Effect of sleep restriction on orthostatic cardiovascular control in humans

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Muenter, N. K., D. E. Watenpaugh, W. L. Wasmund, S. L. Wasmund, S. A. Maxwell, and M. L. Smith. Effect of sleep restriction on orthostatic cardiovascular control in humans. J. Appl. Physiol. 88: 966–972, 2000.—We hypothesized that sleep restriction (4 consecutive nights, 4 h sleep/night) attenuates orthostatic tolerance. The effect of sleep restriction on cardiovascular responses to simulated orthostasis, arterial baroreflex gain, and heart rate variability was evaluated in 10 healthy volunteers. Arterial baroreflex gain was determined from heart rate responses to nitroprusside-phenylephrine injections, and orthostatic tolerance was tested via lower body negative pressure (LBNP). A Finapres device measured finger arterial pressure. No difference in baroreflex function, heart rate variability, or LBNP tolerance was observed with sleep restriction (P > 0.3). Systolic pressure was greater at −60 mmHg LBNP after sleep restriction than before sleep restriction (110 ± 6 and 124 ± 3 mmHg before and after sleep restriction, respectively, P = 0.038), whereas heart rate decreased (108 ± 8 and 99 ± 8 beats/min before and after sleep restriction, respectively, P = 0.028). These data demonstrate that sleep restriction produces subtle changes in cardiovascular responses to simulated orthostasis, but these changes do not compromise orthostatic tolerance.

blood pressure; lower body negative pressure; heart rate variability; arterial baroreflex; partial sleep deprivation

ORTHOSTATIC INTOLERANCE is commonly seen after a period of prolonged bed rest (9), as well as in astronauts after their return to Earth (22). Although some of the mechanisms contributing to postspaceflight orthostatic intolerance have been identified, their relative importance is unknown, and additional mechanisms may also be involved. Demonstrated and possible contributing factors include 1) hypovolemia, which contributes to a decrease in stroke volume and increase in heart rate on reentry into the gravitational field (22), 2) increased lower body venous compliance perhaps due in part to muscle atrophy and reduction of venous smooth muscle tone (22), which would augment pooling of blood in gravity, 3) decreased or insufficient systemic sympathoexcitatory (10) and vasoconstrictor (3, 10, 14) responses to orthostasis, compromising the body’s ability to maintain arterial blood pressure, and 4) possible decreased cerebral vascular compliance as an adjustment to the increased arterial and intracranial pressures during 0 g, which may jeopardize 1 g orthostatic cerebral perfusion (22).

Although significant differences in heart rate and stroke volume responses to orthostasis were not found between orthostatic tolerant and intolerant astronauts after flight, insufficient vasoconstrictor responses appeared only in individuals unable to tolerate 10 min of standing after flight (3). Another study also found that postflight total peripheral resistance responses to orthostasis had decreased in comparison to preflight responses, although this study did not mention whether these astronauts tolerated the orthostasis (14). Whitson et al. (23) found no significant change in total peripheral resistance from before to after flight (including data from orthostatically tolerant astronauts); however, postflight plasma catecholamine levels were significantly increased relative to preflight levels, suggesting that the peripheral vascular response to sympathetic nerve activity (SNA) had been decreased by microgravity. Fritsch-Yelle et al. (10) found that astronauts who could not tolerate 10 min of orthostasis on landing day had significantly decreased standing peripheral vascular resistance and significantly smaller increases in standing plasma norepinephrine levels than astronauts who could tolerate the 10 min of orthostasis.

Because astronauts often experience substantial sleep restriction and interruption (11, 19), we hypothesized that this sleep restriction can lead to attenuated vasoconstrictor responses to orthostasis and possibly other changes in autonomic control, thereby compromising the ability to maintain blood pressure and contributing to orthostatic intolerance. To test this hypothesis, we studied human subjects before and after 4 nights of sleep restriction (4 h total sleep/night) to determine the effect of sleep restriction on baroreflex function, cardiovascular responses to lower body negative pressure (LBNP), LBNP tolerance, and heart rate variability (a generally accepted measure of vagal activity).

METHODS

This study was approved by the University of North Texas Health Science Center Institutional Review Board. Ten healthy volunteers (4 women and 6 men, ages 22–46 yr) participated in the study after giving written, informed consent. All subjects completed a medical history-health questionnaire and passed a physical examination. The sub-
subjects reported sleeping 7.7 h/night on average (range 6.3–9.5 h), with occasional naps of 0.3- to 1.4-h duration. Subjects were not taking any medication routinely (prescription or over-the-counter). Female subjects tested negative for pregnancy and were not studied during or within 2 days of menses to eliminate potential confounding effects of menses on fluid metabolism, blood volume, and cardiovascular function. During the study period, subjects maintained their normal, pre-sleep-restriction caffeine intake and abstained from alcohol as well as vigorous exercise. Moderate exercise consistent with the subjects’ normal routine was allowed.

