Vestibular and Cardiovascular Responses After Long-Duration Spaceflight

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BACKGROUND: The vestibulo-sympathetic reflex operates during orthostatically challenging movements to initiate cardiovascular responses in advance of a baroreceptor-mediated response. The objective of this study was to determine whether there was an association between changes in vestibular function and cardiovascular responses during a prone-to-stand movement in astronauts after return from long-duration spaceflight.

METHODS: Thirteen crewmembers who participated in International Space Station missions were tested before spaceflight and 1 d after landing. Vestibular function was evaluated by computerized dynamic posturography while their head was erect and while they performed dynamic head tilts. Heart rate and mean arterial blood pressure were measured while the subjects were in prone and standing positions.

RESULTS: The 21.4% increase in the astronauts' heart rate during the prone to stand maneuver after spaceflight correlated significantly with their spaceflight-induced 48.7% decrease in postural stability during dynamic head tilts. The larger mean arterial pressure in the prone position after spaceflight compared to preflight (+7%) also correlated with the postflight decrease in postural stability during dynamic head tilts.

CONCLUSION: These results indicate that an appropriate vestibular function is important to evoke optimum vestibulo-sympathetic response during orthostatically challenging voluntary movements performed after spaceflight. They also suggest that there may be a greater need to generate an anticipatory cardiovascular response after spaceflight.

KEYWORDS: vestibular system, dynamic posturography, orthostasis, cardiovascular system, microgravity.

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When the body maneuvers into an upright stance the cardiovascular system must respond rapidly to minimize pooling of blood in the lower body, protect venous return and stroke volume, and maintain blood supply to the brain.[32] Emerging evidence suggests that the vestibular system, particularly the otolith organs, helps protect against presyncope (e.g., lightheadedness, dizziness) and syncope (fainting) by detecting head movements and evoking the vestibulo-sympathetic reflex (VSR). In humans, the VSR increases muscle sympathetic nerve activity, lower limb vascular resistance, and heart rate; this occurs independently of the baroreceptor-mediated response to decreased arterial blood pressure.[37] In patients with deficient vestibular systems, there is a delay in the VSR that may induce a delayed cardiovascular response to a postural change that could contribute to orthostatic intolerance.[29,38]

Exposure to microgravity during spaceflight induces physiological and structural adaptations to multiple physiological systems including the vestibular and cardiovascular systems. Maladaptive responses of the vestibular system result from the cumulative effects of suppression of the otolith-induced reflexes, altered interpretation of otolith information, and structural changes in the otoconia.[5,18,27] Decrements in cardiovascular function, including inadequate maintenance of blood pressure during orthostatic stress, are commonly observed in astronauts after they return from space and are more severe after

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long-duration missions.[20,21] Several studies have suggested that vestibular dysfunction contributes to the orthostatic intolerance experienced by returning astronauts (see review in Yates and Kerman[39]). For example, Hallgren et al.[12] demonstrated a significant relationship between the decrease in the otolith-driven ocular-counter rolling reflex and the mean arterial pressure in astronauts after a long-duration spaceflight. In that study, orthostatic stress was imposed by passively tilting subjects on a tilt table, and the ocular counter-rolling was elicited by passive eccentric body rotation.

The cardiovascular system must respond appropriately during active movements that can precipitate orthostatic intolerance. Voluntary contractions of the lower limb muscles are capable of generating venous pressures required to return blood to the heart from the lower limbs to partially offset the gravitational pull. However, increased otolith-induced sympathetic activity is also important for maintaining blood pressure because it responds more rapidly than the baroreflex.[35] Therefore, to better understand the interactions between the vestibular and cardiovascular systems after spaceflight, we examined the cardiovascular responses during a test protocol consisting of 2 min of quiet prone rest followed by a voluntary transition from prone to standing, and then quiet standing for 3.5 min performed before spaceflight and 1 d after landing from a long-duration spaceflight. This prone-to-stand test allowed us to assess physiological changes while the astronauts performed a functional task that they might have to perform during a space mission, i.e., recovery from a fall during normal activities or an emergency situation after landing.[25] The cardiovascular parameters we measured included heart rate and mean arterial pressure. Changes in vestibular function were evaluated using a computerized dynamic posturography (CDP) protocol that imposed a high demand on vestibular information for maintaining vertical balance.

METHODS

Subjects

There were 13 crewmembers (11 men, 2 women; age 47 ± 5 yr; height: 178 ± 6 cm; body mass: 84 ± 14 kg; mean ± SD) who participated in long-duration missions (159 ± 17 d) on the International Space Station (ISS) and participated in this study. All subjects passed a U.S. Air Force Class II flight physical and had no known vestibular or cardiovascular complications prior to launch. The test procedures were approved by the NASA Johnson Space Center Institutional Review Board and were performed in accordance with the ethical standards established by the 1964 Declaration of Helsinki. All subjects provided written informed consent before participating in the study.

