INTERACTION OF SEMICIRCULAR CANAL STIMULATION WITH CAROTID BARORECEPTOR REFLEX CONTROL OF HEART RATE

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Abstract — The carotid–cardiac baroreflex contributes to the prediction of orthostatic tolerance; experimental attenuation of the reflex response leads to orthostatic hypotension in humans and animals. Anecdotal observations indicate that rotational head movements about the vertical axis of the body can also induce orthostatic bradycardia and hypotension through increased parasympathetic activity. We therefore measured the chronotropic response to carotid baroreceptor stimulation in 12 men during varying conditions of vestibulo-oculomotor stimulation to test the hypothesis that stimulation of the semicircular canals associated with head movements in the yaw plane inhibits cardioacceleration through a vagally mediated baroreflex. Carotid-cardiac baroreflex response was assessed by plotting R-R intervals (ms) at each of 8 neck pressure steps with their respective carotid distending pressures (mmHg). Calculated baroreflex gain (maximal slope of the stimulus–response relationship) was measured under 4 experimental conditions: 1) sinusoidal whole-body yaw rotation of the subject in the dark without visual fixation (combined vestibular–oculomotor stimulation); 2) yaw oscillation of the subject while tracking a small head-fixed light moving with the subject (vestibular stimulation without eye movements); 3) subject stationary while fixating on a small light oscillating in yaw at the same frequency, peak acceleration, and velocity as the chair (eye movements without vestibular stimulation); and 4) subject stationary in the dark (no eye or head motion). Head motion alone and with eye movement reduced baseline baroreflex responsiveness to the same stimulus by 30%. Inhibition of cardioacceleration during rotational head movements may have significant impact on functional performance in aerospace environments, particularly in high-performance aircraft pilots during high angular acceleration in aerial combat maneuvers or in astronauts upon return from spaceflight who already have attenuated baroreflex functions.

Keywords — vestibular function; autonomic function; heart rate; baroreflex.

Introduction

Effective autonomic functions involved in regulation of blood pressure are essential for successful performance of crew members during high-G maneuvering in military aircraft, for reentry to the gravity of earth upon return from spaceflight, and for performance of emergency egress from air and space vehicles. For more than a decade, our laboratory has supported numerous investigations for the National Aeronautics and Space Administration (NASA) and for the United States Air Force (USAF) designed to investigate effects of altering gravitational environments on orthostatic performance in humans and on associated autonomic functions (1–11). During the application of stand tests, we frequently observed that subjects who rotated their heads around the vertical axis of the body became hypotensive and syncopal. When we implemented instructions that subjects fixate on an object in front of them so that their heads would remain stationary, most syn-
copal episodes were eliminated. These observations became more intriguing with anecdotal reports from USAF personnel that G-induced loss of consciousness was often associated with "checking six" (looking back over the shoulder for the enemy), a common maneuver used by pilots during aerial combat in high performance aircraft (12). Since vestibular stimulation can cause parasympathetic activation that results in bradycardia and hypotension under some conditions (13-18), we became interested in the investigation of possible interactions between the semicircular canals and control of heart rate by the primarily vagally mediated carotid baroreflex (19).

It seems reasonable to hypothesize that angular vestibular stimulation in which the semicircular canals receive substantial acceleration stimuli during turning of the head may increase the risk for development of orthostatic hypotension and intolerance by elevating parasympathetic nerve output (16). If this is true, then cases of syncope and G-induced loss of consciousness associated with head rotation could, at least in part, be explained by inhibition of vagal withdrawal by the carotid-cardiac baroreflex response. The purpose of this paper is 1) to present evidence that supports the contribution of carotid-cardiac baroreflex function to orthostatic performance; 2) to describe the effect of exposure to microgravity on carotid-cardiac baroreflex function; and 3) to present new evidence of a direct inhibitory interaction between semicircular canal stimulation and normal car-plasma volume, compliance of the lower extremities, carotid-cardiac baroreflex responsiveness, cardiopulmonary-vascular baroreflex function, and heart rate variability were measured in all subjects. Multivariate analysis was applied to evaluate the unique contribution of each of these six predictor variables to a model that predicted time to failure (vasovagal response) during LBNP. The amount of explained variation under cross-validation of the model was calculated by leaving out one subject, fitting the model from the remaining 13 subjects, and then obtaining a predicted value for the observation that was not used to determine the parameters of the model (leave-out-one cross-validation). This process was repeated for each of the 14 subjects and the squared correlation was calculated between the predicted and actual times to syncope. The results (Figure 1) indicated that 83.1% of the variation under cross-validation of the model could be explained by height, plasma volume, and responsiveness (gain) of the carotid-cardiac baroreflex. From an operational standpoint, this model predicts that shorter individuals with large plasma volumes and sensitive baroreflex responses will have an advantage during orthostatic challenges and that conditions that reduce the latter two factors will compromise orthostatic tolerance. Consistent with previous observations (2,4,20), these data also provide evidence that carotid-cardiac baroreflex function makes a unique contribution to orthostatic performance, independent of vascular volume.