Measurements

Standard polysomnography was used to assess sleep architecture and included the following measurements. Electroencephalography with either of the two lead combinations C4-A1 or C3-A2 (10–20 electrode placement system) was used to monitor brain electrical activity. Electrooculography with two leads, left outer canthus referenced to A2 and right outer canthus referenced to A1, was used to monitor eye movements. Electromyography was used to monitor muscle activity via electrodes placed under the chin over the mentalis/submentalis muscles and on the side of the jaw overlying the masseter muscle. Electrocardiography was used to monitor heart rhythm with a standard, three-lead electrocardiogram (ECG).

During the experimental protocols the following measurements were obtained. Heart rate was obtained using a standard limb-lead ECG. Arterial blood pressure was measured noninvasively from beat-to-beat photoplethysmographic recordings at the finger (Finapres blood pressure monitor 2300, Ohmeda, Englewood, CO). Noninvasive pulsed Doppler flow velocity measured at the brachial artery was used with two-dimensional ultrasonically measured artery cross-sectional area to calculate forearm blood flow (InterSpec XL, Conshohocken, PA, presently owned by ATL, Bothell, WA). This technique has been commonly utilized in previous studies and validated against occlusion plethysmography (4, 12, 20). Briefly, brachial arterial blood flow velocity was quantified for 10 cardiac cycles during each measurement time period. Brachial artery cross-sectional area was measured at the probe site and quantified for each measurement time by built-in software. Forearm blood flow was then calculated as the product of velocity and vessel area. Forearm vascular resistance was calculated as mean arterial pressure divided by forearm blood flow.

Protocol

The effect of sleep restriction was evaluated by comparing baseline, pre-sleep-restriction measurements with measurements after 4 nights of sleep restriction consisting of 4 h of sleep per night. Sleep time was set from 2:30 to 6:30 AM. For most subjects, this presented a late bedtime with a relatively normal awakening time. Subjects spent 2 nights in the sleep laboratory before the 1st night of sleep restriction, the first for familiarization and the second for baseline polysomnographic data collection, for which subjects were instrumented for recording of electroencephalography, electrooculography, electromyography, and electrocardiography. Polysomnographic data were continuously collected during the baseline night and the 4th (final) night of sleep restriction and stored to an IBM-compatible computer by utilization of data acquisition/analyses software (SensorMedics, Yorba Linda, CA).

Baseline cardiovascular testing was performed on the day after baseline sleep monitoring, and post-sleep-restriction cardiovascular testing was performed on the day after the 4th night of sleep restriction. Subjects were tested during a morning or an afternoon session, but the time of testing for each individual was maintained between baseline and post-sleep-restriction sessions. Subjects were instrumented for recording of ECG, arterial blood pressure, and forearm blood flow. ECG and arterial blood pressure data were stored to an IBM-compatible Pentium-based computer with utilization of WINDAQ data acquisition hardware and software (Dataq Instruments, Akron, OH), and forearm blood flow data were recorded to VHS tape. A catheter was also inserted for drug administration during the arterial baroreflex tests. All tests were performed with the subjects supine.

Arterial baroreflex function was determined from blood pressure and heart rate responses to injections of nitroprusside followed by phenylephrine (6, 7). Phenylephrine was administered at the nadir in systolic pressure caused by the nitroprusside. Sodium nitroprusside and phenylephrine were given in increasing doses until a 10- to 20-mmHg change in systolic pressure from baseline was seen in both directions. The dose combination producing the desired response was then repeated a second time. Subjects were closely monitored to ensure a return to baseline heart rates and blood pressures between trials.

Orthostatic tolerance was determined with LBNP. Subjects were placed in an airtight chamber enclosing them from the waist (superior iliac crests) down. A vacuum cleaner attached to the chamber created the negative pressures. Subjects were exposed to progressively more negative pressures: −10, −20, −40, −50, and −60 mmHg. Each pressure was maintained for 3 min, except −60 mmHg, which was maintained for the duration of the subject’s tolerance, with a limit of 18 min at −60 mmHg. The test was terminated when 1) the subject’s blood pressure began to fall significantly and recovery without test termination was not anticipated, 2) the subject reported symptoms of nausea or dizziness, or 3) the subject tolerated −60 mmHg for 18 min. The test was preceded by 1 min of recorded baseline and followed by 1 min of recorded recovery.