Subjects were tested on 253 ± 101 d, 105 ± 56 d, and 60 ± 10 d before the spaceflight, and 36.5 ± 3.3 h after return to Earth. The first preflight session familiarized the astronauts with the study protocol, and data from this session were not used in the analysis. The average of the second and third preflight sessions represented baseline performance (referred to as Pre) for each variable. All pre- and postflight tests were conducted at the NASA Johnson Space Center, Houston, TX, USA.

Procedure

The prone-to-stand test was used to induce orthostatic stress and test balance control while performing a functional task. This test was performed as part of a larger battery of seven functional tasks used to assess astronaut performance after spaceflight.[25] During the test, subjects lay prone on a foam mat for 2 min. Then, at the sound of an audible tone, subjects stood as quickly as possible onto a force plate and positioned themselves with their feet about shoulder-width apart, eyes looking forward, and arms at their side. They maintained this quiet standing position for 3.5 min. The subjects were instructed not to move, sigh heavily, or speak during the standing period, except to report any symptoms to the operators (e.g., lightheadedness, dizziness, tunnel vision). An operator stood on the subject's right side in case assistance was needed. Previous results from 80° tilt tests performed on landing day indicated that 3.5 min of standing was of sufficient duration to provide an orthostatic cardiovascular stress without inducing presyncope, even for long-duration ISS crewmembers.[20,21] If an astronaut had experienced presyncope or syncope during this test, they would have been precluded from participating in later protocols in the test battery on that day.[25]

R-R interval and heart rate (HR) were recorded by a high-fidelity 12-lead Holter monitor (1 kHz, Mortara Instruments, Milwaukee, WI) sampled at 1 kHz, and finger blood pressure was recorded continuously using photoplethysmography (Portapres System, Finapres Medical Systems, Netherlands) at 100 Hz. To protect the blood pressure signal, subjects were instructed not to press on the finger cuff while maneuvering from prone to stand. We calculated the average HR and mean arterial pressure (MAP; average of the continuous waveform) during the 2-min rest in the prone position. For the stand component, the first 20 s of data after standing were not considered prospectively so that the subjects had sufficient time to move to the upright posture and were stationary. The average time from prone to standing was greater after flight than before flight (Pre: 4.9 ± 1.1 s; Post: 6.4 ± 1.3 s, mean ± SD).[22] The average HR and MAP values for standing were calculated over the next 3 min, which is more than enough time for the vestibular system to influence cardiovascular responses.[30] The increase in HR and MAP from prone to standing and the percent change in these responses from preflight to postflight were then calculated.

The R-R interval data were obtained from the Holter monitor data and resampled at 4 Hz. The frequency component was then extracted by the Burg Method of autoregressive analysis with the autoregressive order preset at 16.[1] The low frequency/high frequency (LF/HF) ratio of R-R interval was calculated as the index of the sympathovagal balance, with a higher ratio indicating higher sympathetic bias.[24] The preflight to postflight change in LF/HF ratios was calculated separately for prone and stand components.

Computerized dynamic posturography (CDP) is routinely used to examine postflight postural ataxia in astronauts following exposure to microgravity.[3] In particular, the Sensory Organization Tests (SOTs) provided by EquiTest System platform (NeuroCom, Clackamas, OR, USA) have been used to assess the relative importance of visual, vestibular, and somatosensory feedback for control of postural stability. The greatest spaceflight-induced decrements in performance are revealed when vision is removed (eyes closed) and somatosensory information from the lower limbs is ineffectual (standing on a sway-referenced support surface).[27] In this condition, postural stability depends entirely on a well-functioning vestibular system.[7] The sensitivity of the test is further enhanced with the addition of dynamic head tilts in pitch,[13] which is consistent with crewmembers' reports that activities requiring head tilts are more challenging during the postflight recovery period.[36]

On the basis of these observations, we used a short, focused CDP protocol to quantify the deficits in postural control that could be attributed to maladaptive changes in vestibular function. This CDP protocol was performed approximately 20 min before the prone-to-stand test. During CDP, the crewmembers were instructed to maintain a stable upright posture for six 20-s trials with their feet positioned shoulder width apart, eyes closed, and arms folded across the chest while standing on a sway-referenced support surface. During three trials, subjects were asked to maintain their head in a naturally upright orientation. During three additional trials, crewmembers were asked to pitch their heads ± 20° at 0.33 Hz when cued by an oscillating tone provided over headphones. Head movements were measured by a motion analysis instrument mounted on the headphones (OPTOTRAK System, Model 3020, Northern Digital Inc., Ontario, Canada; or MEMS inertial sensors, Xbus Kit, Xsens Technologies B.V., Enschede, The Netherlands). Before each trial with dynamic head tilts, the test operator trained the subjects by giving corrective instruction over several cycles.