Relationship Between Carotid-Cardiac Baroreflex Function and Orthostatic Performance

In a recent investigation (10), the contribution of physical and physiological factors thought to be associated with orthostatic performance was assessed. Graded lower body negative pressure (LBNP) designed to induce onset of vasovagal presyncope (for example, hypotension, bradycardia) and its symptoms (for example, sweating, nausea, dizziness) was used to measure orthostatic tolerance in 14 subjects. Height, V. A. Convertino

Impairment of Carotid-Cardiac Baroreflex Function in Microgravity

Impairment of the carotid baroreceptor-cardiac reflex response has been demonstrated in humans after their exposure to actual and ground analogues of spaceflight (2,4,5,8,9,20,21,22). Changes in carotid-cardiac baroreflex function are illustrated in Figure 2. A prominent feature of adaptation induced by exposure to microgravity is a shift of the carotid-cardiac stimulus-response relationship downward and to the right, producing a lower gain (less maximum response slope). This indicates that for a given reduction in arterial pressure, there is smaller

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compensatory increase in heart rate (decrease in R–R interval) after adaptation to microgravity. Since there is little change in baseline mean arterial pressure, elevation in baseline heart rate places the operational point at a lower position near the threshold on the response curve. This relocation of operational point on a less responsive part of the stimulus–response relationship further compromises the capacity of this reflex to increase heart rate in the face of an orthostatic challenge such as simple standing.

These alterations in carotid–cardiac baroreflex provide mechanisms that can explain several clinical observations regarding the development of orthostatic hypotension and intolerance following long-term exposure to low gravity. Elevated standing heart rate following spaceflight may be partially explained by hypovolemia that elicits an exaggerated cardiac response from aortic baroreceptor stimulation (23). However, pronounced orthostatic hypotension
upon standing after prolonged exposure to a ground analogue of microgravity was predicted by greater reduction in the gain of the carotid-cardiac baroreflex (Figure 3). Orthostatically hypotensive individuals have demonstrated less tachycardia during standing than subjects who maintained blood pressure (2), and orthostatic instability after spaceflight was associated with a lower operational setpoint on the baroreflex stimulus–response curve (24). These results are similar to those reported in carotid-denervated dogs (25). The observation that reduced maximum gain or lower operational point of the carotid-cardiac baroreflex stimulus–response relationship predicted orthostatic intolerance after exposure to simulated or actual spaceflight as well as in ambulatory subjects (10) supports the notion that impairment of this reflex can produce adverse consequences on functional performance under severe orthostatic environments such as standing upon return from spaceflight and acceleration in high performance aircraft.

