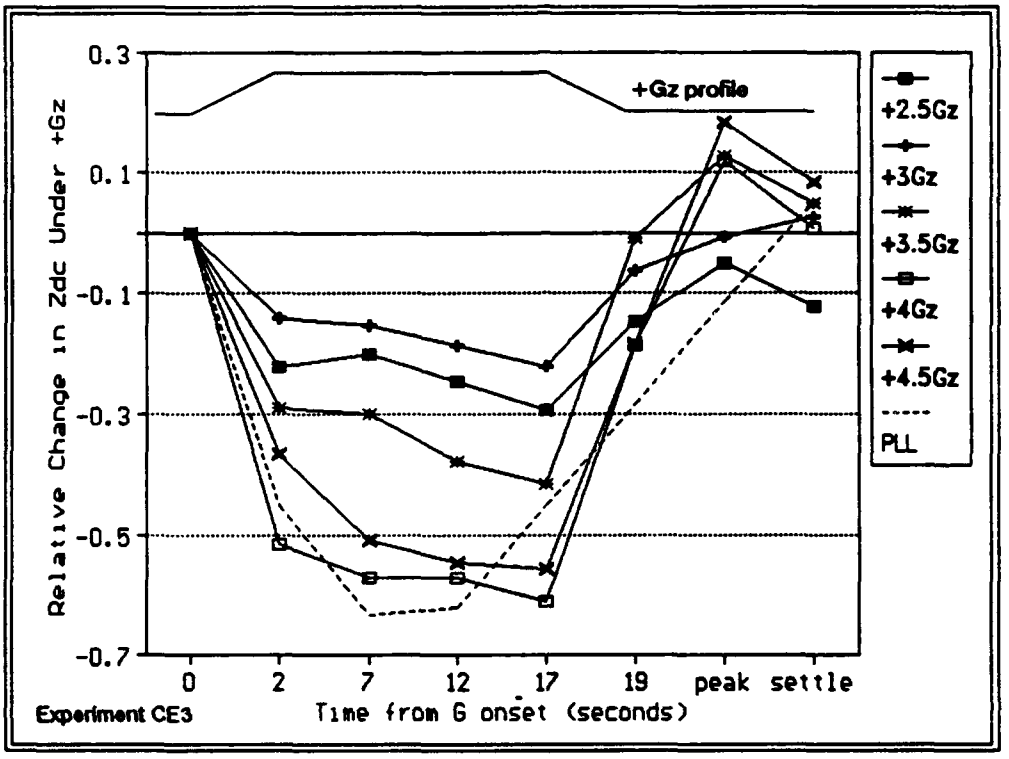


Figure 15. Relative change in Zdc during rapid onset run (average of four subjects). +Gz-onset from 0 to 2 sec, plateau from 2 to 17 sec, +Gz-offset from 17 to 19 sec. "Peak" occurs at height of post +Gz hyperemic response and "settle" is its value after 30 sec of recovery.

	Time Into Run From +Gz Onset						
+Gz	0-2s	2-7s	7-12s	12-17s	17-19s	peak	settle
2.5	-.222	-.200	-.247	-.295	-.148	-.05	-.122
3.0	-.142	-.152	-.186	-.22	-.062	-.006	.026
3.5	-.291	-.300	-.379	-.416	-.009	.129	.05
4.0	-.516	-.571	-.572	-.611	-.186	.121	.008
4.5	-.367	-.509	-.547	-.556	-.184	.184	.084
PLL	-.451	-.634	-.621	x	x	x	.053
AGSM	-.180	.132	.266	.348	.214	.440	.040

Table 4. Percent change in Zdc with respect to +1.03 Gz levels during various points throughout the ROR. See text for explanation. x = no data at these points due to end-of-run condition.

From this data several observations can be made. As +Gz-stress increases, so does the magnitude of %Zdc. Upon offloading of +Gz-stress, there was an overshoot corresponding to the influx of blood reentering the head due to the CV reflex. The relative amount of this overshoot tended to rise with increasing +Gz-load, which corresponds to the increased amount of CV compensation necessary to restore the neural tissues to normal conditions. After the run, %Zdc returned to the previous unstressed level within approximately 10%. This change in Zdc level indicated that the subject's CV system had readjusted and blood flow had been restored. Unfortunately, with this measure we cannot conclusively predict just by the magnitude of %Zdc whether or not the onset of 60° PLL is imminent.

One way analysis of variance (ANOVA) was performed on %Zdc with respect to +Gz-load to discover if a significant statistical relationship existed between the dc impedance and increasing +Gz level at plateau. While there was some biological variability in the data, i.e. %Zdc at +2.5 Gz was greater than at +3 Gz, the relationship between increasing acceleration load and rising %Zdc was highly significant ($F=34.7$ with Probability $> F = 0.000$). This relationship seen with Zdc is consistent with measures of cerebral blood volume made by Glaister and Jobsis-VanderVliet (13) using a near infrared cerebral oxygen status monitor.

The data in Table 4 indicate that %Zdc during straining was different from relaxed runs. Two tailed paired t-tests were performed comparing relaxed runs (all grouped together) with straining runs. These tests were performed for each time period during plateau. At two seconds, the difference was insignificant ($p<0.12$) while at plateau the difference between the means was highly significant ($p<0.005$). One would like to be able to predict the onset of a PLL terminated run from the previous run time performance. Again, two tailed paired t tests were performed to judge the significance between the means at +4.0 and at +4.5 Gz with the PLL terminated run. From this limited set of data, changes in %Zdc alone could not predict the onset of PLL.

However, it should be noted that 60° PLL endpoint was used as a conservative safeguard to avoid inadvertent G-LOC. There is no specific physiological change which would jeopardize a mission associated with the point at which vision closes down to 60°. Therefore, the jury is still out as to whether %Zdc has the ability to predict the onset of blackout or G-LOC.

Therefore, this measure gives a good indication of the relative state of the cephalic circulation with increasing acceleration load and shows that straining is indeed an effective means to increase cephalic blood flow.

Effects Of Straining On Zdc

During the performance of an AGSM, such as the "HOOK" maneuver, there are very definite changes in the form and level of Zdc that can be used to gauge the effectiveness of the respiratory portion of the AGSM. The form and reference points for the straining Zdc waveform are shown in Figure 16 and are as follows:

1. I wavelet: Following a relatively flat or slightly sloped period corresponding to the forced expiration portion of the maneuver, there is a rise, the I wavelet, corresponding to the rapid expiration immediately preceding the inhalation phase (the "KAH").

2. II wavelet: Next is a depression that corresponds to the first part of the rapid (< 30 sec) inspiratory phase, the II wavelet.

3. III wavelet: The second part of the inspiratory phase including the beginning of the forced expiration and muscle tensing is manifested by a large peak, the III wavelet, that corresponds to the "HOO."

4. IV wavelet: This is a relatively flat portion of the curve that corresponds to the forced expiratory phase of the AGSM.

5. Strain amplitude: The difference between the minimum of the II wavelet and the peak of the III wavelet gives a relative indication of the strength of the strain during the breath exchange portion of the AGSM.

6. Strain duration: This is measured from the peak of the I wavelet to the end of the III wavelet. An indication of the speed of the air exchange is evident from this measure. Ideally, this takes about 0.5 seconds (12).

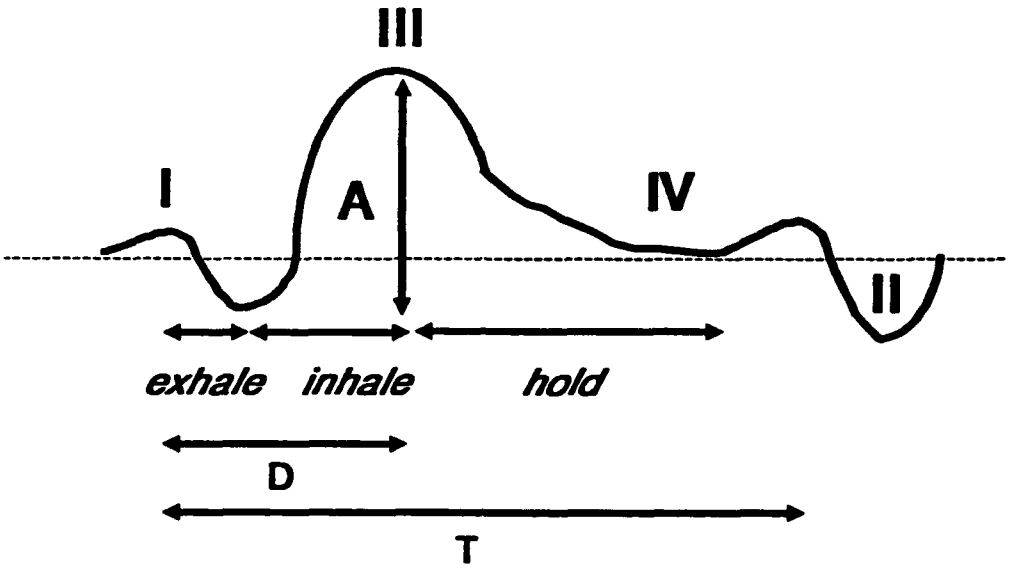


Figure 16. Zdc waveform during an anti-G straining maneuver (AGSM).

KEY

I : End of forced expiration period, the "KAH" sound;
II : Start of inspiration, the "HOO" sound;
III : Peak of inspiration;
IV : Start of forced exhalation period;
A : Magnitude of AGSM (relative strength of strain);
D : Duration of AGSM (speed of breath exchange);
T : Period of AGSM (length of maneuver).

7. Strain period: Measured between two I wavelet minima, this indicated the length of time the entire maneuver takes. Ideally, this should take three seconds (12).

In order to compare the effects of straining on bulk movement of blood under acceleration, one can compare Zdc levels when not straining under +Gz-stress to IV wavelets while performing an AGSM.

Figure 17 shows the changes in Zdc during straining at +5.5Gz along with a respiration trace. The latter was obtained by placing a strain gauge type device across the thorax of the subject. The timing and patterns recorded with this device were mirrored by changes in Zdc. By studying the Zdc traces one can determine the speed of air exchange, relative strength of the respiratory effort, and the length of the strain. As an example, during the SACM phase of CE3, as time progressed during the runs and the subjects started to tire, some subjects exhibited some or all of the following responses: the straining period (I wavelet to I wavelet interval) decreased, strain duration (i.e. speed of breath exchange) lengthened, and the peak of the strain amplitude wavelet (III wavelet) decreased in magnitude and flattened. Clearly, exhibition of these trends would indicate that the effectiveness of their straining technique was diminished. However, while straining amplitude and period both declined as SACM time increased, strain duration either lengthened or shortened depending upon the individual. The amount of straining effort an individual produces in the centrifuge, however, depends in large part to their level of motivation. During these trials, blood lactate measurements were made before and after SACM runs in order to determine whether subjects were engaged in anaerobic metabolism. These indicated that some subjects expended much more energy than others. It was difficult to determine for most of the subjects who truly reached a fatigue end point. Results from this experiment were presented at the 1988 Annual Scientific Meeting of the Aerospace Medical Association (see 52 for the abstract).

In order to gain a complete assessment of straining effort, electromyographic recordings of the arms, legs, and neck muscles are needed to complement the Zdc respiratory information. Once the additional information has been attained and baseline values and trends are known, the REG has the potential to be used as a training aid in the instruction of effective AGSM techniques in a noninvasive unobtrusive manner. Currently, one can monitor AGSM performance by measuring intrathoracic pressure by using an intraesophageal balloon.