The center of pressure in both anterior-to-posterior and medial-to-lateral directions was calculated from the force plate signals. The angle of the anterior-to-posterior peak-to-peak sway was used to compute a continuous equilibrium score scaled relative to a maximum theoretical peak-to-peak sway of 12.5°, and normalized by the percent time of the trial completed.[36] Trials were terminated if subjects moved their feet, began to take a step, or raised their arms. The normalized equilibrium scores ranged from 0 to 100. If the subject was not able to perform the head movements appropriately during the dynamic head tilt test (defined as 2 SD from the subject's mean amplitude or frequency) the data from that test was not included in the analysis. Because intrasession performance varies during CDP,[36] we calculated the median equilibrium score for each condition. We then compared the pre- and postflight equilibrium scores for the head erect condition (SHE) and the dynamic head tilts condition (SDT).

Statistical Analysis

The normality of distribution of the variables was determined using the Shapiro-Wilk test. Variables that were not normally distributed were $\log_{10}$ transformed. The $\log_{10}$ transformed yielded a dataset that more closely conforms to a normal distribution. A repeated-measures analysis of variance (ANOVA) with two factors (head: erect, dynamic tilts; day: Pre, Post) was used to detect differences between pre- and postflight vestibular responses (SHE, SDT). A repeated-measures ANOVA with two factors (position: prone, stand; day: Pre, Post) was used to detect differences between pre- and postflight cardiovascular responses (HR, MAP, LF/HF) during the prone-to-stand test. Bonferroni correction was used to adjust for multiple comparisons.

We used correlation analyses to gain insight into the association between postflight cardiovascular responses (i.e., increase in HR) and postflight vestibular responses (i.e., decrease in SDT). Since HR modulation is a marker of autonomic nervous system function and the LH/HF ratio is an index of sympathovagal balance, we also examined the relationship between the postflight decrease in HR and the percent increase in prone and standing LF/HF ratios. Next, correlations of MAP variables (percent increase in prone and standing MAP postflight) were tested with postflight SHE, SDT, and LF/HF measures.

Data were analyzed using IBM SPSS 22 (IBM SPSS Statistics, IBM Corporation, NY, USA). Statistical significance was determined at $P < 0.05$.

RESULTS

Pre- to Postflight Changes

The equilibrium score during SDT was significantly lower than during SHE [$F(1,51) = 49.74$; $P < 0.001$], indicating that the subjects were less stable during dynamic head tilts. Both SDT and SHE equilibrium scores were lower after flight than before flight [$F(1,51) = 57.71$; $P < 0.001$], indicating that the subjects were unstable after spaceflight in both conditions. Importantly, the interaction between head position and days was significant [$F(1,51) = 29.89$; $P = 0.001$], indicating that the equilibrium score during SDT decreased significantly more after flight than the SHE equilibrium score [$F(1,51) = 29.89$; $P = 0.001$] (**Fig. 1A**).

HR was significantly higher on standing than in the prone position [$F(1,51) = 108.82$; $P < 0.001$] across days. HR also was higher after flight than before flight [$F(1,51) = 18.53$; $P = 0.001$], with a significant interaction term [$F(1,51) = 25.13$; $P < 0.001$], indicating that HR increased significantly more after the flight for standing than prone (**Fig. 1B**).

LF/HF values were not normally distributed and were $\log_{10}$ transformed for ANOVA. Overall, the LF/HF ratio was higher after flight than before flight [$F(1,51) = 9.96$; $P = 0.008$] and was higher on standing than in the prone position [$F(1,51) = 30.43$; $P < 0.001$] (**Fig. 1C**). There was marginal interaction between position and pre- to postflight [$F(1,51) = 4.54$; $P = 0.054$], indicating that the relative increase in LF/HF ratio from prone to standing tended to be larger after flight than before flight.

MAP was lower on standing than in the prone position [$F(1,51) = 14.84$; $P = 0.002$], and was higher after flight than

