Cardiovascular adaptation to repetitive +Gz in fighter pilots: a role for the vestibulosympathetic reflex

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Fighter pilots are routinely exposed to high levels of repetitive +Gz acceleration (ie, acceleration equivalent to more than the force of gravity).[1] The adverse cardiovascular and neural consequences of exposure to the high +Gz environment are well known, with G-induced loss of consciousness (G-LOC) the most significant of these.[2-9] High levels of applied +Gz challenge the body's ability to maintain the appropriate arterial blood pressure. The physiological countermeasures to these adverse +Gz effects include activation of the arterial baroreflexes.[2,10] There is now evidence suggesting that these reflex arcs develop a degree of adaptation, reflected in improved cardiovascular performance, as a result of repetitive exposure to the high +Gz stimulus.[11-13] There is also an emerging body of research that suggests a link between the vestibular system and the regulation of arterial pressure, known as the vestibulosympathetic reflex.[14] This reflex has potential implications for the pilot of a high performance fighter aircraft operating in the high +Gz environment.

This article examines the role of the vestibulosympathetic reflex in the regulation of arterial pressure, and its possible involvement in cardiovascular adaptation to the high +Gz environment. I begin by reviewing the essential elements of cardiovascular regulation of arterial pressure, then examine the vestibular system, its neural connections and primary functions in some detail. This is followed by a consideration of the evidence linking the vestibular system with cardiovascular control. Finally I present a theoretical case for the vestibulosympathetic reflex's role in adaptation to the high +Gz environment.

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Synopsis

- Arterial pressure is regulated by the baroreflex system, a relatively simple negative-feedback control system involving arterial and cardiopulmonary baroreceptors.
- The vestibular system, which comprises the semicircular canals and the otolith organs, is involved in maintaining balance and orientation.
- There are good theoretical grounds for the existence of a link between these two systems, a vestibulosympathetic reflex.
- The vestibular system could provide feed-forward adjustment of arterial pressure before the baroreflexes become active.
- Some experimental evidence supports the existence of vestibulosympathetic reflexes.
- If the vestibulosympathetic reflexes can adapt to frequent exposure to +Gz, this would help protect fighter pilots from G-induced loss of consciousness.

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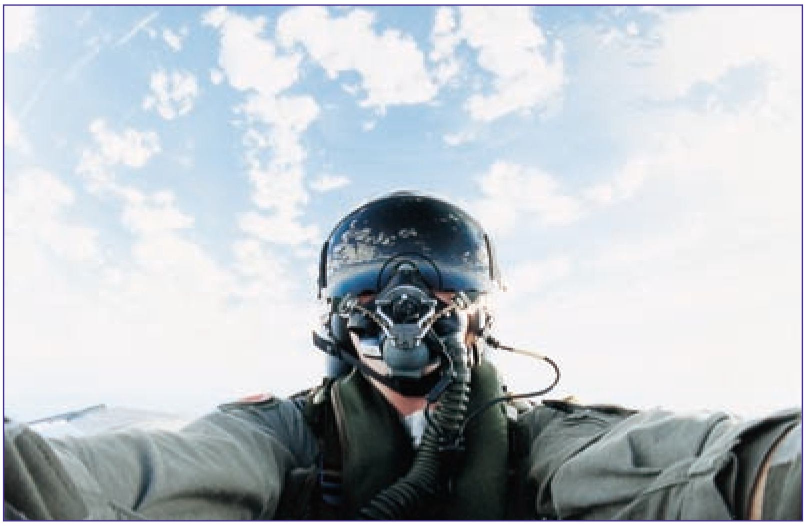
Cardiovascular regulation of arterial pressure

When a fighter pilot is exposed to +Gz acceleration, the sudden increase in hydrostatic force leads to a fall in mean arterial pressure. As mean arterial pressure is the key regulated variable of the cardiovascular system, various physiological countermeasures are activated to restore it to its previous level.[15] Perhaps the most significant and well-studied of these are the baroreflexes. These consist of the arterial baroreflexes on the high-pressure side of the circulation, and the cardiopulmonary baroreflexes on the low-pressure side.