Pulsatile Impedance, Zpul

Analysis of the pulsatile impedance waveform, Zpul, focused upon characterization of +Gz-induced changes in magnitude and

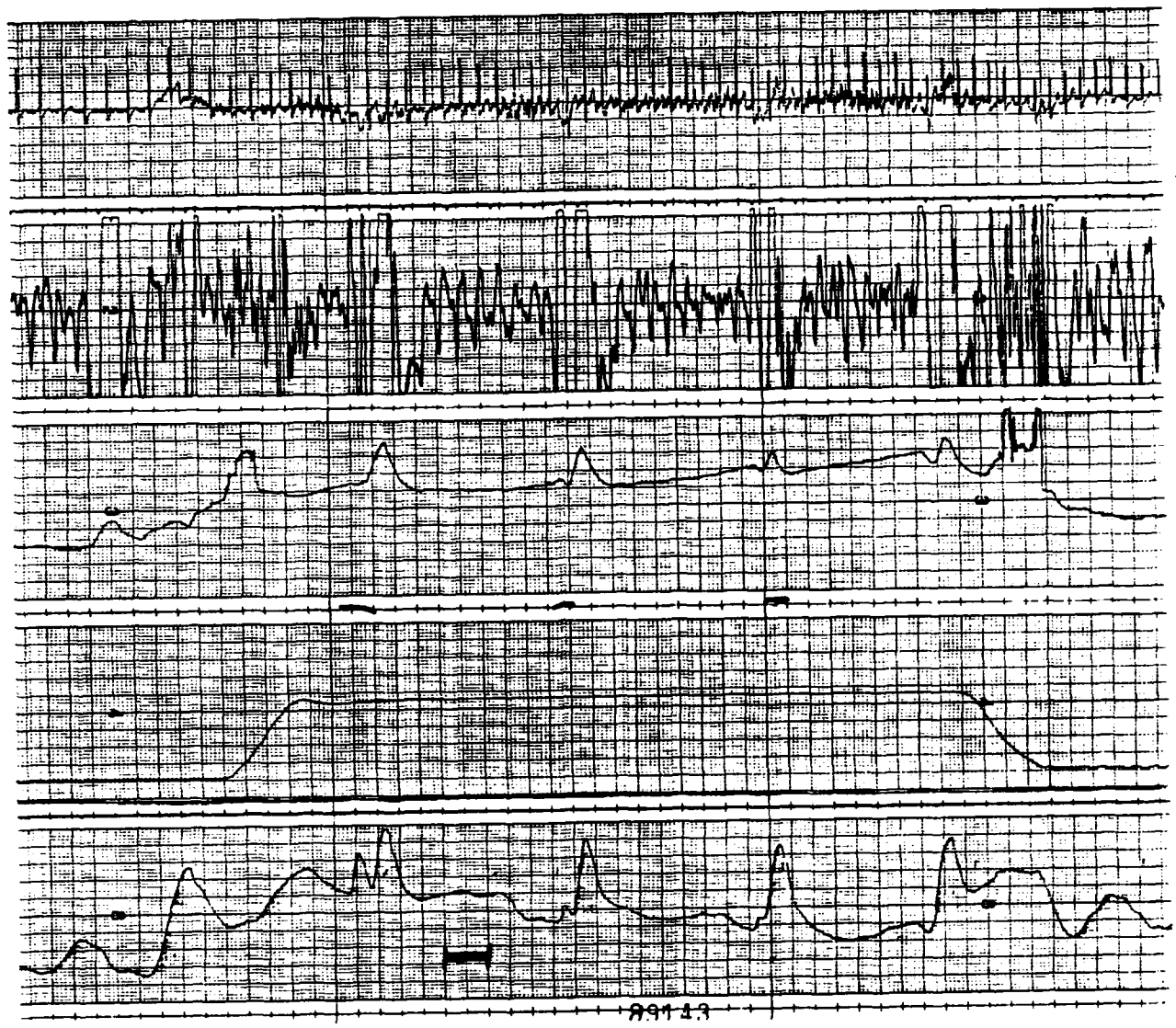


Figure 17. Effects of AGSMs on Zdc during +5.5 Gz plateau. From the top: ECG, Zpul, Zdc, +Gz, thoracic respiration. Horizontal bar on the bottom represents 1 sec.

timing and attempting to explain those alterations with respect to the hydrostatic column theory of physiological response to acceleration stress. A sample strip chart showing the effects of +4.5 Gz on Zpul is found in Figure 18.

Under high a +Gz-load, the Zpul wavelets A (systolic volume), B, and C (venous pressure/degree of impeded venous outflow) all increase in magnitude. As the level of stress rises, more and more of the relatively highly conductive blood plasma and cerebrospinal fluid is redistributed within the skull or is drained out of the cephalic space. Therefore, the impedance of the head rises with respect to an increase in acceleration stress.

For each index, five waveforms were averaged to eliminate the effects of random noise for each of four subjects for nine relaxed runs and six straining runs each. While there was some variability among these subjects, their respective values for each +Gz level and point in time during the runs were averaged together since the overall trend in these indices was the same. Impedance data was then expressed in terms of the percent change between prestress and stressed values. This presentation is similar to one taken by Lifshitz (30). Results from this experiment were presented at the 15th Annual IEEE Northeast Bioengineering Conference (see 51 for the abstract).

Tables 5, 6, and 7 contain the percentage change from prestressed to stressed levels for wavelets A, B, and C, respectively. The prestress period is defined as five seconds prior to acceleration onset. In these tables, run time is broken down as follows: 0-5 seconds, 5-10 seconds, and 10-15 seconds at +Gz plateau, 5-10 seconds and 15-20 seconds after acceleration offset. In this way, it ought to be possible to see any effects of cardiovascular compensation occurring after ten seconds of high +Gz exposure. Recall that the onset of this compensation, on average, can occur after approximately ten seconds of exposure (7). We also wanted to monitor how Zpul reflects physiological recovery after acceleration offset.

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	.152	.222	.265	.027	
3.0	.319	.391	.434	.207	.128
3.5	.299	.445	.393	.044	-.022
4.0	.308	.487	.503	.061	-.034
4.5	.491	.547	.595	.166	.098
PLL	.410	.434		.073	-.179

Table 5. Percent change from prestress levels (+1.03 Gz) of the A wavelet of Zpul with respect to run time and +Gz.

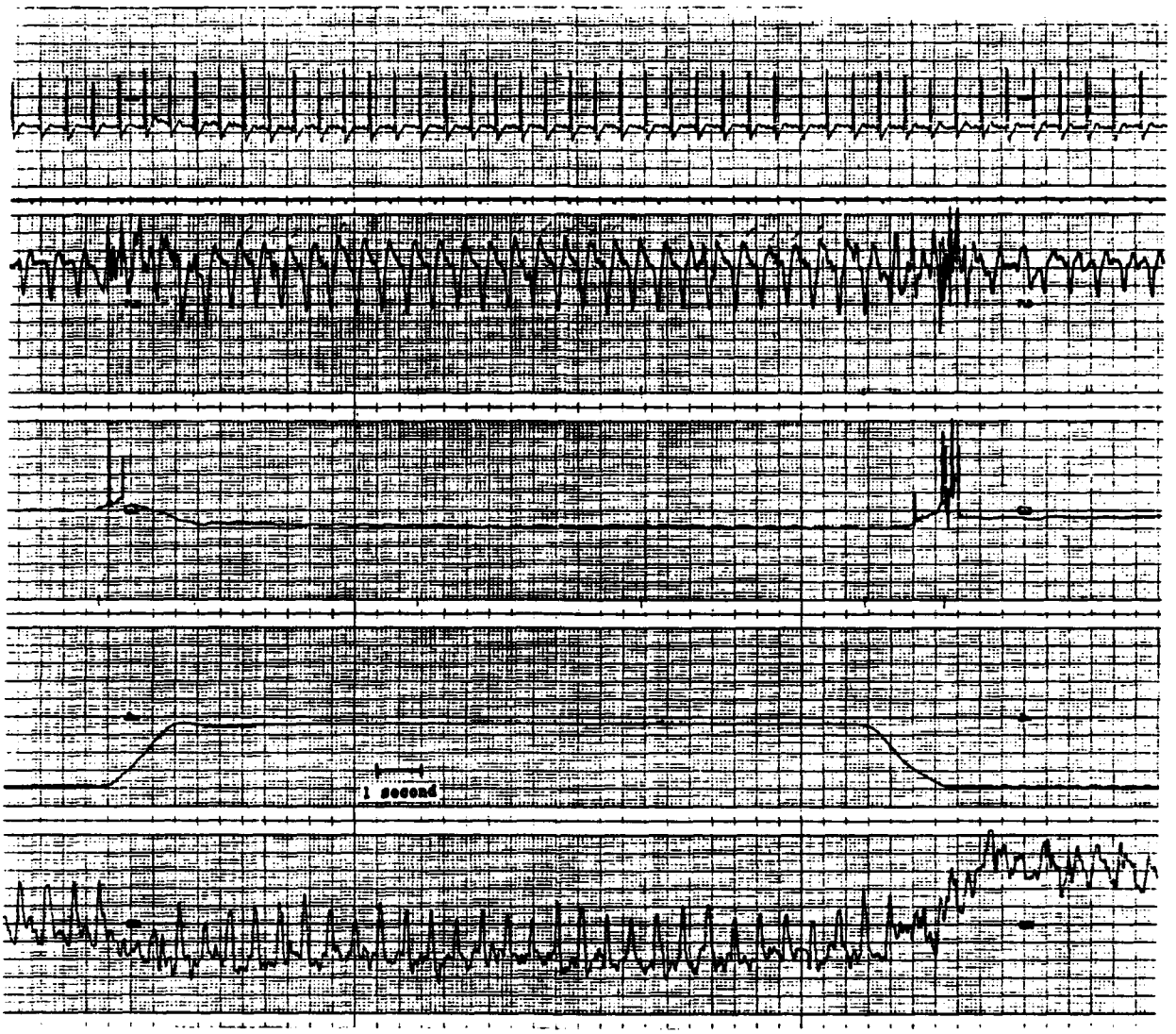


Figure 18. Effects of +4.5 Gz-stress on Zpul. From the top: ECG, Zpul, Zdc, +Gz, ultrasound doppler of superficial temporal artery. Note change in magnitude and period of Zpul.

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	.047	.236	.305	0.0	
3.0	.275	.197	.388	.108	.066
3.5	.275	.453	.398	.055	-.119
4.0	.227	.453	.411	.024	-.077
4.5	.404	.45	.441	.024	-.032
PLL	.360	.343		.048	-.163

Table 6. Percent change from prestress levels (+1.03 Gz) of the B wavelet of Zpul with respect to run time and +Gz.

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	.161	.228	.289	.054	
3.0	.264	.279	.338	.161	.108
3.5	.253	.367	.315	.059	0.0
4.0	.182	.301	.288	.023	-.049
4.5	.320	.325	.359	.107	.045
PLL	.274	.247		.064	-.154

Table 7. Percent change from prestress levels (+1.03 Gz) of the C wavelet of Zpul with respect to run time and +Gz.

No effects of CV compensation were seen with the A wavelet. At +3.5 Gz and above, the B wavelet did indicate increased tone after ten seconds at plateau with respect to the first ten seconds of stress. The C wavelet was a bit more variable in that during some of the runs, at +3.5 and +4.0 Gz, compensation may have begun, also after ten seconds at plateau. It is important to emphasize that compensation may have occurred. There is great variability within individuals as to when their cardiovascular compensatory responses begin in earnest. The nature of this response also depends upon the rate of onset and level of acceleration stress. Impedance changes can be quite useful in determining these responses if they are used in conjunction with other correlative measures. This is brought out by the fact that the A wavelet showed no changes similar to those seen with B and C wavelets. By fifteen seconds after offloading from high +Gz, all wavelets return to within approximately 15% of the previous unstressed levels.

ANOVA for each time period and wavelet were performed to assess the differences between Zpul and run time and/or +Gz value. One way ANOVA tests comparing the means of the percent changes in A, B, and C wavelets with respect to run time show that the pulsatile impedance waveform changes significantly as the length of time under acceleration stress continues (F=18.64,

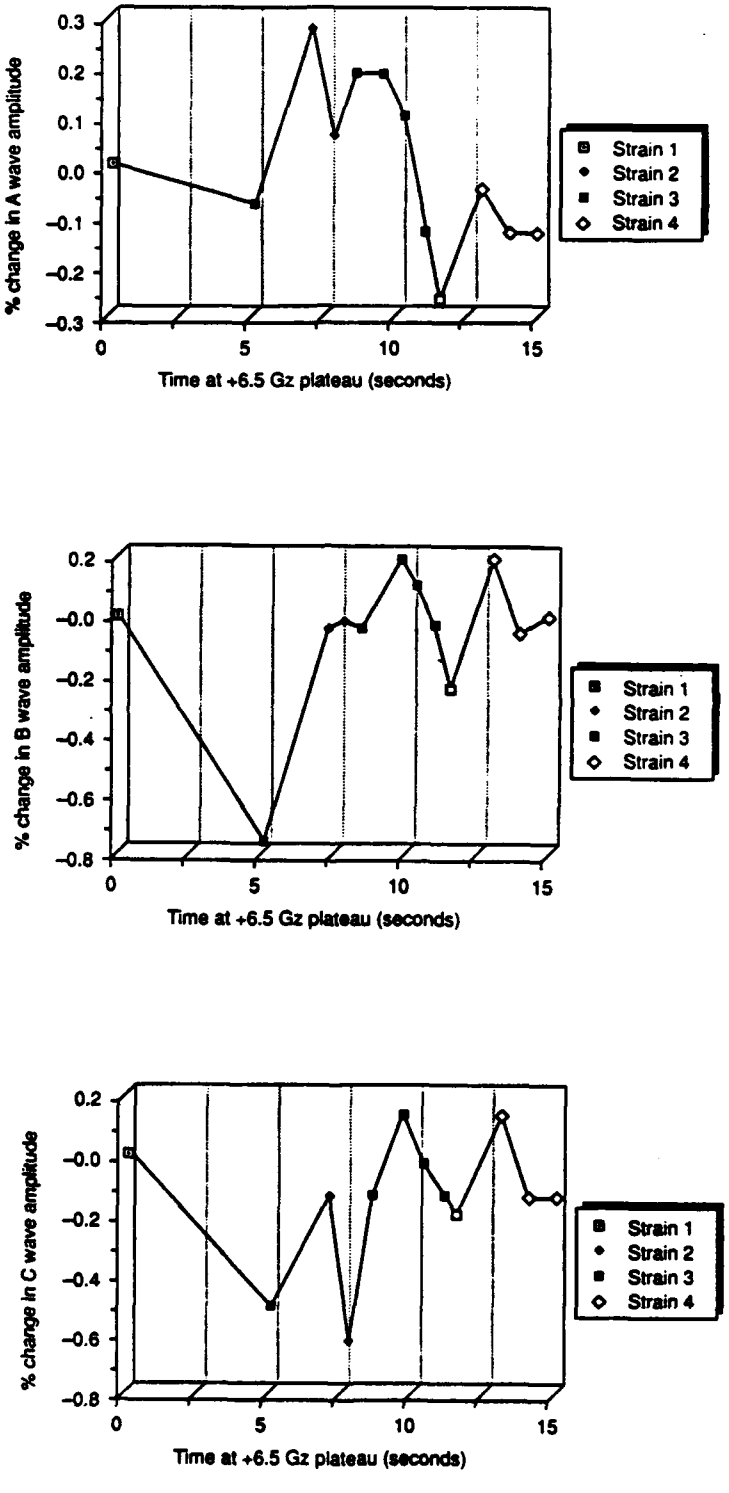
Prob.>F=.000; F=22.91, Prob.>F=.000; F=39.39, Prob.>F=.000, respectively). The results of two way ANOVA comparisons between percent changes in A, B, and C wavelets with respect to run time and +Gz level indicate significant differences between calculated impedance values and run time. However, only analysis of the A and C wavelets demonstrated a significant difference between impedance, run time, and acceleration load (F=7.31, Prob.>F=.001; F=5.198, Prob.>F=.005, respectively). One cannot state that changes in the B wavelet, as analyzed under conditions of this test, did not occur due to chance alone (F=1.679, Prob.>F=.194).