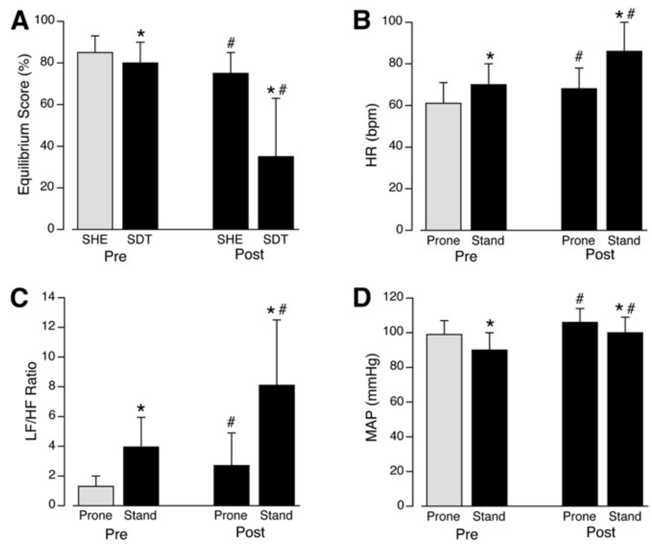

Fig. 1. A.) Mean ± SD of equilibrium scores from 13 crewmembers while standing with the head erect (SHE) and while standing and performing dynamic head tilts (SDT) before the flight (Pre) and 1 d after the flight (Post). B.) Mean ± SD of heart rate (HR) in prone and standing positions before and after flight. C.) Mean ± SD of LF/HF ratio of R-R interval in prone and standing positions before and after flight. D.) Mean ± SD of mean arterial pressure (MAP) in prone and standing positions before and after flight. * $P < 0.05$ between SHE and SDT or between Prone and Stand; # $P < 0.05$ between Pre and Post.

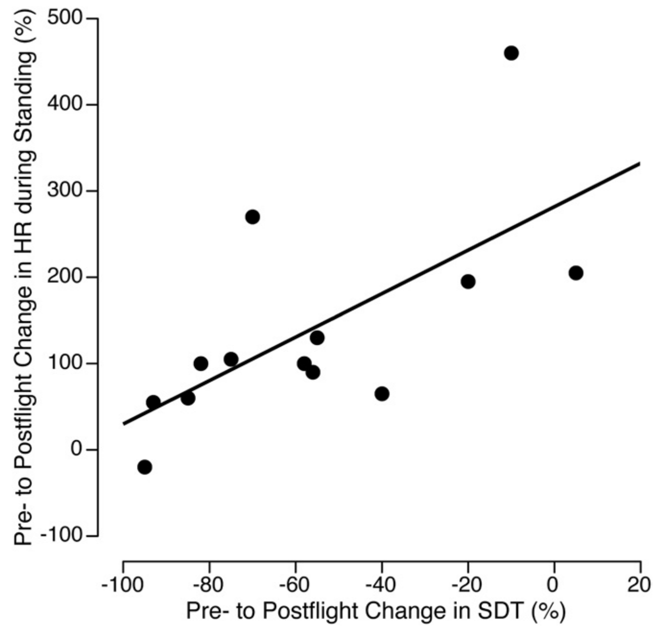

Fig. 2. Correlation between the pre- to postflight percent change in the heart rate response to standing (Stand-Prone) and the pre- to postflight percent change in equilibrium score during dynamic head tilts (SDT) for the 13 astronauts (r = 0.666, $P = 0.013$).

before flight [$F(1,51) = 13.07$; $P = 0.004$]. However, the decrease in MAP from prone to standing was not significantly different during preflight and postflight tests [$F(1,51) = 0.57$; $P = 0.465$] (**Fig. 1D**).

Correlations

The pre- to postflight percent change in the HR response to standing (Stand-Prone) was significantly correlated with the pre- to postflight percent decrease in equilibrium score during SDT (**Fig. 2**), but was not correlated with the percent decrease in equilibrium score during SHE postflight (**Table I**).

The pre- to postflight percent increase in LF/HF ratio in the standing position, but not in prone, was significantly correlated with the pre- to postflight percent increase in HR (Table I).

A multiple linear regression analysis was performed using the postflight increase in HR as a criterion variable, and the postflight decrease in SDT equilibrium score and increase in LF/HF ratio during standing as predictor variables (**Fig. 3**). Both spaceflight-induced decrease in SDT equilibrium score and increase in LF/HF ratio during standing were significant independent determinants of the postflight increase in HR, and together explained a total of 78% of its variability (**Table II**).

The pre- to postflight percent increase in MAP in the prone position was significantly correlated with the postflight decrease in SDT equilibrium score (r = −0.582; $P = 0.037$) (**Fig. 4**), but not with the postflight decrease in SHE equilibrium score (r = 0.066; $P = 0.830$). No relationship was found between the pre- to postflight percent increase in MAP in the standing position and the equilibrium scores ($P = 0.785$ and 0.974).

DISCUSSION

This study demonstrated that there is a relationship between spaceflight-induced changes in vestibularly-mediated balance control and the cardiovascular responses to an orthostatically challenging movement of standing up quickly from a prone position. Decreased vestibular function and exaggerated cardiovascular responses in the upright posture have been previously reported after both short- and long-duration spaceflight,[2,20,21] but this is the first report demonstrating an association during a functionally relevant task. Our findings suggest that countermeasures designed to protect vestibular function during and after spaceflight also may be beneficial for orthostatic tolerance after exposure to microgravity.