A negative-feedback control system

The application of engineering control theory to physiological research has led to the baroreflexes being considered as a closed-loop negative feedback control system, the sole purpose of which is to control mean arterial pressure within a specific range. The human baroreflex system is designed to maintain blood pressure at an optimum functional level. It does this by using any deviation from normal values as a mismatch or error signal with which to drive the control loop towards restoration of the optimum level.[16] The error signal is proportional to the difference between the actual and the desired value, and the goal of the baroreflex system is to eliminate this difference. Cerebral perfusion is therefore maintained, and loss of consciousness is prevented. The system is expressly designed to ensure that all organ systems of the body are adequately perfused despite any postural alterations, such as in going from a lying to a standing position, or when experiencing high +Gz loads.[2,7,10,12,17,18]

The operation of the baroreflexes is relatively simple. Increases in perfusing pressure cause a stretching of the walls of the major arteries and the cardiac chambers, which stimulates stretch receptors within these structures. These stretch receptors (or mechanoreceptors) transmit electrical signals to the vasomotor centre in the medulla oblongata region of the brainstem. In accordance with the normal operation of such reflex arcs, signals are then transmitted via effector nerves to the heart (to decrease heart rate) and blood vessels (to vasodilate), which eventually results in a lowering of arterial pressure. The converse applies when pressure decreases. This reflex is physiologically very important, as it produces a generally stable arterial pressure level despite wide-ranging external influences.[2,10]



Worldview from an F/A-18 Hornet. Pilots who fly such fighter aircraft develop an adaptation to the high G forces involved. The mechanisms underlying this adaptation are the subject of much research. (Photograph courtesy Squadron Leader David Newman.)

Arterial baroreflexes

The arterial baroreflexes have been the most widely studied. Details of their role and function began to emerge in 1900 through the work of two Italian physiologists, Pagano and Siciliano, who discovered that the pressor effect of common carotid artery occlusion in dogs depended on certain nervous structures within the neck.[10] In the 1920s, the German physiologists Hering and Koch discovered that these structures were branches of the glossopharyngeal nerve.[10] Research since then has established that these reflexes are of paramount importance in the regulation of the human circulatory system.

There are two principal arterial baroreflex arcs, named after the anatomical locations of their receptors: the carotid sinus baroreflex and the aortic baroreflex. The carotid sinus is a segmental fusiform dilatation of the upper part of the common carotid and the adjacent part of the internal carotid arteries. The walls of the sinus are very elastic, largely because of the significantly higher collagen and elastin content of the sinus wall compared with that of adjoining segments of the carotid system.[19] Within the walls of the carotid sinus are a multitude of spray-type nerve endings that function as stretch receptors. These receptors are located predominantly in the adventitia of the sinus wall next to the media. The nerve terminals or sensory fibres are unmyelinated, 2–4 μm in size, and morphologically quite variable.[19]

The aortic baroreceptors are located in the arch of the aorta, and consist of the same form of spray-type stretch receptor nerve endings, located within the artery walls at the medial–adventitial interface in great numbers. There is less morphological variation in the nerve endings in the aortic receptors than in the carotid receptors.[19]

Cardiopulmonary baroreflexes

The cardiopulmonary baroreflexes have not been as extensively investigated owing to significant methodological and practical limitations.[20] These mechanoreceptors are functionally and morphologically similar to the high-pressure arterial receptors.[21] They are concentrated within the walls of the pulmonary arteries, near the bifurcation of the main pulmonary artery into right and left branches, and in the subendocardial part of the atria near the venoatrial junctions.