During the performance of an AGSM during a two second rise, 15 second plateau ROR, reductions in magnitude of the A, B, and C wavelets indicate an elevated level of blood flow towards the head as straining time increases. During each approximately three second strain, one to four Zpul waveforms were readable and measured for subjects P7 and P10. These values have been expressed as percentages as above. The effects of straining on the A, B, and C wavelets for subject P10 are found in Figure 19. In general, during the performance of an effective AGSM the overall percentage magnitude change declines within an individual straining period and during the entire +Gz exposure at plateau. Note that there was an increase in index magnitude during the post-stress recovery period which then returns to values close to prestress levels. This change indicates that after performance of AGSMs over a fifteen second period, which caused an abnormal increase of blood flow into the head, a compensatory response to decrease this extra volume occurs, causing a rise in measured impedance.

The main physiological responses of the body to +Gz-stress are tachycardia and a rise in arterial pressure that occurs was a consequence of increased vasoconstriction. Concurrently with this rise in pressure in the lower regions of the body is a decrease in blood pressure in the head. Recall that the venous and, to a lesser extent, the arterial circulation of the head is protected under a high +Gz-load by the CSFP (44). Gillies (10, page 599) cites experiments that showed <u>decreased</u> vasoconstriction, particularly in the pial system, occurs in the cranium under acceleration stress. The CNS has the ability during periods of reduced cerebral perfusion to actively shift resources (e.g.blood) to more critical areas of the brain. Also, the larger arteries in the brain play a greater vasomotor role than in other organs. The rheographic indices of tone (B/A, C/A, a and a/T) provide an indication of overall tone changes and are not sensitive enough to provide precise regional information. Therefore, to interpret these indices the special physiological compensatory vasomotor action of the CNS autoregulatory system must be considered.

Table 8 contains the averaged percent change in B/A (arteriolar tone) for four subjects from prestress to stressed values for +2.5 to +4.5 Gz. Also included are values from runs

Figure 19. Effects of AGSM on Zpul indices A, B and C during 15 seconds at +6.5 Gz (subject P10).



terminated due to 60° PLL. The changes in B/A during relaxed +Gz runs were quite variable. For all +Gz levels, during the first five seconds at plateau, arteriolar tone decreased. During the rest of the time at plateau and during recovery, arteriolar tone either increased or decreased depending upon the acceleration load, though not in any particular pattern. Results of a two way ANOVA comparing these values to run time and +Gz-load his analysis show that there was no significant change in B/A with respect to +Gz levels during relaxed acceleration exposures (F=1.165, Prob.>F=.356) though there was significant change with respect to run time (F=3.64, Prob.>F=.017).

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	-.125	.007	-.018	-.082	-.071
3.0	-.058	-.121	-.068	-.056	-.081
3.5	-.028	-.047	-.036	-.033	-.104
4.0	-.109	-.016	-.059	-.039	-.047
4.5	-.063	-.044	-.122	-.133	-.111
PLL	-.066	-.075		.055	.023

Table 8. Percent change from prestress levels (+1.03 Gz) of the averaged ratio B/A (arteriolar tone) with respect to run time and +Gz.

The results determining the effects on changing venous tone, C/A, under high +Gz were quite different. The ratio C/A were expressed as percentages in the same manner as above. These values are presented in Table 9. With each +0.5 Gz increase, C/A indicated a decrease in tone, except for the first run at +2.5 Gz. Results of a two way ANOVA comparing these values to run time and +Gz-load his analysis show that there was a highly significant change in venous tone with respect to +Gz levels while relaxed (F=7.46, Prob.>F=0.0) and run time (F=6.20, Prob.>F=.002).

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	-.004	.023	-.013	.006	.014
3.0	-.027	-.071	-.071	-.063	-.023
3.5	-.086	-.074	-.083	-.015	-.021
4.0	-.103	-.105	-.126	.001	-.006
4.5	-.128	-.134	-.159	-.025	-.040
PLL	-.138	-.168		-.043	.025

Table 9. Percent change from prestress levels (+1.03 Gz) of the averaged ratio C/A (venous tone) with respect to run time and +Gz.

The third index of cerebrovascular resistance (intermediate and large vessel tone) is the rheographic time a/T. These values were averaged for each time period during the run as above (see Table 10). In contrast to the rheographic ratio results above which indicated a decrease in tone, a/T tends to increase under acceleration. According to Hadjiev (17), this increase is indicative of greater levels of CVR. His measurements were performed on patients with ischemic cerebrovascular disorders and there was no indication of the heart rate of these subjects. Figure 20 displays the change in a/T with increasing +Gz-load. Note on this figure that there is a change in inflection between five and ten seconds at plateau. This may be due to a decrease in tone with the onset of cardiovascular compensation or may only be due to biological variability. Figure 21 is a 'blowup' of Figure 20 in which a/T responses at +4.0 and +4.5 Gz can be compared with a/T during PLL runs. In this case, the PLL values were quite different during the first ten seconds at plateau. More data needs to be obtained to objectively verify this change. One sample t tests performed comparing prestress levels to stressed levels showed highly significant differences ($p < 0.01$ or better) at +3.5 Gz and above. By 15 seconds after offset of acceleration, a/T returned to prestress values. However, a two way ANOVA comparing a/T with time at plateau and +Gz showed there was no significant interaction between a/T and acceleration load ($F=1.31$, Prob.>$F=.285$).

+Gz	0-5 s	5-10 s	10-15 s	20-25 s	30-35 s
2.5	.113	.215	.084	-.018	-.040
3.0	.151	.143	.170	.046	-.077
3.5	.263	.186	.215	.069	-.057
4.0	.255	.227	.198	.089	.028
4.5	.077	.054	.061	-.051	-.175
PLL	.328	.294		.113	-.029

Table 10. Percent change from prestress levels (+1.03 Gz) of the averaged ratio a/T (large and intermediate vessel tone) with respect to run time and +Gz.

Experiment CE4

The primary purpose of CE4 was to train DOD volunteers to become members of the NADC Acceleration Subject Panel. Subjects became accustomed to the centrifuge gondola, experimental procedures, and the nature of +Gz-stress. They became proficient in tracking the limits of their peripheral field of vision using the NADC Dynamic Light Bar as well as fixed lights and to perform efficient anti-G straining maneuvers (AGSM). Their individual tolerances to a variety of anti-G protective modalities was determined. These modalities included no protection ("relaxed"

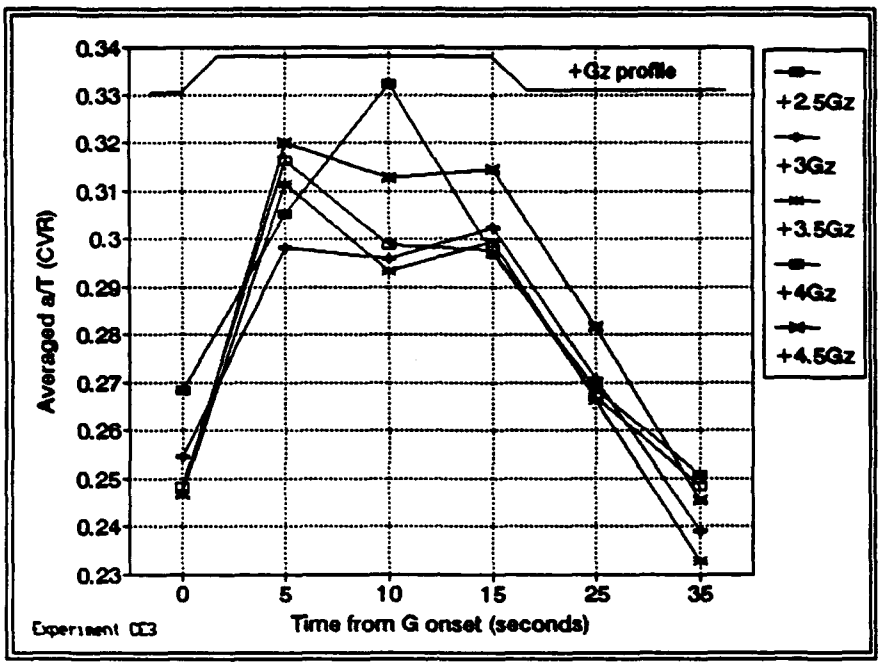


Figure 20. Effects of +Gz on a/T (average of four subjects).

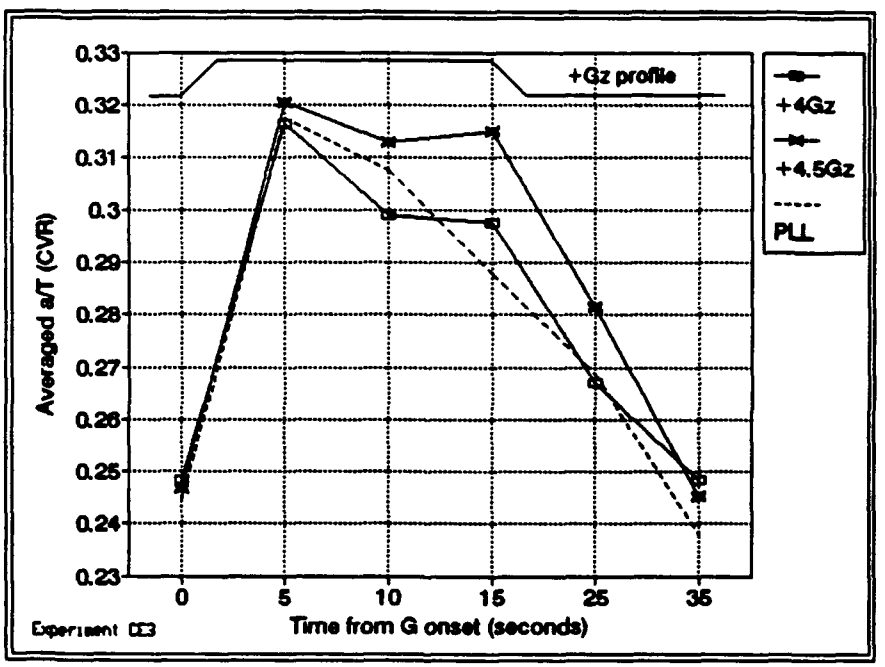


Figure 21. Change in a/T as +Gz-load approaches PLL level (average of four subjects).

tolerance), Navy AGS alone ("AGS"), AGSM alone, or a combination of AGS with AGSM ("AGS/AGSM") during either gradual onset (GOR at 0.1 G/sec), rapid onset (2 second onset/offset, 15 second plateau haversine) exposures or SACM (as described in CE3, above).

The following is a summary of the rheoencephalographic results to GOR exposures. A representative sample is presented below. Data analysis consisted of measurements taken at 0.4 to 0.5 G steps during the G exposure and up to 60s after G offset. Four waveforms were averaged during the 15 seconds prior to G-onset to serve as the "pre-stress" data. During each 0.5G period and during recovery, four waveforms were averaged and the relative difference between these averages and the prestress average were calculated. Rheographic indices A, B, C, B/A, C/A, a, and a/T were calculated. Changes in Zdc and SaO_2 were also determined. Recall that when interpreting changes in "A" that an decrease in impedance reflects an increase in blood volume.

There was great variability both intra- and inter-subjects and individual subjects served as their own controls, using pre-stress data. On any given day subjects exposed to the same test condition would present different responses in terms of G tolerance as well as tracking and straining performance. For a given subject, for example, the trend of changes in his rheographic indices were similar but the magnitudes were not leading to a potentially invalid interpretation of standard one-way ANOVA analysis. All in all, the difference between subjects were too great for a logical grouping of responses. Therefore, Tables 11 and 12 below contain the relative values of the rheographic indices for two subjects as a representative sample. In these tables, prestress levels are set to 0. Relative differences are expressed in percentages, where 1.0 is a 100% magnitude increase. Figures 22a through 22f graphically show how the REG indices are affected by G-load during AGS versus AGS/AGSM conditions for subject S12. (In these figures, the solid vertical line indicates the point in which a PLL endpoint occurred during AGS runs. The dashed vertical lines indicate the period in which AGSM were performed with the line to the right indicating the PLL endpoint.) When possible, one way ANOVA were performed to judge the effect of anti-protection modes on these parameters. In general, during relaxed conditions (no AGS or AGSM), these indices indicated that overall systolic volume decreased and venous outflow was increasing impeded. Arteriolar tone increased and venous tone increased slightly. Cerebrovascular resistance varied but for the most part was within +/- 15% of prestress levels. Zdc indicates bulk fluid outflow increased with increasing G-load and that flow was abruptly reversed with the offset of G.