Changes in Vestibular Responses

Postural stability declined in our subjects after they returned from space, especially when they performed voluntary head movements in pitch. Clinical studies have shown that CDP during dynamic head tilts is sensitive for detecting mild vestibular impairment.[23] During static upright posture, there is a coupling of head and trunk segments to reduce complexity of postural control.[28] With the superimposed head movements, this stiffening strategy is no longer possible. The greater postural instability during dynamic head pitch after spaceflight could be the result of reduced axial segmental control.[4] Investigators who used specific tests of the otolith system, such as ocular counter-rolling reflex, off-vertical axis rotation, and centrifugation, have also shown that astronauts' otolith system is impaired after spaceflight.[8,11,31] In addition to stimulating the otolith organs,

Table I. Pearson Correlation r and *P* Values of Postflight Percent Increase in Heart Rate (HR) and Postflight Decrease in Equilibrium Scores (SHE, SDT) During CDP, and Increase in LF/HF Ratio in the Prone and Stand Components of the Prone-to-Stand Test.

	%SHE DECREASE	%SDT DECREASE	LF/HF INCREASE (PRONE)	LF/HF INCREASE (STAND)
% HR increase	r = 0.139	r = 0.666	r = -0.038	r = 0.757
	P = 0.649	P = 0.013*	P = 0.902	P = 0.003*

* $P < 0.05$.

the head movements in our CDP protocol also stimulated the semicircular canals and the neck proprioceptors. Therefore, future studies should assess the relationship between postural stability during dynamic head tilt and specific otolith responses using techniques such as the ocular-counter rolling reflex or the vestibular evoked myogenic potentials.

Change in Cardiovascular Responses

Collectively, data from our laboratory indicates that astronauts have an exaggerated HR response to tilt with the same or lower blood pressure on the day they return from a long-duration spaceflight.[20,21] Within a relatively short time after landing (1–2 d), the HR response to standing is reduced compared to landing day, the blood pressure response is closer to the preflight pattern, and the incidence of presyncope during these tests is low. While the cardiovascular system responds more appropriately during orthostatic stress as recovery progresses, full recovery may take several weeks.[2,20] In agreement with these previous reports, the current findings demonstrate an exaggerated HR response 1 d after return from ISS and sufficient MAP to prevent presyncope, particularly during this short standing period.

An increase in sympathetic bias after spaceflight has been reported previously.[10] This increase also was observed in the present study, as indicated by the overall increase in HR, LF/HF, and MAP after the flight. However, the postflight increase in LF/HF or HR in the prone position were not related to the postflight increase in MAP when prone. This result suggests that a stronger anticipatory cardiovascular response is generated after spaceflight when the vestibular system is not fully functional. It is also possible that the weaker anticipatory response in MAP requires an augmented response initiated by the vestibulo-sympathetic reflex. These findings are in line with previous findings in animals that demonstrated higher magnitude of vestibulo-sympathetic response with lower blood pressure.[17] Other measures of increased sympathetic activity, such as peripheral vasoconstriction or MSNA, would be helpful to identify the mechanism underlying this postflight increase in MAP in prone.

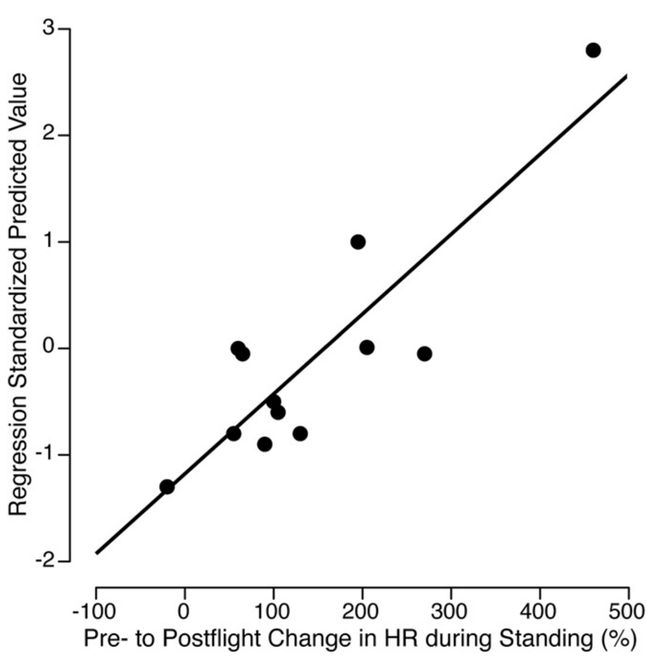

Fig. 3. Result of the multiple regression between pre- to postflight percent change in heart rate during standing (x axis) and the predicted percent change in heart rate (y axis) obtained using postflight decrease in SDT and postflight change in LF/HF ratio during standing for the 13 astronauts (r = 0.869, $P < 0.001$).

In addition to an increase in HR, an augmented sympathetic activity induces vasoconstriction that helps counteract the orthostatic stress. However, deficient vasoconstriction has been reported in returning astronauts.[9] Therefore, the greater HR seen during our postflight test likely reflects a transient alteration in cardiovascular function. Our results also indicate that in addition to an overall increased reliance on the sympathetic system, a dysfunctioning of the vestibular system after returning from space could affect the changes in HR when performing an orthostatically-challenging body movement. Furthermore, an increase in HR initiated by the vestibulo-sympathetic reflex may be required when there is a weaker anticipatory increase in MAP just prior to the movement.