Heart rate variability was assessed during baseline conditions and during LBNP (−50 or −60 mmHg). Baseline data collection consisted of the subject breathing to a metronome at 15 breaths/min for 5 min. Subjects were asked to breathe at a relatively constant tidal volume, representative of normal respiration under quiet, restful conditions. Baseline data were collected before the arterial baroreflex and LBNP tests. Heart rate variability was also assessed during −60-mmHg LBNP, unless the subject did not tolerate −60 mmHg for a reasonable number of heartbeats, in which case −50-mmHg data were used.

Analyses

Arterial baroreflex. We quantified arterial baroreflex function by determining the change in R–R interval and heart rate for a given change in systolic arterial blood pressure during the drug-induced rise in blood pressure, a method that has been utilized by previous investigators (17, 21). Arterial blood pressure pulses were matched with a following R–R interval presumed to be affected by that blood pressure pulse, as described previously (16).

R–R intervals were plotted against systolic arterial blood pressures, and linear regressions were produced. Slopes of these regression lines were then determined, as well as confidence levels for these slopes. Cutoff values for these confidence levels were determined from the statistics table of critical values of correlation coefficients (24) (1-tailed, \( P = 0.05 \)), and slopes with confidence values at or below these cutoff values were not used. Remaining slopes (73%) were
then analyzed for significant differences between pre- and post-sleep-restriction values with a paired t-test. Systolic arterial pressures were also plotted against heart rate, and the same analyses were performed on the regression lines. This was done to address concerns regarding potential false-positive results when R-R intervals are used (18).

LBNP. Orthostatic tolerance was calculated as the sum of the products of each level of negative pressure multiplied by the duration of tolerance of that pressure. Responses to LBNP were assessed by determining changes from baseline in systolic, diastolic, and mean arterial blood pressure, heart rate, forearm blood flow, and forearm vascular resistance for each level of negative pressure. Data were analyzed during the last 30 s at each pressure level, except −60 mmHg, for which data were analyzed during the last 30 s of every 3-min interval as well as the final 30 s of tolerance. Baseline and recovery values were obtained from 1-min data segments. Two-factor repeated-measures ANOVA determined whether significant differences existed between experimental conditions for each variable (factors: LBNP level and sleep restriction status). Post hoc paired t-tests were then used to delineate which specific changes were significant.

Heart rate variability. Heart rate variability estimated in the time domain was used to determine whether sleep restriction caused changes in basal parasympathetic activity levels as well as changes in autonomic responses to a physiological stress (LBNP in this case). Baseline data, as well as data collected during −60-mmHg LBNP, were used in the comparison between before and after sleep restriction. R-R intervals from LBNP data were taken only after subjects had equilibrated to the negative pressure but well before any presyncopal symptoms developed. Equal numbers of R-R intervals were analyzed within each subject, with a minimum of 138 R-R intervals analyzed. Heart rate variability was quantified by calculating the root mean square of sequential intervals from LBNP analysis. As described above, two-factor repeated-measures ANOVA and post hoc paired t-tests determined effects of sleep restriction and LBNP on heart rate variability. All statistical analyses were performed at a significance level of 0.05. Values are means ± SE.

RESULTS

Sleep Architecture

Sleep latency decreased with sleep restriction (8 ± 2 and 1 ± 0 min before and after sleep restriction, respectively, P < 0.001). The average number of minutes spent in rapid-eye-movement sleep decreased with sleep restriction (59 ± 6 and 33 ± 5 min before and after sleep restriction, respectively, P < 0.001), while subjects maintained the average number of minutes spent in slow-wave sleep from before to after sleep restriction (81 ± 11 and 81 ± 5 min before and after sleep restriction, respectively). Thus the percentage of total sleep time spent in rapid-eye-movement sleep decreased slightly with sleep restriction, although this change was not significant (16 ± 2 and 14 ± 2% before and after sleep restriction, respectively, P = 0.06), whereas the percentage of total sleep time spent in slow-wave sleep significantly increased with sleep restriction (22 ± 4 and 54 ± 5% before and after sleep restriction, respectively, P = 0.002). Sleep restriction had no effect on average heart rate during sleep (53 ± 3 and 56 ± 2 beats/min before and after sleep restriction, respectively).

Arterial Baroreflex Function

Figure 1 shows that sleep restriction had no effect on arterial baroreflex gain. Paired t-tests were run on R-R interval data and heart rate data (R-R interval data: −10 ± 2 and 11 ± 1 ms/mmHg before and after sleep restriction, respectively, P = 0.49; heart rate data: −0.7 ± 0.1 and −0.7 ± 0.1 beats·min⁻¹·mmHg⁻¹ before and after sleep restriction, respectively, P = 0.97). Three subjects were omitted from this test because an intravenous line was not achieved, and a fourth subject was omitted because of a wandering pacemaker. A fifth subject was omitted from the R-R interval analysis because the confidence value for the slope of the regression line was below the statistically critical value. Therefore, six subjects make up the data pool for heart rate, whereas only five were included in the R-R interval analysis.