With the addition of an operational AGS, the overall steady rise in the values of the indices with increasing +Gz-stress was changed. All index values tended to oscillate. Initial response of systolic volume (A) ranged from oscillating +/- 10% with respect to prestress to a 40% increase in impedance (drop in

CONDITION	Gz	TIME FROM ONSET (s)	%A	%B	%C	%B/A	%C/A	%a/T
Relaxed	1.03	0	0.00	0.00	0.00	0.00	0.00	0.00
	1.30	4	0.01	-0.02	0.04	-0.05	0.01	0.11
	1.70	8	0.19	0.36	0.31	0.13	0.10	0.12
	2.10	12	0.36	0.64	0.49	0.21	0.09	0.09
	2.50	16	0.38	0.46	0.43	0.06	0.03	0.15
	2.90	20	0.57	0.61	0.64	0.03	0.05	0.09
	3.20	24	0.46	0.67	0.55	0.12	0.04	0.11
	3.60	28	0.38	0.61	0.48	0.16	0.07	-0.00
PLL	4.00	32	0.64	1.08	0.75	0.26	0.06	-0.05
	2.00	36	0.57	0.96	0.84	0.25	0.16	-0.11
	1.20	48	0.50	0.76	0.55	0.17	0.02	-0.04
	1.03	60	0.54	0.88	0.75	0.22	0.13	-0.01
AGS	1.03	0	0.00	0.00	0.00	0.00	0.00	0.00
	1.30	4	0.04	0.00	-0.20	-0.04	-0.23	0.18
	1.70	8	0.33	0.50	0.29	0.12	-0.03	0.08
	2.00	12	0.23	0.32	0.24	0.08	0.01	0.30
	2.40	16	0.17	0.21	0.34	0.04	0.15	0.27
	2.80	20	0.04	0.14	0.07	0.10	0.03	0.41
	3.20	24	0.42	0.64	0.37	0.16	-0.04	0.50
	3.60	28	0.25	0.68	0.41	0.34	0.13	0.61
	3.90	32	0.54	0.82	0.41	0.18	-0.08	0.57
	4.30	36	0.50	0.75	0.41	0.17	-0.06	0.48
	4.60	40	0.50	0.79	0.32	0.19	-0.12	0.59
	5.00	44	0.56	1.00	0.54	0.28	-0.02	0.57
PLL	5.20	48	0.25	0.54	0.29	0.23	0.03	0.74
	3.40	50	0.38	0.89	0.71	0.38	0.24	0.43
	1.80	52	0.38	0.75	0.46	0.27	0.06	0.51
	1.30	56	0.21	0.14	0.00	-0.05	-0.17	0.18
	1.10	60	0.33	0.18	0.34	-0.12	0.01	0.17
	1.03	64	0.21	0.21	0.12	0.00	-0.07	0.27

Table 11. Relative difference with respect to prestress levels of pulsatile REG indices for subject S8. PLL indicates highest +Gz-level reached prior to peripheral light loss endpoint.

CONDITION	Gz	TIME FROM ONSET (s)	%A	%B	%C	%B/A	%C/A	%a/T
AGS with	1.03	0	0.00	0.00	0.00	0.00	0.00	0.00
AGSM	1.50	8	0.12	0.04	0.19	-0.08	0.07	0.41
	2.00	13	0.29	0.16	0.20	-0.11	-0.07	0.38
	2.50	18	0.25	0.32	0.31	0.06	0.06	0.66
	3.00	24	0.49	0.57	0.42	0.05	-0.05	0.42
	3.50	30	0.39	0.49	0.27	0.06	-0.09	0.96
	4.00	35	0.25	0.27	0.11	0.00	-0.11	0.62
	4.50	40	0.32	0.40	0.14	0.05	-0.14	0.68
	5.00	45	0.34	0.27	0.08	-0.07	-0.20	0.75
Straining	5.30	48	-0.03	-0.18	-0.21	-0.19	-0.20	0.77
Period	5.60	51	0.00	-0.85	-0.76	-0.85	-0.76	0.08
	6.00	56	0.03	-0.07	-0.21	-0.13	-0.25	-0.08
	6.20	58	-0.26	-0.78	-0.70	-0.70	-0.59	0.31
	6.80	65	0.53	0.49	0.46	-0.03	-0.04	0.71
PLL	7.70	76	0.16	0.01	0.07	-0.13	-0.07	0.36
	1.50	86	0.50	-0.01	-0.15	-0.35	-0.43	0.67
	1.10	96	0.39	0.21	0.10	-0.14	-0.22	0.31
	1.03	116	0.00	-0.31	-0.25	-0.31	-0.24	0.21
	1.03	136	0.09	-0.01	0.07	-0.10	-0.02	0.20

Table 11 (con'd). Relative difference with respect to prestress levels of pulsatile REG indices for subject S8. PLL indicates highest +Gz-level reached prior to peripheral light loss endpoint. Straining period contains the +Gz range during which AGSMs were performed.

CONDITION	Gz	TIME FROM ONSET (s)	%A	%B	%C	%B/A	%C/A	%a/T	Zdc (ohm)	SaO2 %
AGS	1.03	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
	1.50	4	0.07	0.25	0.00	0.17	-0.07	-0.02	1.50	0.96
	1.90	8	0.00	0.08	-0.07	0.08	-0.07	-0.05	1.00	0.97
	2.20	12	0.21	0.33	0.00	0.10	-0.18	0.01	0.50	0.97
	2.50	16	-0.02	-0.08	-0.05	-0.06	-0.03	0.34	-0.50	0.98
	2.90	20	-0.10	0.21	-0.07	0.34	0.02	0.26	-1.00	0.99
	3.30	24	0.05	0.25	-0.20	0.19	-0.24	0.20	-1.25	1.00
	3.70	28	0.05	0.21	-0.20	0.15	-0.24	0.31	-2.00	1.00
	4.00	32	0.00	0.42	0.00	0.42	0.00	0.32	-2.00	1.00
	4.40	36	-0.05	0.04	-0.32	0.09	-0.29	0.45	-2.25	0.99
	4.80	40	-0.07	0.13	-0.15	0.21	-0.08	0.41	-2.50	0.98
	5.10	44	-0.05	0.08	-0.30	0.14	-0.26	0.46	-3.00	0.98
	5.50	48	0.00	0.17	-0.20	0.17	-0.20	0.70	-3.00	0.98
	5.90	52	-0.14	0.21	-0.15	0.41	-0.01	0.63	-3.00	0.97
	6.30	56	-0.12	0.08	-0.25	0.23	-0.15	0.62	-3.50	0.96
	6.70	60	-0.14	0.00	-0.30	0.17	-0.18	0.51	-3.50	0.94
	7.10	64	-0.12	0.08	-0.32	0.23	-0.23	0.65	-3.75	0.91
	7.50	68	-0.12	0.13	-0.25	0.28	-0.15	0.67	-4.00	0.89
PLL	7.60	72	-0.17	0.25	-0.25	0.50	-0.10	0.75	-4.00	0.89
	2.10	76	0.12	0.33	0.03	0.19	-0.08	0.63	-2.00	0.89
AGS with AGSM	1.03	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
	1.50	9	0.30	0.31	0.27	0.02	0.00	0.00	0.00	1.00
	2.00	14	0.05	0.23	0.08	0.20	0.00	0.00	0.00	1.00
	2.50	19	0.05	0.11	-0.05	0.06	0.00	0.00	0.00	1.00
	3.00	24	0.32	0.52	0.12	0.14	0.00	0.00	0.00	1.00
	3.50	30	0.05	0.11	-0.08	0.06	0.00	0.00	0.00	1.00
	4.00	36	-0.04	0.15	-0.10	0.21	0.00	0.00	0.00	1.00
	4.50	42	0.03	-0.05	-0.13	-0.07	0.00	0.00	0.00	1.00
	5.00	46	0.21	0.31	-0.15	0.08	0.00	0.00	0.00	1.00
	5.50	51	-0.04	-0.09	-0.18	-0.04	0.00	0.00	0.00	1.00
Straining Period	6.40	61	0.16	0.01	-0.08	-0.14	0.00	0.00	0.00	0.99
	7.10	68	0.00	0.07	0.08	0.03	0.00	0.00	0.00	0.98
	7.30	70	0.23	0.35	0.03	0.10	0.00	0.00	0.00	0.98
	7.50	73	-0.11	-0.05	-0.12	0.00	0.00	0.00	0.00	0.97
	7.90	78	0.23	0.35	-0.03	0.00	0.00	0.00	0.00	0.91
PLL	8.20	81	0.10	-0.13	-0.31	0.00	0.00	0.00	0.00	0.89
	1.60	93	0.82	0.90	0.62	0.00	0.00	0.00	0.00	0.91
	1.25	121	0.46	0.19	0.21	0.00	0.00	0.00	0.00	0.98

Table 12. Relative difference with respect to prestress levels of pulsatile REG indices for subject S11. PLL indicates highest +Gz-level reached prior to peripheral light loss endpoint. Straining period contains the +Gz range during which AGSMs were performed.

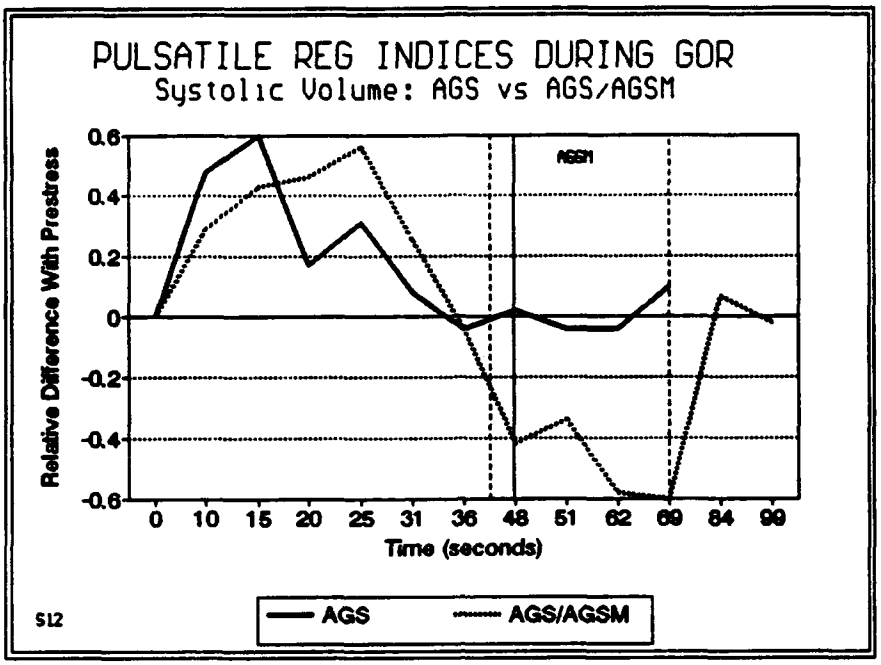


Figure 22a. Change in "A" wavelet (systolic volume) during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

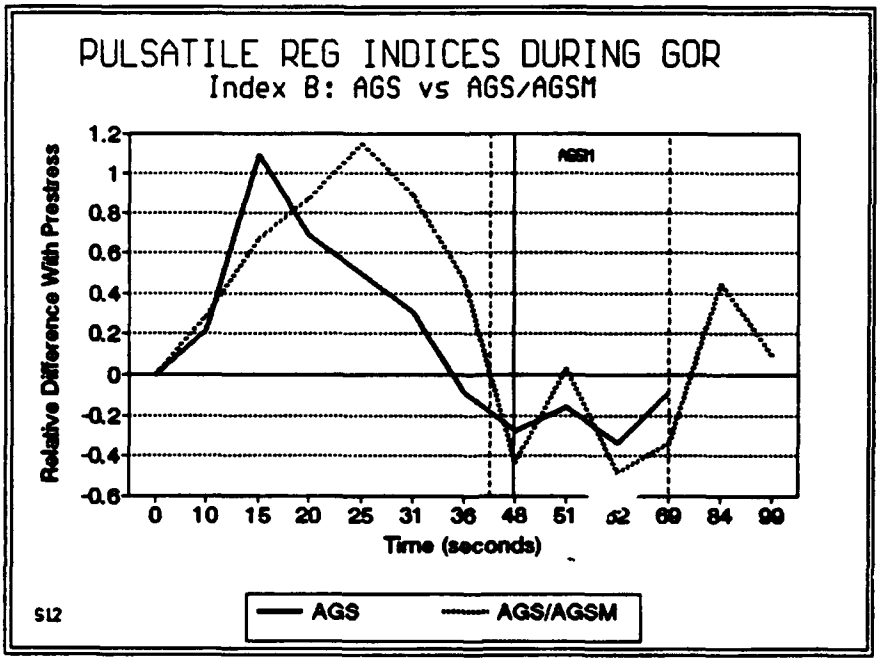


Figure 22b. Change in "B" wavelet during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