It is well-known that spaceflight induces decreases in plasma volume, which are commonly observed in astronauts during and after return to Earth.[21] These observations are common across spaceflight missions even though crewmembers, including those in the present study, participate in oral fluid loading countermeasures prior to re-entry.[6,19] By the time that the subjects were tested in our study on the day after landing, the spaceflight-induced reduction in plasma volume appears to have been fully restored,[25] perhaps because ISS astronauts routinely receive oral and/or intravenous fluids after landing. Therefore, the changes in cardiovascular parameters in our study were presumably not due to a reduction in plasma volume.

Interactions

Our primary objective was to determine whether there is a relationship between changes in vestibular function and cardiovascular responses to standing as a result of spaceflight. Our primary finding is that astronauts who experienced a greater pre- to postflight decrement in postural stability during head movements while performing the dynamic posturography tests also experienced smaller increases in HR when moving from the prone to standing positions. One interpretation of these

Table II. Results of the Multiple Linear Regression Analysis Using the Pre- to Postflight Percent Change in HR as a Criterion Variable, and the Pre- to Postflight Percent Change in SDT and Pre- to Postflight Percent Change in LF/HF Ratio During Standing as Predictor Variables.

	B	STD ERROR	STANDARDIZED B	*t*	*P*
%SDT change	1.908	0.628	0.476	3.036	0.013*
LF/HF change (stand)	0.249	0.064	0.609	3.883	0.003*
Constant	200.145	45.002	N/A	4.446	0.001*

* $P < 0.05$.

findings is that those astronauts who were more posturally unstable were more likely to have engaged core and lower limb muscles while standing, thus activating the "muscle pump". This would aid the return of blood from the lower body toward the heart, provide a better maintenance of stroke volume, and thus reduce the HR response relative to those astronauts who were able to maintain a more static posture. In clinical populations, it has been noted that individuals with low blood pressure commonly shift their weight and feet to instinctively engage the muscle pump.[35]

An alternative explanation is that subjects who experienced a smaller decrement in postural stability have maintained their otolith function to a greater degree after spaceflight and this contributes to an elevated HR response mediated by the VSR. All our subjects were able to maintain MAP while standing, but those with a greater HR response might have had a greater capacity to respond to the orthostatic stress, integrating both central and peripheral responses. In a previous study, Hallgren et al.[12] observed no relation between otolith function (ocular counter-roll reflex) and HR when astronauts were tilted to 60° head-up 4 d after they returned from an ISS mission, yet otolith function was positively correlated with the change in MAP after a maneuver from supine to tilt. Studies also have demonstrated an increase in muscle sympathetic nerve activity (MSNA) during head-down head flexion in healthy participants.[33] Therefore, a postflight decrement in postural stability and a lesser increase in HR response could be the result of a dysfunction of the otolith system after long-duration microgravity exposure.

Vestibular stimulation increases sympathetic nerve activity, which can induce vasoconstriction and increased heart rate to counteract orthostatic stress.[16] By contrast, studies using animal models[15] and human studies on vestibular deficient patients[26] have demonstrated that suboptimal vestibular information can lead to orthostatic hypotension. A poor modulation of HR has also been observed in patients with bilateral vestibular hypofunction.[14] Maintaining the VSR during spaceflight and recovery of VSR response when the otoliths are activated may be an important contributor to the prevention of orthostatic intolerance after spaceflight.

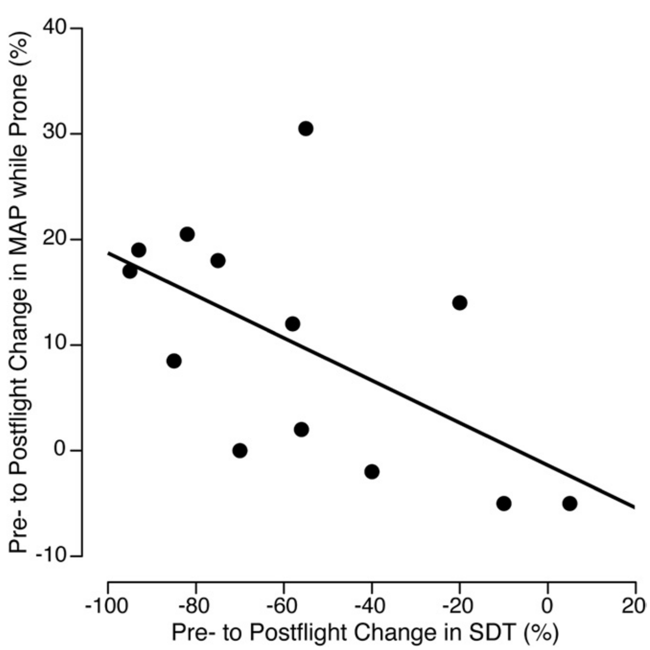

Fig. 4. Correlation between pre- to postflight percent change in SDT and pre- to postflight percent change in MAP in the prone position for the 13 subjects ($r = -0.582$, $P = 0.037$).