Operation of the baroreflexes

Afferent impulses are transmitted from the various baroreceptors to the nucleus of the tractus solitarius in the posterolateral medulla and lower pons.[21] The carotid sinus impulses are transmitted along a small branch of the glossopharyngeal nerve (cranial nerve IX) known as the sinus nerve (or Hering's nerve), while afferent impulses from the remaining baroreceptors travel via the vagus nerves.[19] From the nucleus of the tractus solitarius, secondary fibres communicate with vasodilator and vasoconstrictor areas in the anterolateral medulla. These three areas constitute the vasomotor centre,[21] which lies close to the dorsal motor nucleus of the vagus (the vagal centre). Secondary impulses from the tractus solitarius also travel to the vagal centre. Efferent sympathetic impulses from the vasomotor centre are then transmitted to the heart and blood vessels via the paravertebral sympathetic chain, while efferent parasympathetic impulses are conducted along the vagus nerves (cranial nerve X) via the vagal centre. The vasomotor centre thus receives afferent inputs from several sources and integrates this information before dispatching the appropriate efferent impulses via common output arms.

Baroreceptor inputs maintain both a tonic inhibitory influence on the vasomotor centre, which tends to limit vasoconstriction, and a tonic excitatory influence on the vagal centre, which tends to produce the parasympathetically mediated decreases in heart rate and cardiac contractility. This set of circumstances represents the normal balance between sympathetic and parasympathetic tone in the cardiovascular system, and results in a certain resting heart rate and resting arterial blood pressure in a given individual.[10,21]

If arterial pressure falls, the arterial baroreceptor input decreases. It loses its normal inhibitory effect on the medullary vasomotor centre, allowing this centre to produce a degree of peripheral vasoconstriction mediated by the sympathetic nervous system. The reduced excitation of the vagal centre results in less parasympathetic influence, leading to an increase in both heart rate and cardiac contractility. The tone of the circulatory system thus shifts in favour of the sympathetic system. These measures tend to return arterial pressure to its normal level.[19]

Conversely, any increase in arterial pressure will cause activation of the baroreceptors and an increase in the degree of vasomotor inhibition and vagal excitation. The parasympathetic system becomes dominant. This will lead to vasodilatation, bradycardia and a relative reduction in cardiac contractility, resulting in a reduction in arterial pressure until the normal blood pressure level is restored.

The reflexes produced by the cardiopulmonary baroreceptors are in parallel with those of the arterial baroreceptors. Although they do not detect systemic pressure, they respond to small pressure differences in the low-pressure side of the circulation, thereby minimising the effect of central blood volume changes (due to postural changes, for example). The combination of high- and low-pressure baroreceptors results in a significantly more powerful system for regulation of arterial pressure.[21] This is well illustrated by an experiment in which dogs were infused with a bolus of 300 mL of blood. With all reflexes intact, arterial pressure rose by 15 mmHg. With the arterial baroreceptors denervated, pressure rose by 50 mmHg, but with denervation of the cardiopulmonary receptors as well it rose by 120 mmHg.[21]

Thus, any deviation in arterial pressure from the normal level will be detected by the baroreceptors, and attempts made to return pressure to normal values via the activation or deactivation of the baroreflex mechanisms. However, the arterial baroreflexes tend to be more effective at preventing a fall in blood pressure than a rise.[10,19]

The vestibular system and its neural connections

The vestibular system, composed of the semicircular canals and the otolith organs, is a complex arrangement of sensory receptors and neural projections. A comprehensive review of the anatomy and physiology of the semicircular canals and the otoliths is beyond the scope of this article; what concerns us here are the neural connections and projections between these vestibular end-organs and the central nervous system. Readers with an interest in more detailed information regarding end-organ function in terms of basic orientation mechanisms are directed to the relevant articles.[22-24]

Afferent traffic from the mechanoreceptive sensory hair cells in the canals and otoliths is transmitted via the vestibuloacoustic nerve (cranial nerve VIII).[25,26] This is composed of three ampullary nerves (from the canals), the utricular nerve and the two saccular nerves (from the otoliths), and the nerve bundles from the acoustic end-organs.[23-27] Scarpa's ganglion, located at the internal auditory meatus, consists of the cell bodies of the bipolar vestibular neurons, and lies within the nerve.[24-26] Neuronal dendrites terminate within the labyrinthine architecture, attaching to the sensory hair cells of the cristae and maculae of the canals and otoliths, respectively.