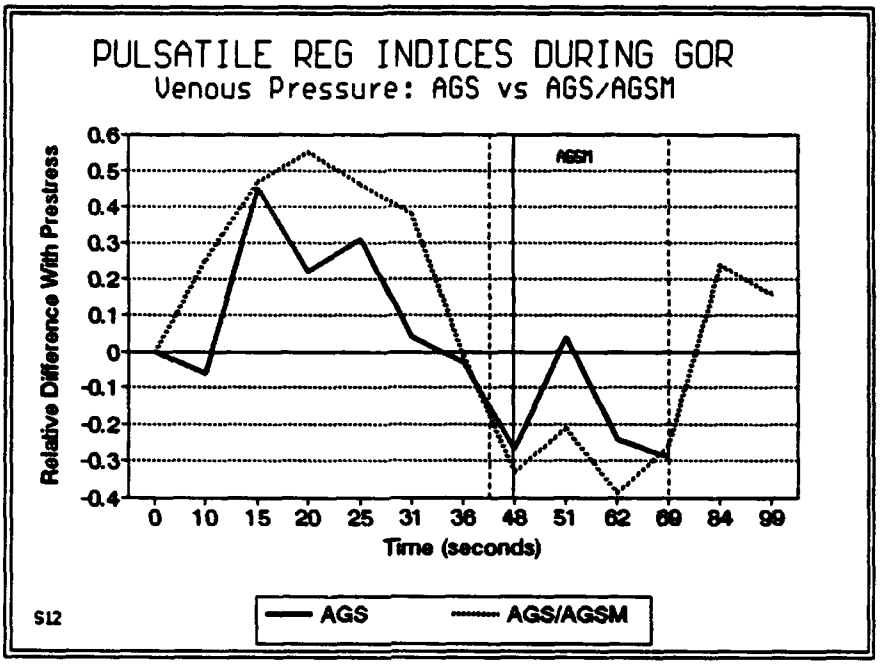


Figure 22c. Change in "C" wavelet (venous pressure) during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

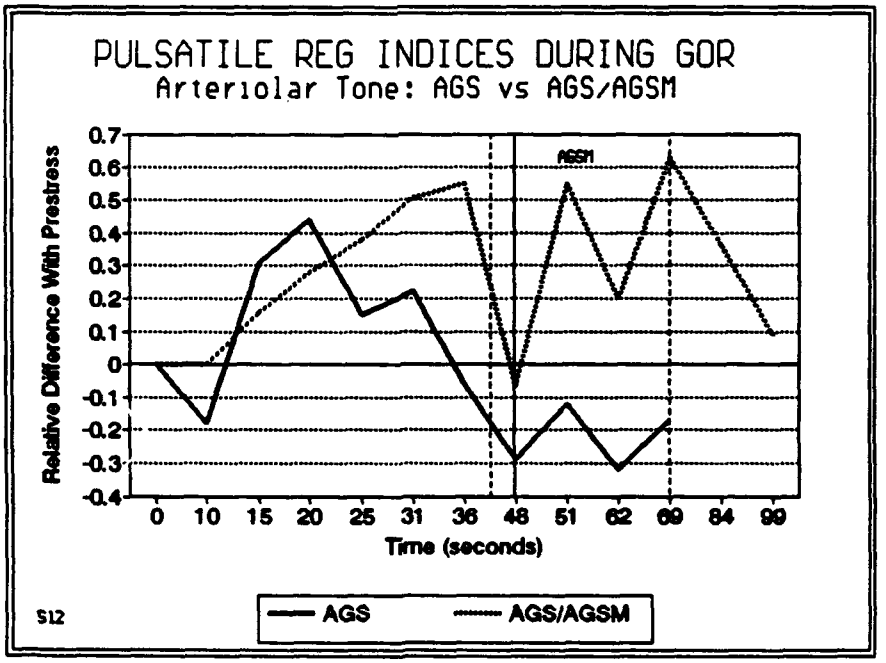


Figure 22d. Change in B/A ratio (arteriolar tone) during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

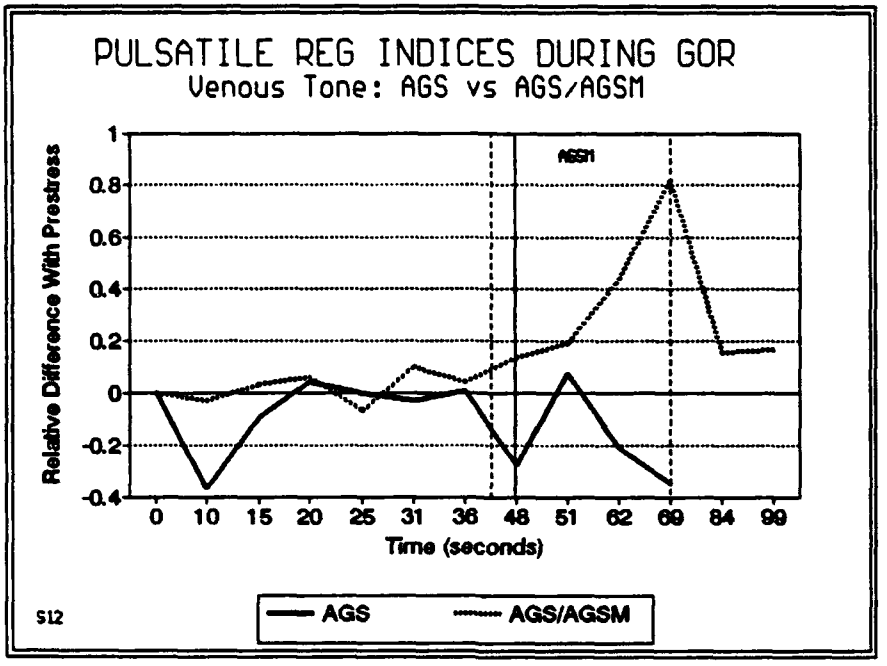


Figure 22e. Change in C/A ratio (venous tone) during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

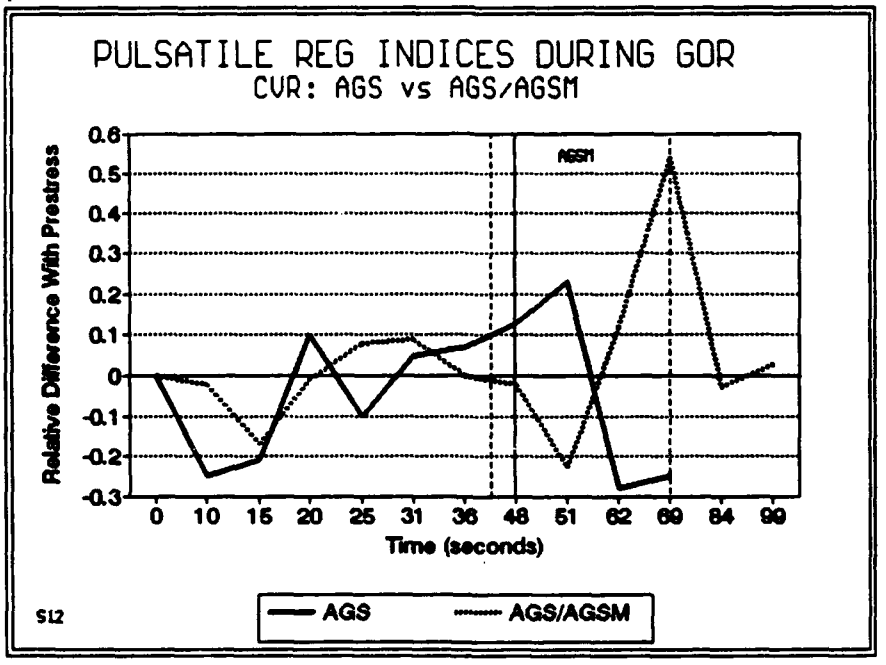


Figure 22f. Change in a/T ratio (cerebrovascular resistance) during GOR: AGS (+6Gz max) vs AGS/AGSM (+7Gz max).

volume). These responses typically were followed by a drop in impedance and a large change at the peripheral light loss (PLL) endpoint, usually an abrupt increase, occurred. (This was not always the case. For example, Subject S8's systolic volume index steadily decreased until PLL when a 30% change in index indicated an increase in volume). With offset, systolic volume tended to rise towards +/- 15% of prestress within 20 seconds. Venous pressure (or resistance to venous outflow) was variable within and between subjects. Usually there was a change in inflection at PLL, typically indicating a rise in pressure. Arteriolar tone tended to oscillate at low G then typically increased towards PLL with a peak either at or just after (within four seconds) PLL. Venous tone initially fell then tended to rise approaching PLL. Changes in venous tone were typically less pronounced than the other tone indices. Large and intermediate sized vessel tone (a/T) was the most consistent of the tone indices. This implied a steadily increasing vasoconstriction of these vessels which peaked at or within four seconds of PLL, followed by a return towards prestress during G-offset.

The most remarkable difference in indices occurred when subjects strain. Subjects were instructed to strain when their peripheral vision closed down to 60^{o}. Because of the large excursions in breathing, four clearly defined pulsatile REG waveforms were not evident so averages consisted of two or three waveforms. Zdc however, was clearly defined showing the AGSM timing and by following the hold period, it was evident that the bulk outflow was reversed with straining. SaO_2 also dropped during straining down to 89% in some individuals. There was an abrupt increase in systolic volume at the higher G-levels during straining with respect to lower G-levels in the same run. Venous pressure tended to decrease. Arteriolar, venous, and larger vessel tone changes were variable depending upon the subject.

Results of one-way ANOVA for a sample of individual subjects were as follows. For subject S8, when comparing relaxed with AGS conditions showed that with straining, systolic volume was marginally reduced ($F=3.14$, $Prob>F = .090$), venous pressure and tone fell ($F=7.06$, $Prob>F = .014$ and $F=4.88$, $Prob>F = .038$, respectively) and larger vessel tone increased ($F=19.3$, $Prob>F = .0002$). When comparing responses between wearing an AGS and wearing an AGS while straining for subject S11, systolic volume increased ($F=10.9$, $Prob>F = .002$), venous pressure increased ($F=7.04$, $Prob>F = .012$), arteriolar tone and larger vessel were less ($F=13.73$, $Prob>F = .001$ and $F=11.87$, $Prob>F = .002$, respectively).

As in CE3, the REG was able to monitor +Gz-induced alterations in blood volume in the head and was responsive to the effects anti-G protection modalities. The variance obtained in analyzing GOR exposures may be traced to the complicated interplay of compensation reflexes occurring during long periods of +Gz-stress. While the duration ROR exposures may or may not be long enough for reflexes to be fully activated, GOR exposures

allow sufficient time for both cardiovascular and neurologic reflexes to be "on-line". As such, it is not unusual to see oscillations and inflections in the indices. These may simply reflect the attempts of the body to redirect resources during stress through changes in vasomotor tone.

Experiment CE5

The purpose of this experiment was to test various forms of acceleration protection via body positioning to reduce the hydrostatic column. The higher +Gx loads generated required that additional respiratory support be given. Pressure breathing for G (PBG) using a standard PBG mask and helmet and a counter pressure jerkin was employed. PBG started at +4G at which point it increased at 12 mmHg per G to a maximum of 60 mmHg at +9G. Subjects were either upright (27^{o} seat-back-angle, SBA) or supine (67^{o} SBA) during +Gz exposures. This experiment was the first in which REG measurements were taken during PBG and while cognitive tasks under +Gz were performed. Because of the movement of the subject in the acceleration field (the PALE SBA begins changing at 2.5G), G values below are expressed in radial or aircraft G (Gr), i.e. the acceleration imposed on the centrifuge ball. Results of this experiment were presented at the 1991 Annual Scientific Meeting of the Aerospace Medical Association (see 55 for abstract).

Data analysis consisted of measurements taken at throughout the G exposure and 15s after G offset. Time analysis, were performed on data which had been normalized to isolate the effects of PBG. Data are presented as relative differences with respect to resting or pre-stress levels. Results of the analysis of Zdc and the dc portion of the infrared plethysmograph (IRPdc) are given below. This allowed a comparison of bulk volume movements within the deeper areas of the brain (with Zdc) and the peripheral areas (with IRPdc).

There was great variability both intra- and inter-subjects and individual subjects served as their own controls, using pre-stress data. Runs were compared for similar G and light loss levels. Data comparisons were organized to isolate the effects of anti-G protection, SBA and/or PBG and were compared based on similar peripheral light loss levels. For this experiment, the following abbreviations are used: REL = anti-G suit was worn but not inflated; PBG = same as REL except with pressure breathing; AGS = anti-G suit was operational; BOT = same as AGS except with pressure breathing.