Limitations

The primary limitation of this work is that our subjects did not experience orthostatic hypotension or presyncope to the degree previously seen in astronauts when they stand after returning from space.[20] This effect is presumably due to the activation of muscles during the transition from prone to standing, the short duration of the standing period, and the fact that testing did not occur until one day after landing.[25] Thus, we could not assess the relationship between vestibular function and the full range of orthostatic responses. Furthermore, only two female astronauts participated in this study. Women are more likely to suffer postflight orthostatic intolerance,[34] and thus this may reduce any broad application of our results. Finally, it was not possible to assess vestibular function and orthostatic responses simultaneously. Our subjects performed other tests between the CDP and the prone-to-stand test (see Mulavara et al.[25]), but we believe that this design had no significant effect in the present findings.

To understand the operational efficiency of crewmembers after spaceflight, it is important to gain more insight into cardiovascular responses during active movements that can precipitate orthostatic intolerance. Future studies should focus on the relative contributions of the 'central command' on the sympathetic response, the voluntary muscle contractions on venous return, and the modulatory role of the vestibulo-sympathetic response to changes in critical cardiovascular parameters while actively performing orthostatically challenging body movements.

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REFERENCES

1. Arzeno NM, Stenger MB, Bloomberg JJ, Platts SH. Spaceflight-induced cardiovascular changes and recovery during NASA's Functional Task Test. Acta Astronaut. 3; 92(1):10–14.
2. Baevsky RM, Baranov VM, Funtova II, Diedrich A, Pashenko AV, et al. Autonomic cardiovascular and respiratory control during prolonged spaceflights aboard the International Space Station. J Appl Physiol. 2007; 103(1):156–161.
3. Black FO, Paloski WH. Computerized dynamic posturography: What have we learned from space? Otolaryngol Head Neck Surg. 1998; 118(3):S45–S51.
4. Bloomberg JJ, Reschke MF, Huebner WP, Peters BT, Smith SL. Locomotor head-trunk coordination strategies following space flight. J Vestib Res. 1997; 7(2–3):161–177.
5. Boyle R, Mensinger AF, Yoshida K, Usui S, Intravaia A, et al. Neural readaptation to Earth's gravity following return from space. J Neurophysiol. 2001; 86(4):2118–2122.
6. 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.
7. Cohen HS, Kimball KT. Usefulness of some current balance tests for identifying individuals with disequilibrium due to vestibular impairments. J Vestib Res. 2008; 18(5–6):295–303.
8. Clément G, Wood SJ. Eye movements and motion perception during off-vertical axis rotation after spaceflight. J Vestib Res. 2013; 23(1):13–22; https://doi.org/10.3233/VES-130471. Additional information can be found at https://doi.org/10.3389/fneur.2017.00414 and https://doi.org/10.1038/srep42071.23549051.
9. Convertino VA. Mechanisms of microgravity induced orthostatic intolerance: implications for effective countermeasures. J Gravit Physiol. 2002; 9(2):1–13.
10. Eckberg DL, Halliwill JR, Beightol LA, Brown TE, Taylor JA, Goble R. Human vagal baroreflex mechanisms in space. J Physiol. 2010; 588(Pt. 7):1129–1138.
11. Hallgren E, Kornilova L, Fransen E, Glukhikh D, Moore ST, et al. Decreased otolith-mediated vestibular response in 25 astronauts induced by long-duration spaceflight. J Neurophysiol. 2016; 115(6): 3045–3051.
12. Hallgren E, Migeotte PF, Kornilova L, Delière Q, Fransen E, et al. Dysfunctional vestibular system causes a blood pressure drop in astronauts returning from space. Sci Rep. 2015; 5:17627.
13. Jain V, Wood SJ, Feiveson AH, Black FO, Paloski WH. Diagnostic accuracy of dynamic posturography testing after short-duration spaceflight. Aviat Space Environ Med. 2010; 81(7):625–631.
14. Jáuregui-Renaud K, Reynolds R, Bronstein AM, Gresty MA. Cardio-respiratory responses evoked by transient linear acceleration. Aviat Space Environ Med. 2006; 77(2):114–120.
15. Jian BJ, Cotter LA, Emanuel BA, Cass SP, Yates BJ. Effects of bilateral vestibular lesions on orthostatic tolerance in awake cats. J Appl Physiol. 1999; 86(5):1552–1560.