An idea of the complexity of the vestibular system can be derived by the diverse array of destinations for this afferent traffic within the central nervous system. The axons enter the brainstem at the junction of the pons and medulla, and bifurcate before terminating in the vestibular nuclear complex. This complex consists of four histologically defined vestibular nuclei in the rostral part of the medulla and caudal part of the pons: the superior, inferior, medial and lateral (or Deiters') nuclei.[14,24-28] The vestibular nuclei project via several secondary vestibular tracts to various centres throughout the brain and spinal cord. As the two complexes normally act as a coordinated pair, there are extensive connections between the vestibular nuclei on both sides. There are even efferent fibres which travel back to the vestibular end-organs. These are thought to be involved with a feedback function, but their role is poorly understood.[26]

The cerebellum receives a number of nerve fibres directly from the vestibular nerve, as well as a substantial number of interneuronal fibres from the vestibular nuclei. These fibres enter the cerebellum via the inferior cerebellar peduncle to terminate in the fastigial nucleus, the flocculonodular lobe and the adjacent region of the inferior vermis.[24-26] The efferent connections of the vestibulocerebellum are concerned with influencing muscle tone in relation to postural changes and locomotion.

The ascending medial longitudinal fasciculus carries vestibular nuclei projections to the motor nuclei of the oculomotor, trochlear and abducens nerves, and the accessory oculomotor nuclei of the midbrain, which together control the function of the extra-ocular muscles. This arrangement forms the basis of the vestibulo-ocular reflex.[24-28] The vestibulo-ocular reflex is designed to stabilise the retinal image despite any head movements or postural changes. It facilitates conjugate eye movement, coordinated with head movement, to maintain visual fixation. The eyes will turn in the opposite direction to that of the head movement to prevent smearing of the visual image across the retina. Indeed, without this reflex, an individual would not be able to resolve fine detail and maintain normal visual acuity when walking, running or when exposed to vibration.[22] It is a fundamentally important component of the normal process of acquiring and maintaining a correct sense of spatial orientation.

Descending efferent fibres from the vestibular nuclei are carried in the lateral vestibulospinal tract and descending medial longitudinal fasciculus.[24-26,28] Fibres in the lateral vestibulospinal tract originate in Deiters' nucleus and descend throughout the spinal cord, subserving the critical function of regulating axial muscle tone to maintain equilibrium and balance, particularly in the face of postural changes. Fibres in the descending medial longitudinal fasciculus (also known as the medial vestibulospinal tract) originate in the medial vestibular nucleus and descend into the cervical spinal cord. These fibres are primarily involved with the vestibulocollic reflex, which is concerned with maintaining stability of the head in space. The vestibulocollic reflex results in a pattern of neck muscle activation designed to counteract any head movement detected by the vestibular end-organs.[29]

The vestibular system has a crucial role to play in human spatial orientation. The neural integration of angular and linear acceleration information into commands for the regulation of postural muscle tone and conjugate eye movement serves to maintain balance and orientation with respect to the coordinate reference system of the horizon and the gravitational force environment.

Evidence supporting the existence of a vestibulosympathetic reflex

It would appear from the foregoing that regulation of mean arterial pressure is the function of the cardiovascular system (mediated largely by the sympathetic branch of the autonomic nervous system), while balance and orientation are the functions of the vestibular system, with the two systems being unrelated. However, an emerging body of evidence supports the notion of a vestibulosympathetic reflex, effectively a neural control link between the vestibular and cardiovascular systems.

Theoretical analysis

There are good theoretical grounds for postulating the existence of a vestibulosympathetic reflex. Postural changes invoke a series of physiological events in both the cardiovascular and vestibular systems. The cardiovascular system is exposed to a changing hydrostatic force environment when going from the supine to the fully upright position, and this leads to activation of the baroreflex mechanisms. This same change in body position is accurately transduced by the vestibular system to derive an accurate internal model of spatial orientation, and to maintain balance.