A typical strip chart showing ECG, Zdc and IRPdc during a +5Gz upright run with and without PBG with an inactivated anti-G suit is given in Figure 23. For both Zdc and IRPdc a downward deflection means a shift out of fluid. This figure shows that with PBG as the sole active anti-G protection device, deeper CNS

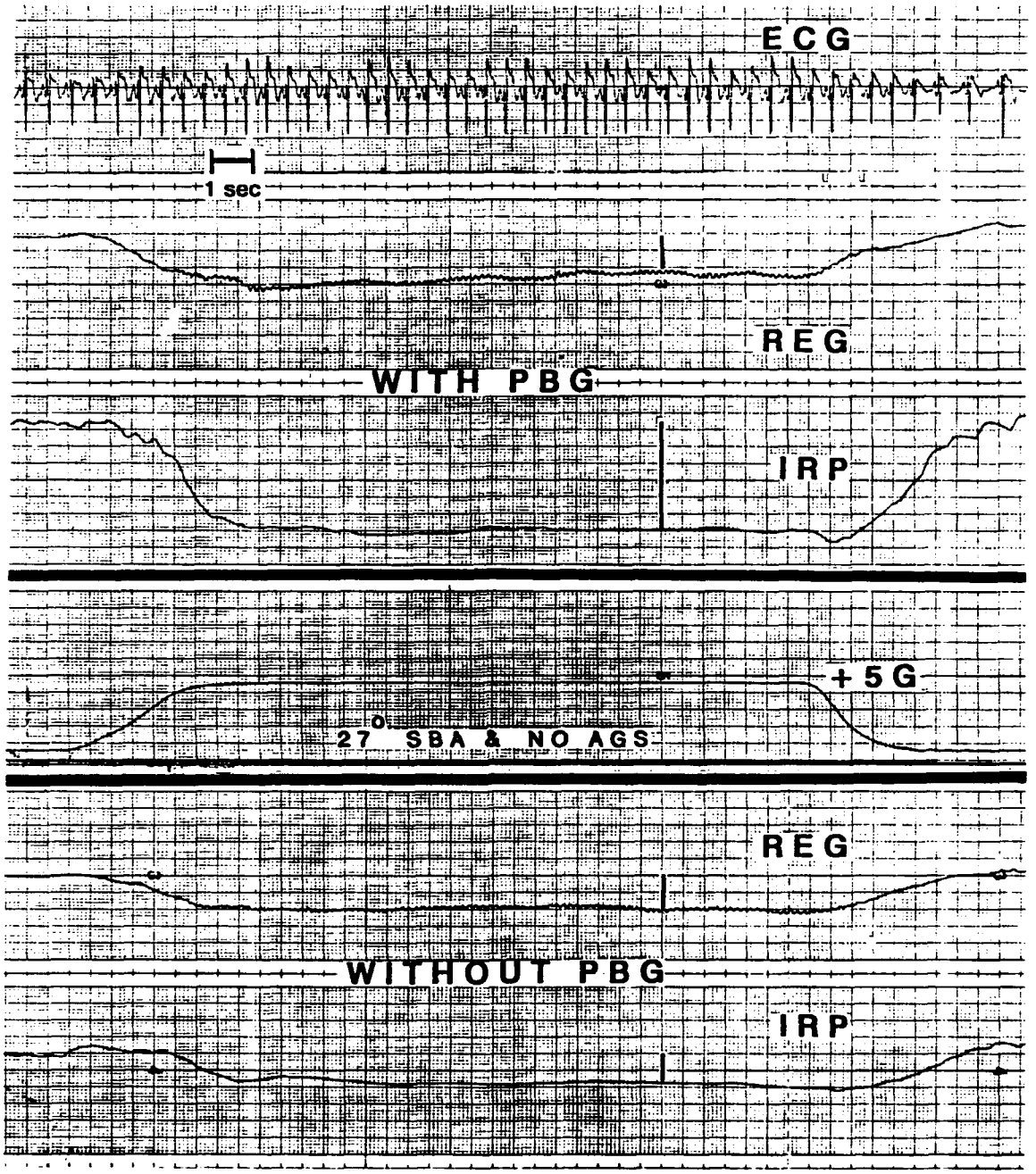


Figure 23. Sample strip chart highlighting effects of +5Gr on Zdc and IRPdc during upright relaxed conditions. From top: ECG, Zdc with PBG, IRPdc with PBG, Gr, Zdc without PBG and IRPdc without PBG.

circulation is aided at the expense of peripheral circulation for this subject.

The results using the infrared plethysmograph were as follows. During the upright condition, when there was a statistically significant difference, whether comparing REL vs PBG or AGS vs BOT, peripheral blood volume reduction was significantly less without PBG. For example, subject D for REL vs PBG at 4.5 Gr, Prob>F = .0014 and at 5 Gr, Prob>F = .0113 and for AGS vs BOT at 4.5 Gr, Prob>F = .0133 and at 5.5 Gr, Prob>F = .0392. Figures 24 and 25 show results for the upright position with and without AGS and PBG, respectively. (Figures 24-33 present representative responses of subject D).

As with the upright data, some supine runs did not present a statistically significant difference. However when significance greater than .05 level was evident, whether comparing REL vs PBG or AGS vs BOT, peripheral blood volume reduction was significantly less without PBG. For example, subject D for REL vs PBG at 4.5 Gr, comparisons using PLL = 0^{o} ranged from not significant to Prob>F = .014 and at 5.5 Gr with PBG at 0^{o} and REL at 30^{o} PLL, Prob>F = .008. For AGS vs BOT: at 4.5 Gr (PLL = 0^{o}) Prob>F = .0002, 5.5 Gr (PLL = 0^{o} to 10^{o}) Prob>F = .0002, at 6.5 Gr (PLL = 0^{o} to 20^{o}), Prob>F = .0255, and at 7.5 Gr (PLL = 10^{o} to 15^{o}), Prob>F = .0046). Figures 26 and 27 show results for the supine position with and without AGS and PBG, respectively.

During performance of the cognitive tasks, IRPdc values were either not significant or indicated that at 4.5 Gr, additional workload lessened the amount of peripheral blood volume loss (Prob>F less than 0.05), while at 5 Gr, save for two comparisons, the differences were not significant. The the supine position at Gr <= 6.5, Prob>F = less than 0.05 that additional workload lessened the amount of peripheral blood volume loss. At 7.5 Gr, most comparisons were not significant. Figure 28 shows the effects of added cognitive tasks during a +6 Gr exposure. The lower solid line curve shows IRPdc while simply riding the profile and the middle three traces show IRPdc while performing cross hair tracking, task B and task B with tracking.

The results with the Zdc were as follows. When subjects were upright, a comparison between REL and PBG indicate that while cerebral blood volume loss was reduced with PBG, the differences were not significant at the Prob>F = 0.05 level. However, with the addition of AGS, when statistically significant at (4 - 5 Gr), PBG decreased the cerebral blood volume loss at the Prob>F = 0.05 level. Figures 29 and 30 show results for the upright position with and without AGS and PBG, respectively. Note that for subject D, the differences were not statistically significant.

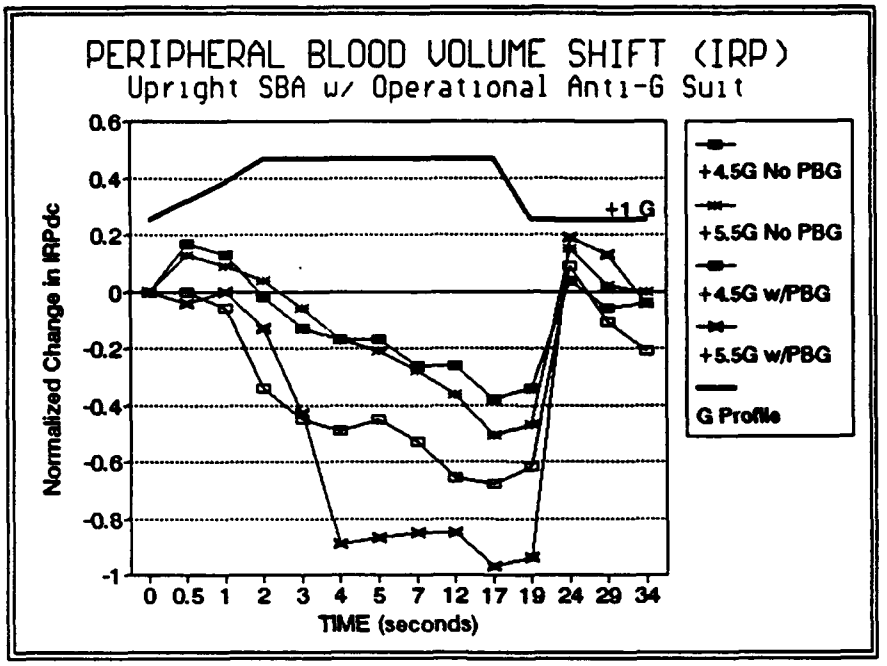


Figure 24. Effects of PBG on peripheral cephalic blood volume shift (IRPdc) with an AGS while upright.

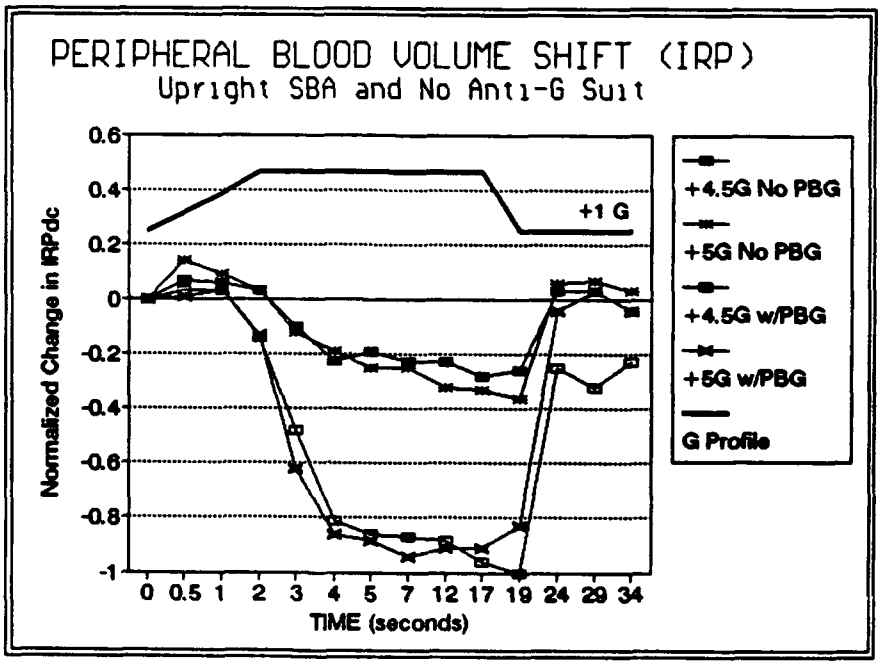


Figure 25. Effects of PBG on peripheral cephalic blood volume shift (IRPdc) without an AGS while upright.

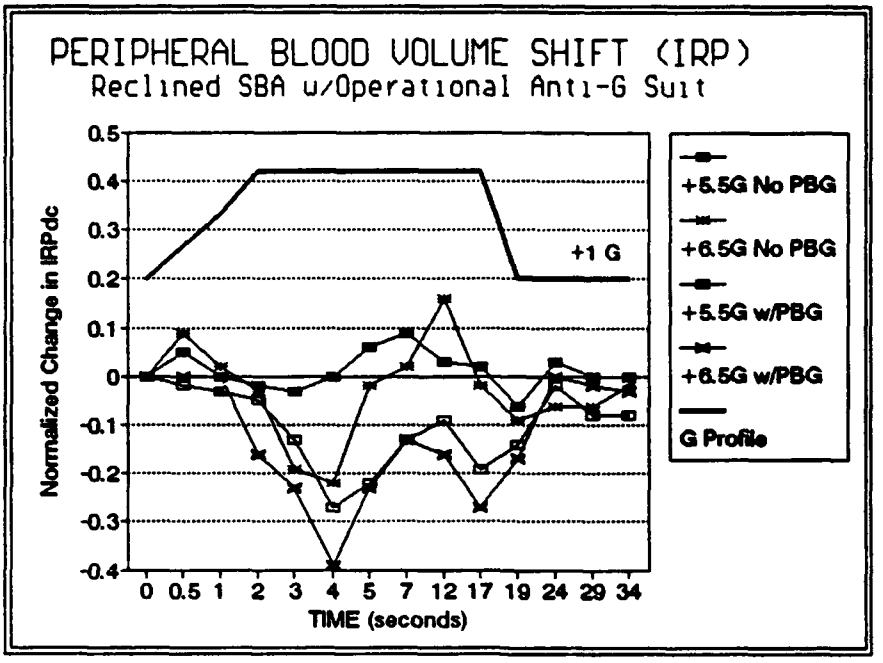


Figure 26. Effects of PBG on peripheral cephalic blood volume shift (IRPdc) with an AGS while supine.