16. Kaufmann H, Biaggioni I, Voustianiouk A, Diedrich A, Costa F, et al. Vestibular control of sympathetic activity. An otolith-sympathetic reflex in humans. Exp Brain Res. 2002; 143(4):463–469.
17. Kerman IA, Yates BJ. Regional and functional differences in the distribution of vestibulosympathetic reflexes. Am J Physiol. 1998; 275:R824–R835.
18. Kornilova LN, Naumov IA, Azarov KA, Sagalovitch VN. Gaze control and vestibular-cervical-ocular responses after prolonged exposure to microgravity. Aviat Space Environ Med. 2012; 83(12):1123–1134.
19. Kozlovskaya IB, Yarmanova EN, Yegorov AD, Stepantsov VI, Fomina EV, Tomilovaskaya ES. Russian countermeasure systems for adverse effects of microgravity on long-duration ISS flights. Aerosp Med Hum Perform. 2015; 86(Suppl., 12):A24–A31.
20. Lee SM, Feiveson AH, Stein S, Stenger MB, Platts SH. Orthostatic intolerance after ISS and Space Shuttle missions. Aerosp Med Hum Perform. 2015; 86(12, Suppl.):A54–A67.
21. Meck JV, Reyes CJ, Perez SA, Goldberger AL, Ziegler MG. Marked exacerbation of orthostatic intolerance after long- vs. short-duration spaceflight in veteran astronauts. Psychosom Med. 2001; 63(6):865–873.
22. Miller CA, Kofman IS, Brady RR, May-Phillips TR, Batson CD, et al. Functional task and balance performance in bed rest subjects and astronauts. Aerosp Med Hum Perform. 2018; 89(9):805–815.
23. Mishra A, Davis S, Speers R, Shepard NT. Head shake computerized dynamic posturography in peripheral vestibular lesions. Am J Audiol. 2009; 18(1):53–59.
24. Montano N, Ruscone TG, Porta A, Lombardi F, Pagani M, Malliani A. Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt. Circulation. 1994; 90(4):1826–1831.
25. Mulavara AP, Peters BT, Miller CA, Kofman IS, Reschke MF, et al. Physiological and functional alterations after spaceflight and bed rest. Med Sci Sports Exerc. 2018; 50(9):1961–1980.
26. Ohashi N, Imamura J, Nakagawa H, Mizukoshi K. Blood pressure abnormalities as background roles for vertigo, dizziness and disequilibrium. ORL J Otorhinolaryngol Relat Spec. 1990; 52(6):355–359.
27. Paloski WH, Black FO, Reschke MF, Calkins DS, Shupert CS. Vestibular ataxia following shuttle flights: effects of microgravity on otolith-mediated sensorimotor control of posture. Am J Otol. 1993; 14(1):9–17.
28. Pozzo T, Berthoz A, Lefort L. Head stabilization during various locomotor tasks in humans. Exp Brain Res. 1990; 82(1):97–106.
29. Radtke A, Popov K, Bronstein AM, Gresty MA. Vestibulo-autonomic control in man: Short- and long-latency vestibular effects on cardiovascular function. J Vestib Res. 2003; 13(1):25–37.
30. Raffai G, Cseko C, Nádasy G, Monos E. Vestibular control of intermediate- and long-term cardiovascular responses to experimental orthostasis. Physiol Res. 2010; 59(1):43–51.
31. Reschke MF, Wood SJ, Clément G. Ocular counter rolling in astronauts after short- and long-duration spaceflight. Sci Rep. 2018; 8(1):7747.
32. Serrador JM, Schlegel TT, Black FO, Wood SJ. Vestibular effects on cerebral blood flow. BMC Neurosci. 2009;10(1):119.
33. Shortt TL, Ray CA. Sympathetic and vascular responses to head-down neck flexion in humans. Am J Physiol. 1997; 272(4):H1780–H1784.
34. Waters WW, Ziegler MG, Meck JV. Postspaceflight orthostatic hypotension occurs mostly in women and is predicted by low vascular resistance. J Appl Physiol. 2002; 92(2):586–594.
35. Wieling W, van Dijk N, Thijs RD, de Lange FJ, Krediet CT, Halliwill JR. Physical countermeasures to increase orthostatic tolerance. J Intern Med. 2015; 277(1):69–82.
36. Wood SJ, Loehr JA, Guilliams ME. Sensorimotor reconditioning during and after spaceflight. NeuroRehabilitation. 2011; 29(2):185–195; https://doi.org/10.3233/NRE-2011-0694. Additional information can be found at https://doi.org/10.3389/fphys.2019.00627.
37. Yates BJ, Bolton PS, Macefield VG. Vestibulo-sympathetic responses. Compr Physiol. 2014; 4(2):851–887.
38. Yates BJ, Bronstein AM. The effects of vestibular system lesions on autonomic regulation: observations, mechanisms, and clinical implications. J Vestib Res. 2005; 15(3):119–129.
39. Yates BJ, Kerman IA. Post-spaceflight orthostatic intolerance: possible relationship to microgravity-induced plasticity in the vestibular system. Brain Res Brain Res Rev. 1998; 28(1–2):73–82.