The regulation of arterial pressure involves responding to inputs from both arterial and cardiopulmonary baroreceptors that register the alteration in applied hydrostatic force (which is due to a changing gravitational force vector, particularly when experiencing high +Gz). This change in gravitational vector is registered by the otolith organs, which, as linear accelerometers, signal the static position of the head with respect to gravity.[24] Why not also use this otolithic information in the integration of information pertaining to postural change and the maintenance of an adequate cerebral perfusing pressure? After all, one determinant of consciousness is an adequate level of cerebral perfusion. Although maintaining this cerebral perfusion is an essential role of the postural baroreflexes, the information provided by the otoliths would be similarly useful in determining the magnitude of the required cardiovascular response to a changing hydrostatic force environment.

The problem with negative feedback systems, such as the baroreflexes, is that their drive relies on an error signal; they only act once homeostasis has been disturbed.[30] In the face of deteriorating conditions, these reflexes must restore the status quo. Owing to the inherent inertia in their activity, they are not always able to do so. The G-LOC phenomenon is a perfect example of this baroreflex overload situation. With the increasing +Gz level, the hydrostatic force drives blood to the lower limbs, reducing venous return, stroke volume and mean arterial pressure. This scenario is a magnified version of what happens in going from the supine to the upright position.[15,31] If the application of +Gz is sufficiently rapid and/or maintained for long enough, the baroreflexes will not be able to correct the adverse circulatory state before cerebral perfusion is affected and unconsciousness supervenes. To prevent this from occurring, it makes sense for the vestibular system to play some role in maintaining a stable mean arterial pressure in the face of rapid postural changes by mediating cardiovascular adjustments before homeostasis is disturbed.[30]

The vestibular system may have a role as a feed-forward mechanism in the regulation of arterial pressure. Researchers have commented on the likelihood that vestibular signals could provide feed-forward adjustment of arterial pressure during unexpected postural change.[32] Ray et al postulated that the vestibular system could signal postural changes (and the attendant cardiovascular consequences) before the baroreflexes become active.[33]

Experimental evidence

The notion of a vestibulosympathetic reflex does have some experimental support. Some of the earliest work was performed by Spiegel and Demetriades in the 1900s.[14] Using both electrical and caloric stimulation of vestibular afferents, they demonstrated increases in blood pressure in a variety of animals such as cats and dogs. Subsequent experiments have determined that vestibular stimulation results in increased sympathetic activity, and that this mediates the cardiovascular changes.[34] Furthermore, this increase in sympathetic outflow can be abolished by experimental lesions in the vestibular nuclei.[14] Woodring et al demonstrated increased sympathetic nervous system activity and a consequent pressor response following nose-up vestibular stimulation in cats.[32] This response was abolished in cats with transected vestibular nerves, a phenomenon also demonstrated by Doba and Reis,[35] who found that cats with bilaterally transected vestibular nerves were unable to compensate for the orthostatic hypotension produced by head-up tilt, whereas normal cats with intact vestibular nerves fared much better.

Studies in humans have also pointed to the existence of a link between the vestibular system and cardiovascular control. Shortt and Ray found that head-down neck flexion in human subjects resulted in increased muscle sympathetic nerve activity and subsequent rises in calf vascular resistance.[36] Essandoh et al demonstrated similar increases in forearm and calf vascular resistance.[37] Skin sympathetic nerve activity does not seem to be affected by head-down neck flexion,[33] whereas reduced baroreceptor stimulation leads to forearm vasoconstriction in both skin and muscle circulations.[38] Interestingly, while peripheral vascular resistance increases have been universally observed, heart rate has been variously reported as undergoing no change or as increasing.[32,33,36]

Finally, there is evidence to suggest that the vestibulosympathetic reflex is indeed primarily the result of otolith activation, as the changes in sympathetic outflow are limited to pitch inputs rather than roll or yaw.[14,30,38] Furthermore, the response characteristics and gain of the vestibulosympathetic reflex to sinusoidal pitch inputs are similar to otolith afferents.[14,38] Researchers have concluded that a specific group of vestibular receptors (otolithic pitch responders) is responsible for vestibulosympathetic responses, and that these responses are appropriate to offset hydrostatic challenges to the circulation, such as postural changes and exposure to the high +Gz environment.[14,38] It has also been suggested that the central site of the vestibulosympathetic reflex is the caudal ventrolateral medullary reticular formation.[39]