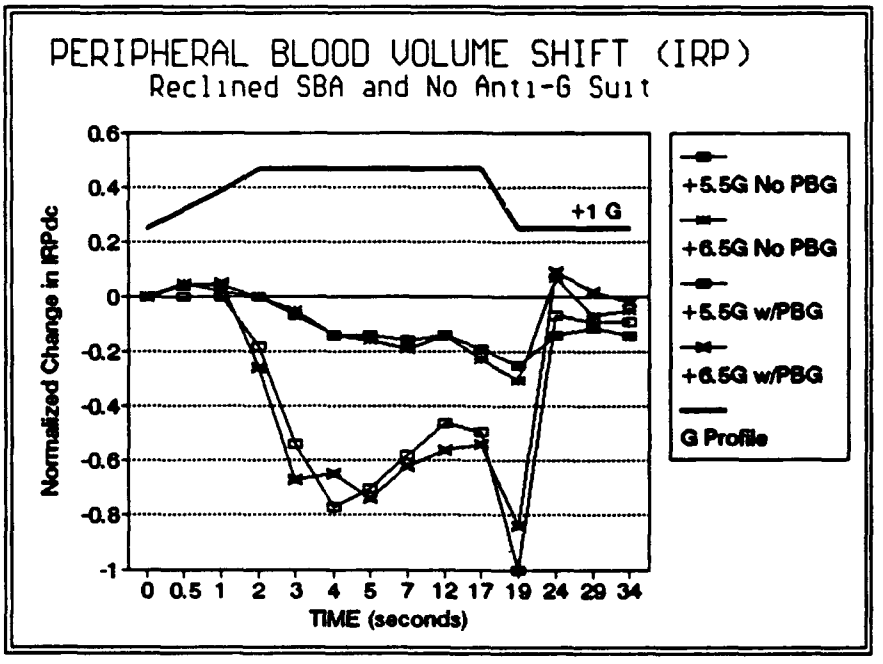


Figure 27. Effects of PBG on peripheral cephalic blood volume shift (IRPdc) without an AGS while supine.

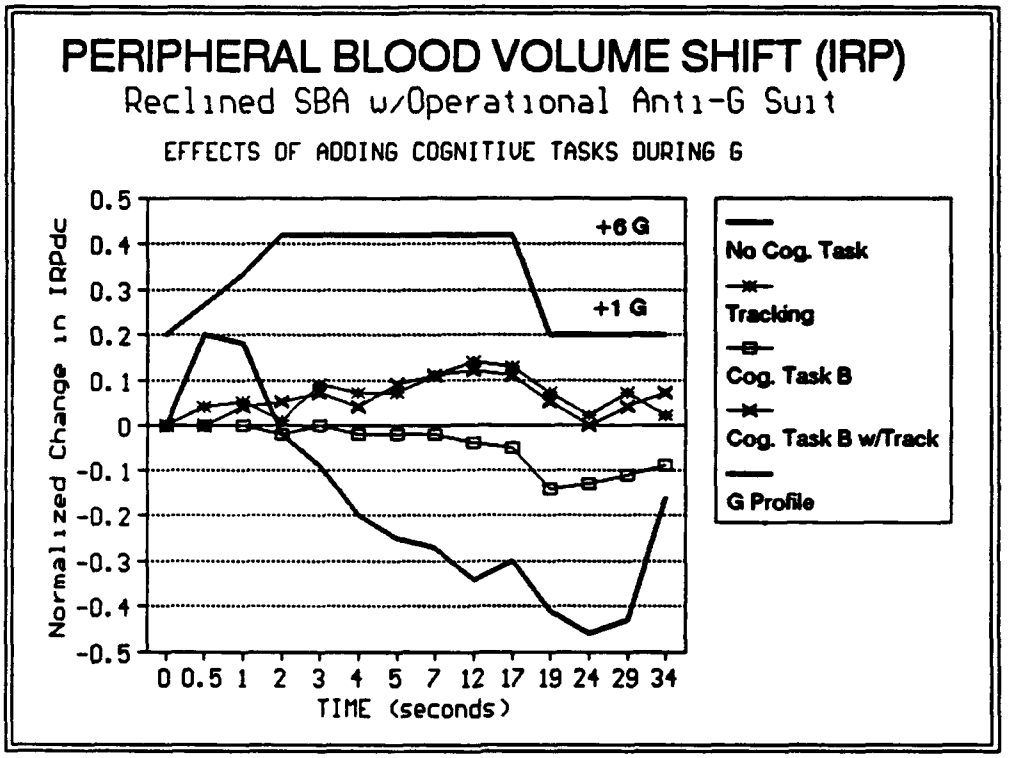


Figure 28. Effects of performance of cognitive tasks on peripheral blood volume shifts (IRPdc) with an AGS and PBG while supine. Lowest curve represents IRPdc without cognitive task performance.

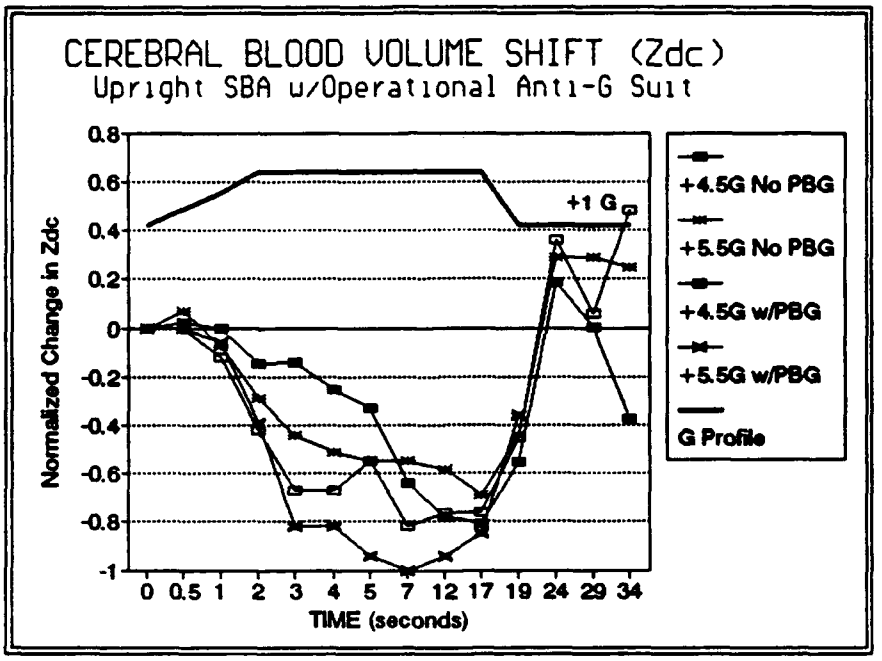


Figure 29. Effects of PBG on cerebral blood volume shift (Zdc) with AGS while upright.

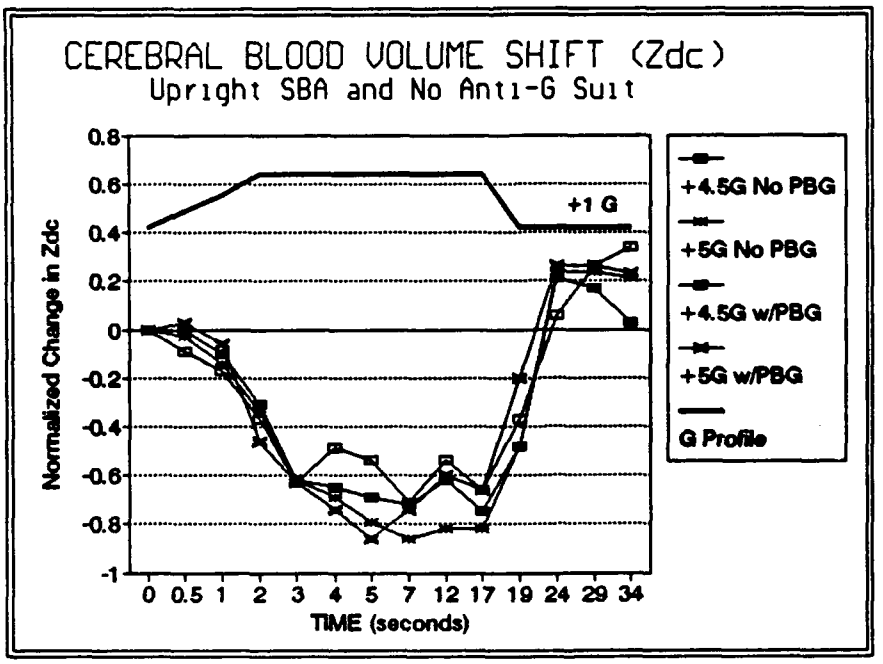


Figure 30. Effects of PBG on cerebral blood volume shift (Zdc) without AGS while upright.

During the supine runs, when comparing REL vs PBG, the data was mixed between subjects and comparisons were either not significant at the 0.05 level or significant at the Prob>F = 0.025 level. The addition of AGS led to interesting results. While a majority of the responses led to either not significant or indicated with a Prob>F at 0.05 level that PBG reduced the outflow of blood volume, in one subject, statistical comparisons were either not significant or indicated that the addition of PBG did not reduced blood volume outflow at Prob>F = 0.03 level.

Figures 31 and 32 show results for the supine position with and without AGS and PBG, respectively.

With the addition of cognitive task performance, Zdc values were mostly not significant in the upright position, however, when statistical significance was shown, the addition of cognitive tasks reduced cerebral blood volume loss (see Figure 33). When the subject were supinated, the results were mixed. Some individuals showed significant reduction in cerebral blood volume loss depending upon the task. Figure 34 shows sample results including significant changes during cross hair tracking and cognitive tasks A and B. In both Figure 33 and 34, the lower trace shows Zdc without performance of cognitive tasks. However, one subject, during most tasks at 6.5 and 7.5 Gr, showed a significant increase in blood volume loss with PBG.

To summarize, it appears that the addition of PBG does not lead to a statistically significant increase in peripheral cephalic blood volume shifts under G regardless of anti-G protection modes. However, the addition of cognitive tasks did decrease blood loss. When the data were significant, deeper cerebral blood volume shifts were aided by the addition of PBG. Addition of cognitive tasks did aid cerebral blood volume in some subjects, but not all. Of interest is the effects of increasing PBG level as G-stress increases. Figure 35 shows an example for subject M during 5.5 and 6 Gr runs. A 6.5 Gr run is shown in which the subject terminated the exposure at 11.3 seconds from onset due to reaching his 60^{o} PLL endpoint. As the PBG level increases (in this case from 18 to 30 mmHg), the amount of outflow of blood as measured by Zdc is reduced with a larger post-G hyperemic response.

These preliminary results do indicate the possibility of regional bulk blood shifts under G stress and that the addition of PBG can influence the magnitude of these shifts. However, the sample size of this experiment was too small to provide a more definitive answer to the effects of PBG under G-stress on the cerebral vasculature.

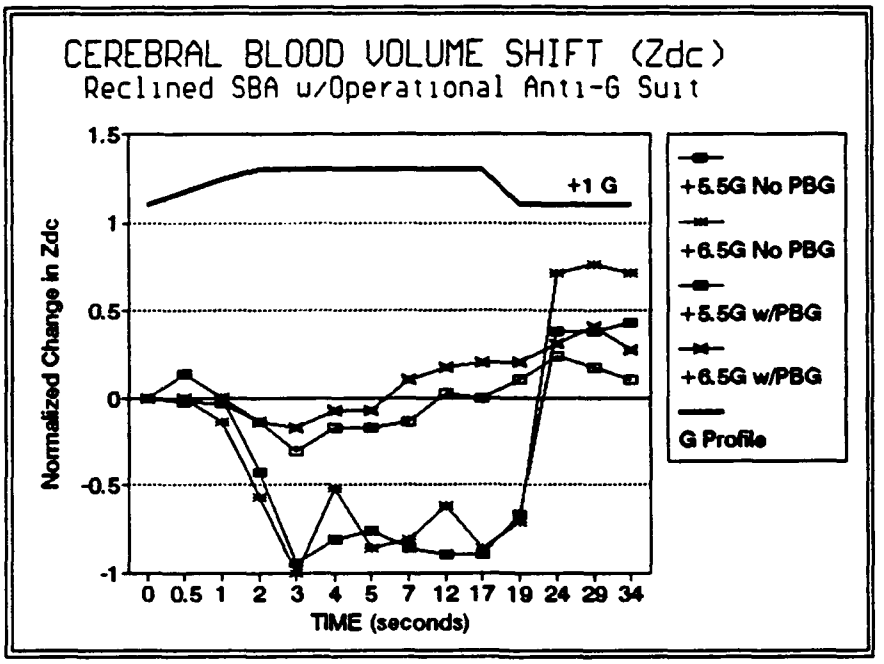


Figure 31. Effects of PBG on cerebral blood volume shift (Zdc) with AGS while supine.

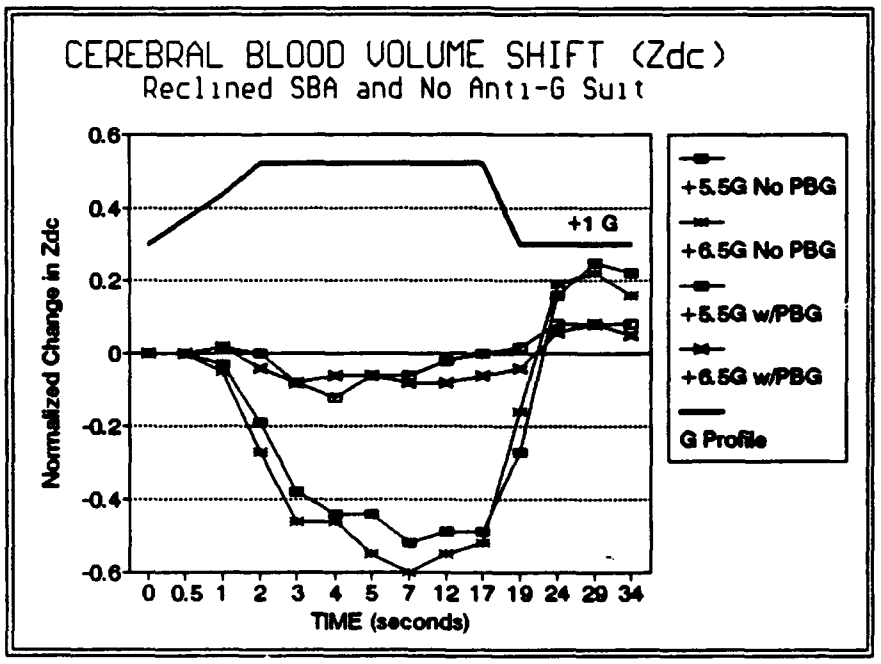


Figure 32. Effects of PBG on cerebral blood volume shift (Zdc) without AGS while supine.