### Impairment of Carotid–Cardiac Baroreflex Function by Semicircular Canal Stimulation

Since orthostatic hypotension and attenuated tachycardia have been associated with impaired carotid–cardiac baroreflex function (2–4.9) and head rotation (14–18), we became interested in determining if there was a direct interaction between semicircular canal stimulation and the normal carotid–cardiac baroreflex response in humans. We hypothesized that the heart rate response to carotid baroreceptor stimulation would be attenuated (that is, baroreflex responsiveness would be reduced) during semicircular canal stimulation. We therefore conducted experiments (26) on 12 male subjects in a 2 by 2 factorial experimental design conducted in 12 randomized blocks (subjects). The vagally mediated cardiac response (that is, R–R interval) to specific carotid baroreceptor stimulation was measured in our subjects with and without isolated semicircular canal stimulation and eye movements to determine if vestibular and/or oculomotor stimulation associated with yaw (lateral movement around the body’s vertical axis) head movements inhibits baroreflex control of heart rate. Baroreflex sensitivity was measured under 4 experimental conditions: 1) oscillation of the subject in the dark without visual fixation (vestibular stimulation with nystagmus); 2) sinusoidal rotation of the subject while fixating a small light moving with the subject (vestibular stimulation without nystagmus); 3) subject stationary while fixating on a small light oscillating in yaw at the same frequency, peak acceleration, and velocity as the chair (eye movements without vestibular stimulation); and 4) subject stationary in the dark (control). Consequently, we had 2 factors (vestibular and oculomotor stimulation) each at 2 levels (present and absent). Each subject received all 4 treatment conditions during a single experimental session, with the order of treatment systematically counterbalanced with three 4 by 4 Latin squares. Rotation was continuous during each oscillation treatment, but was discontinued between treatments. Subjects were rotated in a room isolated from all light in an attempt to minimize extraocularvestibular influences. Stimuli to carotid baroreceptors (neck chamber pressure), semicircular canals (chair rotation), and oculomotor (light rotation) were

![Figure 3. Relationship between change (Δ) in maximal slope of the carotid baroreceptor-cardiac reflex relationship and change in systolic blood pressure during stand test after 30 days' exposure to simulated microgravity (6° head-down tilt). Points represent subjects who completed (nonsyncopal) and those who failed to complete (syncopal) the stand test. Correlation coefficient for all subjects (N = 10) = 0.70 (P = 0.03). Modified from Convertino and colleagues (2).](image-url)
Vestibular and Baroreflex Interaction

accurately controlled and reproducible. Our experiment therefore allowed us to examine 2 main effects (vestibular and oculomotor stimulation) and their interaction.

Carotid baroreceptor-cardiac reflex responses were measured by applying stepwise pressure changes directly to the carotid baroreceptors with a special neck cuff, simultaneously measuring the reflex heart rate response, and calculating the maximum slope (gain) of the stimulus–response relationship (27). Using a chair that was rotated by a servo-controlled motor-driven turntable system allowed us the capability of precise maintenance of vestibular stimulation.

Vestibular stimulation without nystagmus was induced by rotation of subjects with equal oscillation frequency and peak acceleration and velocity, but with the eyes fixated on a small red light placed in front of the subject. Oculomotor stimulation by itself was induced by the eyes' fixation on a small red light placed in front of the subject. Oculomotor stimulation was quantified by electro-oculograms (EOG) measured during the 3 eye movement treatments. These analyses revealed that VOR gains (that is, oculomotor stimulation) in the two experimental conditions that involved eye movement were equal (0.68 ± 0.09 and 0.69 ± 0.04, respectively) while eye movement was virtually eliminated during head motion with fixation (gain = 0.05 ± 0.01).

Figure 4 illustrates the effects of semicircular canal stimulation on the average carotid baroreceptor–cardiac response relationships in the 12 subjects. The major finding of this study was that head movement in the yaw plane reduced (P < 0.0002) the cardiac reflex response to controlled stimulation of the carotid baroreceptors by 30%, from 3.8 ± 0.5 to 2.6 ± 0.5 ms/mmHg. Eye movement alone reduced the carotid–cardiac baroreflex response only slightly (13%) and only when the head was stationary. During head motion, the effect of eye motion acceleration of 125°/s², and peak velocity of 80°/s. This acceleration was sufficient to induce a strong vestibulo-oculomotor reflex response in our subjects (26). The use of a single whole-body oscillation frequency of 0.25 Hz met the requirements of the experimental protocol to assure that all subjects could suppress their vestibular nystagmus during the no-eye-movement intervention and to permit accurate tracking of the moving light target without producing overt somatosensory stimulation that might have caused nausea and other discomforts to the subjects. A harness was used to hold the head stationary. Vestibular stimulation without nystagmus was induced by rotation of subjects with equal oscillation frequency and peak acceleration and velocity, but with the eyes fixated on a small red light placed in front of the subject. Oculomotor stimulation by itself was induced by the eyes' fixating on a small red light placed in front of the subject that was rotated with equal oscillation frequency and peak acceleration and velocity as above while the chair and head were stationary. Subjects were monitored throughout testing using an infrared closed circuit television system to assure proper eye fixations and the equality of the gains in vestibulo-oculomotor reflex (VOR) between the treatment conditions was quantified by electro-oculograms (EOG) measured during the 3 eye movement treatments. These analyses revealed that VOR gains (that is, oculomotor stimulation) in the two experimental conditions that involved eye movement were equal (0.68 ± 0.09 and 0.69 ± 0.04, respectively) while eye movement was virtually eliminated during head motion with fixation (gain = 0.05 ± 0.01).