The implications for adaptation to +Gz in fighter pilots

Baroreflex adaptation to altered gravitational force environments has been well documented, at least in terms of the orthostatic hypotension associated with microgravity and its ground-based analogues.[40-48] My colleagues and I have demonstrated adaptation of the baroreflexes to repetitive occupational exposure to high +Gz forces in fighter pilots.[11-13] Our research suggested that +Gz-adapted fighter pilots were able to activate their baroreflexes more quickly and to a more significant extent than non-pilots, reflecting their enhanced ability to shift the autonomic balance in favour of the sympathetic system.

A case could be made on the basis of the arguments presented here for the repetitive exposure of fighter pilots to the high +Gz environment (and its cardiovascular effects) to lead to an augmented and enhanced vestibular feed-forward mechanism to better protect the pilot from the potential for +Gz-induced circulatory compromise. If the gain of the arterial baroreflex arc can be increased by repetitive exposure to a challenging environment, why should the vestibulosympathetic reflex not experience a similar training effect if exposed to the same stimulus?

In normal individuals exposed to a terrestrial +1 Gz environment, the vestibulosympathetic reflex maintains mean arterial pressure despite the normal hydrostatic perturbations that result from ambulatory movement and postural changes. The vestibulosympathetic reflex of a fighter pilot, regularly and repetitively exposed to high +Gz levels, may well develop an enhanced functional state. As soon as the otoliths begin to register an increase in the applied +Gz level, activation of the enhanced vestibulosympathetic reflex could result in earlier activation of the +Gz-adapted efferent arm of the baroreflexes. This could prevent the precipitous and potentially disastrous fall in mean arterial pressure that would normally be required to trigger the baroreflexes. Clearly, this would be advantageous in the fighter pilot operating in a high +Gz environment, as it would protect against G-LOC.

This theoretical role of the vestibulosympathetic reflex in the cardiovascular adaptation to high +Gz warrants further research. My colleagues and I plan to investigate this by examining the responses to head-down neck flexion in fighter pilots compared with non-pilots. Vestibulosympathetic reflex adaptation to +Gz would be elegantly and simply demonstrated by the finding that increases in peripheral vascular resistance due to head-down neck flexion were more marked in fighter pilots than non-pilots. Such a finding would show that the vestibulosympathetic reflex had developed an enhanced level of functioning due to repetitive exposure to the high +Gz environment.

Conclusion

I have discussed the roles of the vestibular system in cardiovascular control in general and in adaptation to +Gz in particular. It seems logical that regulation of arterial pressure would be achieved via the neural integration of all available information concerning postural or +Gz-induced challenges with their attendant hydrostatic penalties. Such integrated information would clearly include that provided by the otoliths via the vestibulosympathetic reflex. It is quite possible that the vestibulosympathetic reflex also adapts to frequent exposure to high +Gz, by enhancing its normal feed-forward action. This certainly warrants further research attention. In this way we may better understand the complex and intricate mechanisms responsible for regulation of the circulatory system.