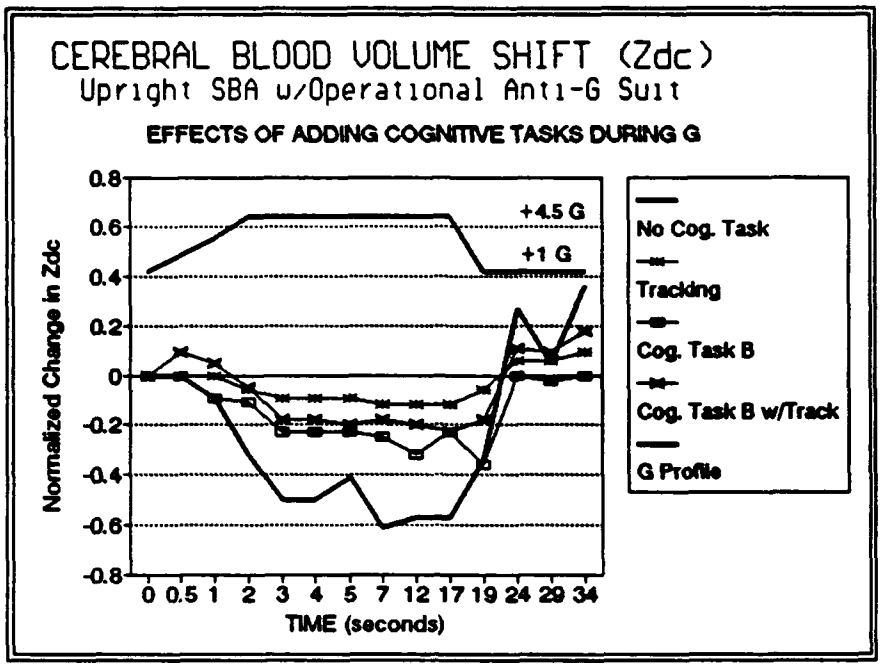


Figure 33. Effects of cognitive task loading on Zdc with AGS while upright. Bottom curve without tasking.

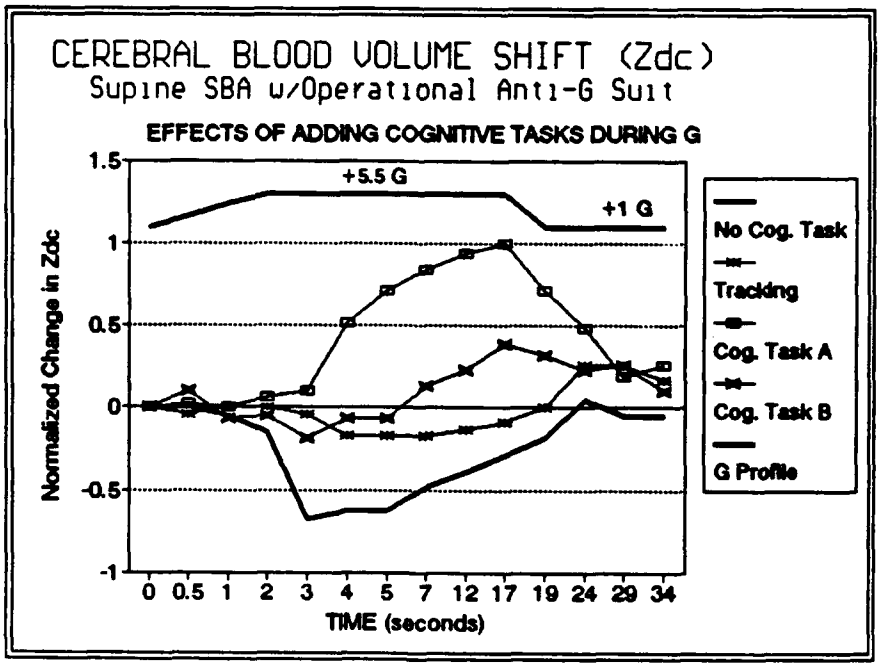


Figure 34. Effects of cognitive task loading on Zdc with AGS while supine. Bottom curve without tasking.

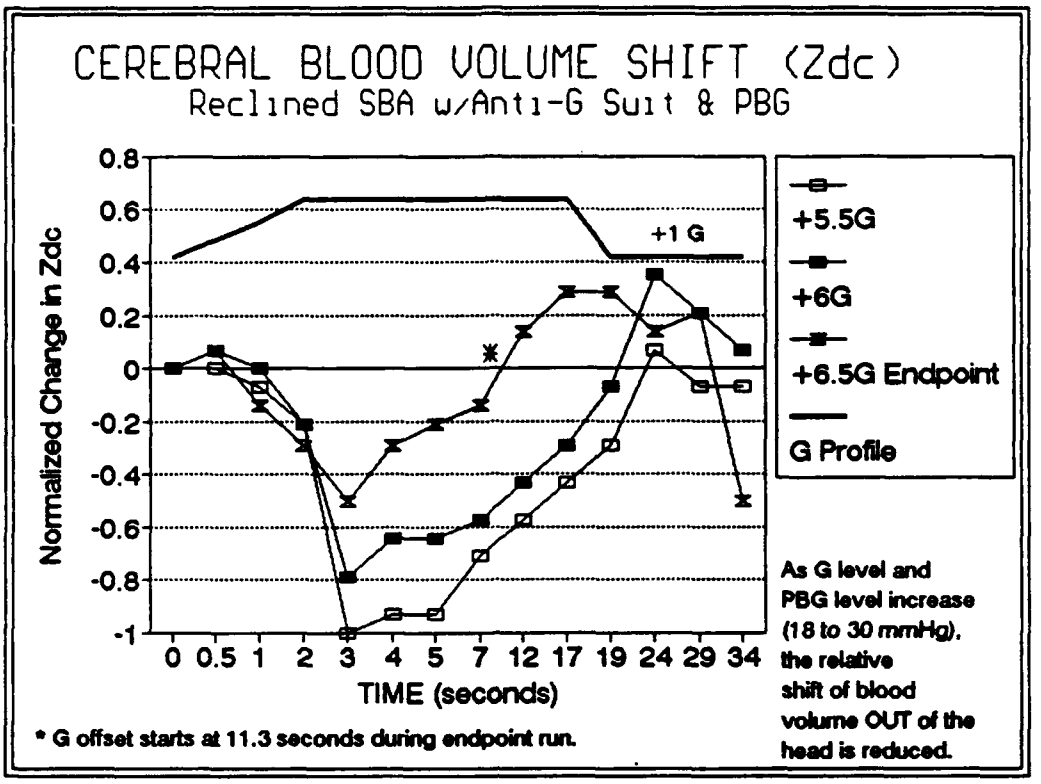


Figure 35. Effects of cognitive task loading on Zdc with AGS while supine. Plot demonstrates that as PBG level increases, the relative shift of cerebral blood volume out of the head is reduced (subject M).

CONCLUSIONS

A convenient, unencumbering, noninvasive, real time, and unobtrusive method for investigating the redistribution of cephalic fluid volume in humans that accompanies exposure to acceleration has been demonstrated. This is the first successful use of this technique at high acceleration levels and onset rates. The REG device has successfully withstood acceleration stresses as high as +14 Gz and -1.5 Gx without compromise. In contrast to the clinical difficulties reported in the literature of the past, rheoencephalography is a useful and easily applied technique in acceleration studies. In the past, the slow moving, or baseline, component of the REG signal has been considered to be an annoying artifact that was removed within the clinical devices. This baseline has been successfully separated from the composite signal in hardware and the utility of monitoring it has been demonstrated. It is now possible to estimate the extent of the bulk movement of cranial blood that occurs under acceleration stress under relaxed conditions and with the performance of AGSM by monitoring changes in the baseline impedance, Zdc. The bulk movement of blood out of the head towards the large capacitance veins of the legs has been postulated in accordance with the hydrostatic column theory of the physiological responses to acceleration stress. This is the first demonstration of the ability to estimate these shifts, whether directly or indirectly. Further, changes in Zdc have been shown to be useful in determining the effects of anti-G protective devices (e.g. a reclining seat) and anti-G protective maneuvers (e.g. as an aid in determining with effectiveness of the performance of the respiratory portion of a AGSM).

The pulsatile component of the REG waveform, Zpul, has been subjected to both classical and contemporary analysis. The form of Zpul shows definite temporal and morphological changes with increasing levels of acceleration stress, particularly those indications related to changes in blood volume and vascular tone. It was possible to demonstrate a frequency content change in Zpul as acceleration load increases. Further, changes seen with other modalities, i.e. pulse wave delay using pulsed doppler ultrasound, were also seen with Zpul.

The instrument has been worn by fifty eight volunteer subjects during five different human centrifuge experiments. A variety of electrode types have been investigated. Large surface area silver-silver chloride electrodes seem to work the best. In all of the configurations, whether placed on the forehead or on the occipital region of the head, none of the subjects experienced any discomfort or after-effects as a consequence of using the REG device.

The relationship between respiratory pressure changes and the REG was hinted at during CE5. One of the effects of positive pressure breathing is to force blood out of the chest into the arms and, presumably, the head. The REG did indicate that

pressure breathing did contribute to an increase in headward blood volume. One can then postulate that the REG could be used to investigate the effects of cerebral perfusion through the use of respiratory maneuvers alone. This would enable the REG to be used in further studies of the physiologic effects of pressure breathing as well as in high altitude studies.

In summation, an old technique configured and used in a new environment has been developed and tested. Use of this device has enhanced the potential for further exploration into the mysteries of the cerebral circulation in both normal and acceleration environments.

RECOMMENDATIONS FOR FUTURE STUDIES

Obviously, it has been impossible to characterize the contribution of cerebrospinal fluid (CSF) to the REG waveform while only performing human trials. Only by the use of animal models in both normal and acceleration stress environments can this be determined. A separate effort under an NADC Independent Research Project is underway to explore this issue. These studies have included the use of physiological and surgical techniques to mimic the effects of +Gz-stress, i.e. reduced cerebral blood supplies and hypoxia, as well as direct manipulations of the CSF space. Preliminary results can be found in references 53 and 54. This information remains to be correlated and integrated with the human responses.

Further analysis on humans can be performed noninvasively. For example, tests on a tilt table to simulate higher acceleration stress can be performed without having to schedule human centrifuge time. Volunteers can inhale 5-7% CO_2 and O_2 mixtures to increase vasodilation while REG, ECG, etc. is recorded. It should be possible to fashion useful electrodes that can be fitted to the nose to measure REG signals. The nose is highly vascularized and contains no CSF. Obtaining this kind of data would be enormously useful.

The use of lower body negative pressure can be used to study the effects of reduced cerebral perfusion. In this technique a suction is applied to the body below the iliac crest causing blood to be drawn into the legs away from the chest and head. By taking REG as well as transcranial doppler (cerebral artery blood velocity) measurements, it will be possible to gauge the ability of the REG to follow deep cerebral vascular changes during orthostatic stress.

Another 1g avenue of research to follow would be to specifically investigate the effects of respiratory pressures on the REG in humans. A controlled laboratory study using a variety of breathing patterns, similar to the animal studies, would enable determination of the effects of breathing pressures on the REG. Preliminary indication from the animal studies is that the

magnitude and timing of the B wavelet as well as a shifting of the A wavelet are related to breathing pressures.

Some consideration might be given for outfitting the REG electrodes in such a way that they do not have to be affixed to a individual in the current fashion. The current method can lead to problems when a subject dons a flight helmet, e.g. wires and electrodes may move and become disconnected. It may be possible to fit electrodes onto a pair of sunglasses with sensors places on the ear pieces. This arrangement should not conflict with other operational gear currently worn.

Several technical refinements and additions should be incorporated into the REG design. Exciting the purposely off-null detection bridge with a +/- 1.4 Vp-p signal has led to a minimum of adjustments necessary for good reproduction of the signal. However, no adjustment would be best. Therefore, some automatic control mechanism for optimally setting the bridge should be considered. In order to compare the results currently obtained with those contained in some previously published clinical studies, a tetrapolar constant current version of the REG ought to be developed. This could use most of the currently installed hardware. This device would probably be less sensitive and more difficult to set up on a subject due to the necessity of good linear alignment of four electrodes on a curved surface, i.e. the head. Lastly, the device itself should be redesigned to reduce the size of the instrument. This could easily be accomplished with new miniaturized circuit components which have recently gone on the market.

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