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evidence of a direct vestibular effect on the reflex control to the heart. Our findings (26) are the first data to our knowledge to demonstrate a direct link between semicircular canal stimulation and attenuated cardiac vagal withdrawal in humans. The vestibular system influences components of the autonomic nervous system that are involved in regulating cardiovascular function during movement and changes in posture, with compelling evidence of direct neural connections between vestibular nuclei and brain stem regions that mediate parasympathetic function that can lead to increase vagal activation during head movements (15,16,28). Impairment of the vagally mediated heart rate response to carotid baroreceptor stimulation caused by whole-body yaw rotation (Figure 4) was consistent with the notion that increased vagal activation caused by rotational head movements could represent a mechanism that inhibits withdrawal of vagal influence on the heart and limits the normal tachycardic responses during orthostatic challenge.

An attenuated tachycardia has been associated with orthostatic compromise (1-4,6,11). This relationship has been directly linked to impairment of vagally mediated carotid-cardiac baroreflex responsiveness. Dogs with sinoaortic baroreceptor denervation demonstrated smaller tachycardia and greater hypotension during upright posture than dogs with intact baroreflexes (25). Orthostatic hypotension in patients confined to wheelchairs as a result of spinal injury was associated with impaired carotid-cardiac baroreflex responsiveness (3) and was eliminated by enhancing cardiac baroreflex responsiveness (7). Attenuation of carotid-cardiac baroreflex responsiveness induced by 12 to 25 days of exposure to a ground analogue of microgravity correlated \(r = 0.7\) with orthostatic hypotension and syncope (2). It is intriguing to note that the reduction in cardiac baroreflex response caused by semicircular canal stimulation (Figure 4) was virtually identical to the magnitude of attenuation induced by simulated microgravity, which was, in turn, associated with a 40% increase in the incidence of orthostatic intolerance and syncope (2). It is therefore reasonable to speculate that inhibition of tachycardia associated with rotational head movement might impair blood pressure regulation in situations where head movements are combined with orthostatic challenges. Such a mechanism would provide a plausible explanation for the anecdotal observations that head rotation can be associated with increased incidence of syncope in some individuals.

**Functional Implications**

Impairment of orthostatically induced tachycardia caused by vestibular stimulation could compromise blood pressure regulation and maintenance of cerebral perfusion and lead to incapacitation of crewmembers during high-G maneuvering in military aircraft or re-entry to earth in spacecraft. Rapid onset rates of G acceleration in addition to head movements routinely required to check enemy positions (12) as well as observe cockpit head-up displays can provide strong vestibular stimulation. Although the vast majority of vestibularly related fatal aircraft mishaps have been attributed to spatial disorientation, the attenuating effect of vestibular stimulation on cardiac baroreflex function demonstrated in the present investigation should not be dismissed as a potential mechanism that might contribute to impaired performance as a result of compromised blood pressure regulation and cerebral perfusion.

Our results have implications for the management of patients or astronauts with orthostatic hypotension or for the training of high-performance aircraft pilots. Orthostatic incompetence is experienced by astronauts following spaceflight, as are disturbances in labyrinthine function (17,29). It is possible that vestibular disturbances caused by adaptation to microgravity might contribute to post-spaceflight orthostatic hypotension by exacerbating already impaired carotid-cardiac baroreflex function. Initial rehabilitation following prolonged confinement to bedrest or spaceflight should therefore include avoidance of head-yaw motions. Pilot training and development of cockpit displays designed to minimize head movements might reduce the risk of G-induced loss of consciousness during rapid acceleration exposures. Enhancing G-tolerance by using current techniques of high-G
training on the centrifuge may overestimate gains in protection if rapid eye and head movements similar to those experienced during engagement with enemy obstacles are not employed during training. Finally, development of countermeasures that enhance baroreflex responsiveness should be considered as an approach to minimize the effects of vestibular inhibition on cardiac function in orthostatic conditions.

Acknowledgments — This research was supported by grants from the Air Force Office of Scientific Research and the National Aeronautics and Space Administration.

REFERENCES