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References

1. Newman DG, Callister R. Analysis of the Gz environment during air combat maneuvering in the F/A-18 fighter aircraft. *Aviat Space Environ Med* 1999; 70: 310-315.
2. Blomqvist CG, Stone HL. Cardiovascular adjustments to gravitational stress. In: Handbook of physiology. The cardiovascular system. Sect 2, Vol III, Ch 28. Bethesda, MD: American Physiological Society, 1983; 1025-1063.
3. Burton RR. G-induced loss of consciousness: definition, history, current status. *Aviat Space Environ Med* 1988; 59: 2-5.
4. Burton RR, Leverett SD, Michaelson ED. Man at high sustained +Gz acceleration: a review. *Aerospace Med* 1974; 45: 1115-1136.
5. Burton RR, Shaffstall RM. Human tolerance to aerial combat manoeuvres. *Aviat Space Environ Med* 1980; 51: 641-648.
6. Glaister D. Long duration acceleration. In: Ernsting J, King P, editors. Aviation medicine. 2nd ed. London: Butterworths, 1988.
7. Howard P. The physiology of positive acceleration. In: Gillies JA, editor. A textbook of aviation physiology. New York: Pergamon Press, 1965.
8. Newman DG. Neurophysiological aspects of G-induced loss of consciousness (G-LOC). *Aust Mil Med* 1997; 6(3): 3-7.
9. Parkhurst MJ, Leverett SD, Shubrooks SJ. Human tolerance to high, sustained +Gz acceleration. *Aerospace Med* 1972; 43: 708-712.
10. Mancia G, Mark AL. Arterial baroreflexes in humans. In: Handbook of physiology. The cardiovascular system. Sect 2, Vol III, Ch 20. Bethesda, MD: American Physiological Society, 1983; 755-793.
11. Newman DG, Clark CL, White SW, Callister R. Baroreflex adaptation to +Gz in pilots of high performance fighter aircraft: a preliminary analysis. Proceedings of the Australian Physiological and Pharmacological Society. Melbourne: The Society, 1995; 26(2): 201P.
12. Newman DG, White SW, Callister R. Evidence of baroreflex adaptation to repetitive +Gz in fighter pilots. *Aviat Space Environ Med* 1998; 69: 446-451.
13. Newman DG, Clark CL, White SW, Callister R. Cardiovascular dynamics in the +Gz-adapted pilot. Proceedings of the Australian Physiological and Pharmacological Society. Brisbane: The Society, 1998; 29(2):20P.
14. Yates BJ. Vestibular influences on cardiovascular control. In: Yates BJ, Miller AD, editors. Vestibular autonomic regulation. Boca Raton: CRC Press, 1996.
15. Rowell LB. Human circulation: regulation during physical stress. New York: Oxford University Press, 1986.
16. Shinners SM. Modern control system theory and design. 2nd ed. New York: John Wiley & Sons, 1998.
17. Sagawa K. Baroreflex control of systemic arterial pressure and vascular bed. In: Handbook of physiology. The cardiovascular system. Sect 2, Vol III, Ch 14. Bethesda, MD: American Physiological Society, 1983; 453-496.
18. Kircheim HR. Systemic arterial baroreceptor reflexes. *Physiol Rev* 1976; 56: 100-176.
19. Downing SE. Baroreceptor regulation of the heart. In: Handbook of physiology. The cardiovascular system. Sect 2, Vol III, Ch 17. Bethesda, MD: American Physiological Society, 1983; 621-647.
20. Folkow B, Heymans C, Neil E. Integrated aspects of cardiovascular regulation. In: Handbook of physiology. Circulation. Sect 2, Vol III, Ch 49. Bethesda, MD: American Physiological Society, 1965; 1787-1824.
21. Guyton AC. Textbook of medical physiology. 8th ed. Philadelphia: WB Saunders, 1991.
22. Benson AJ. Spatial disorientation — general aspects. In: Ernsting J, King P, editors. Aviation medicine. 2nd ed. London: Butterworths, 1988.
23. Gillingham KK, Previc FH. Spatial orientation in flight. In: DeHart RL. Fundamentals of aerospace medicine. 2nd ed. Maryland: Williams & Wilkins, 1996.
24. Kelly JP. Vestibular system. In: Kandel ER, Schwartz JH, editors. Principles of neural science. New York: Elsevier North Holland, 1982.
25. Barr ML, Kiernan JA. The human nervous system: an anatomical viewpoint. 4th ed. Philadelphia: Harper and Row, 1983.
26. Nolte J. The human brain: an introduction to its functional anatomy. St Louis: CV Mosby, 1981.
27. Homick JL, Vanderploeg JM. The neurovestibular system. In: Nicogossian AE, Huntoon CL, Pool SL, editors. Space physiology and medicine. Philadelphia, PA: Lea and Febiger, 1989; 185-191.
28. Lathan CE, Clement G. Response of the neurovestibular system to spaceflight. In: Churchill SE, editor. Fundamentals of space life sciences. Vol 1. Malabar: Krieger, 1997.
29. Schor RH, Kearney RE, Dieringer N. Reflex stabilisation of the head. In: Peterson BW, Richmond FJ, editors. Control of head movement. New York: Oxford University Press, 1988.
30. Yates BJ, Miller AD. Overview of vestibular autonomic regulation. In: Yates BJ, Miller AD, editors. Vestibular autonomic regulation. Boca Raton: CRC Press, 1996.
31. Tanaka H, Sjoberg BJ, Thulesius O. Cardiac output and blood pressure during active and passive standing. *Clin Physiol* 1996; 16: 157-170.
32. Woodring SF, Rossiter CD, Yates BJ. Pressor response elicited by nose-up vestibular stimulation in cats. *Exp Brain Res* 1997; 113: 165-168.
33. Ray CA, Hume KM, Shortt TL. Skin sympathetic outflow during head-down neck flexion in humans. *Am J Physiol* 1997; 273 (Regulatory Integrative Comp Physiol 42): R1142-R1146.
34. Yates BJ, Miller AD. Properties of sympathetic reflexes elicited by natural vestibular stimulation: implications for cardiovascular control. *J Neurophysiol* 1994; 71: 2087-2092.
35. Doba N, Reis DJ. Role of the cerebellum and the vestibular apparatus in regulation of orthostatic reflexes in the cat. *Circ Res* 1974; 34: 9-18.
36. Shortt TL, Ray CA. Sympathetic and vascular responses to head-down neck flexion in humans. *Am J Physiol* 1997; 272 (*Heart Circ Physiol* 41): H1780-H1784.
37. Essandoh LK, Duprez DA, Shepherd JT. Reflex constriction of human resistance vessels to head-down neck flexion. *J Appl Physiol* 1988; 64: 767-770.
38. Rowell LB, Wyss CR, Brengelmann GL. Sustained human skin and muscle vasoconstriction with reduced baroreceptor activity. *J Appl Physiol* 1973; 34: 639-643.
39. Yates BJ, Miller AD. Physiological evidence that the vestibular system participates in autonomic and respiratory control. *J Vestibular Res* 1998; 8: 17-25.
40. Bungo MW. The cardiopulmonary system. In: Nicogossian AE, Huntoon CL, Pool SL, editors. Space physiology and medicine. Philadelphia, PA: Lea and Febiger, 1989: 185-191.
41. Bungo MW, Charles JB, Johnson PC. Cardiovascular deconditioning during space flight and the use of saline as a countermeasure to orthostatic intolerance. *Aviat Space Environ Med* 1985; 56: 985-990.
42. Bungo MW, Johnson PJ. Cardiovascular examinations and observations of deconditioning during space shuttle orbital flight test program. *Aviat Space Environ Med* 1983; 54: 1001-1004.
43. Convertino VA, Doerr DF, Eckberg DL, et al. Carotid baroreflex response following 30 day to simulated microgravity. *Physiologist* 1989; 32 Suppl: 67-68.
44. Convertino VA, Doerr DF, Eckberg DL, et al. Head-down bed rest impairs vagal baroreflex responses and provokes orthostatic hypotension. *J Appl Physiol* 1990; 68: 1458-1464.
45. Convertino VA, Fritsch JM. Attenuation of human carotid-cardiac vagal baroreflex responses after physical detraining. *Aviat Space Environ Med* 1992; 63: 785-788.
46. Fritsch-Yelle JM, Charles JB, Jones MM, et al. Spaceflight alters autonomic regulation of arterial pressure in humans. *J Appl Physiol* 1994; 77: 1776-1783.
47. Schlegel TT, Benavides EW, Barker DC, et al. Cardiovascular and valsalva responses during parabolic flight. *J Appl Physiol* 1998; 85: 1957-1965.
48. Thompson CA, Tatro DL, Ludwig DA, Convertino VA. Baroreflex responses to acute changes in blood volume in humans. *Am J Physiol* 1990; 259 (*Regulatory Integrative Comp Physiol* 28): R792-R798. ❑