Orthostatic Tolerance

Orthostatic tolerance was unaffected by sleep restriction, as shown in Fig. 1 (1,114 ± 130 and 1,170 ± 55 mmHg·min before and after sleep restriction, respectively, P = 0.63). The end of tolerance occurred during an LBNP of −60 mmHg for all subjects after sleep restriction. Orthostatic tolerance was calculated as the sum of the products of each level of negative pressure multiplied by the duration of tolerance of that pressure. Responses to LBNP were assessed by determining changes from baseline in systolic, diastolic, and mean arterial blood pressure, heart rate, forearm blood flow, and forearm vascular resistance for each level of negative pressure. Data were analyzed during the last 30 s at each pressure level, except −60 mmHg, for which data were analyzed during the last 30 s of every 3-min interval as well as the final 30 s of tolerance. Baseline and recovery values were obtained from 1-min data segments. Two-factor repeated-measures ANOVA determined whether significant differences existed between experimental conditions for each variable (factors: LBNP level and sleep restriction status). Post hoc paired t-tests were then used to delineate which specific changes were significant.

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restriction and for all but one subject before sleep restriction. This particular subject reached her tolerance limit at -50 mmHg before sleep restriction.

The normal physiological response to orthostasis was observed before and after sleep restriction. LBNP significantly affected all dependent variables within both sleep conditions as follows: systolic, diastolic, and mean arterial pressures decreased with increasing LBNP (ANOVA: P < 0.001, P = 0.002, P < 0.001, respectively; Fig. 2, Table 1); heart rate increased with increasing LBNP (ANOVA: P < 0.001; Fig. 3); forearm vascular resistance increased with increasing LBNP (ANOVA: P < 0.001; Fig. 4); and forearm blood flow decreased with increasing LBNP (ANOVA: P < 0.001; Table 1).

In contrast to our hypothesis, sleep restriction did not impair the physiological responses to LBNP. Systolic pressure tended to be greater at all levels of LBNP after sleep restriction, and this trend was enhanced at the more severe levels of LBNP (Fig. 2). The relative increase in systolic pressure after sleep restriction was statistically significant during the first 3 min at -60 mmHg (110 ± 6 and 124 ± 3 mmHg before and after sleep restriction, respectively, P = 0.038) and near significance during the last 30 s of tolerance (97 ± 8 and 111 ± 6 mmHg before and after sleep restriction, respectively, P = 0.053). Although sleep restriction did not significantly affect diastolic and mean arterial pressures, both showed the same trend to be higher after sleep restriction, and this trend was also enhanced at the more severe levels of LBNP (Table 1).

Heart rate tended to be lower at all levels of LBNP after sleep restriction, and this relative reduction became more apparent at the more severe levels of LBNP (Fig. 3). During the last 30 s of LBNP, heart rate was significantly lower after sleep restriction than in sleep-replete conditions (108 ± 8 and 99 ± 8 beats/min before and after sleep restriction, respectively, P = 0.028).

Although neither forearm blood flow nor forearm vascular resistance responses to LBNP were significantly affected by sleep restriction, one difference between pre- and post-sleep-restriction responses was noted. When LBNP reached -60 mmHg before sleep restriction, forearm vascular resistance decreased to levels near pre-LBNP baseline and remained there for the balance of the test (Fig. 4). This decrease in forearm vascular resistance at -60 mmHg was reflected in

Table 1. DBP, MAP, and FBF during graded LBNP tolerance tests before and after sleep restriction

<table>
<thead>
<tr>
<th>LBNP</th>
<th>DBP, mmHg</th>
<th>MAP, mmHg</th>
<th>FBF, ml·min⁻¹·100 g⁻¹</th>
<th>DBP, mmHg</th>
<th>MAP, mmHg</th>
<th>FBF, ml·min⁻¹·100 g⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>71 ± 3</td>
<td>92 ± 3</td>
<td>1.16 ± 0.12</td>
<td>72 ± 2</td>
<td>94 ± 2</td>
<td>1.16 ± 0.10</td>
</tr>
<tr>
<td>-10 mmHg</td>
<td>70 ± 3</td>
<td>92 ± 3</td>
<td>1.14 ± 0.13</td>
<td>72 ± 3</td>
<td>94 ± 3</td>
<td>1.00 ± 0.11*</td>
</tr>
<tr>
<td>-20 mmHg</td>
<td>73 ± 4</td>
<td>93 ± 4</td>
<td>0.98 ± 0.13</td>
<td>73 ± 3</td>
<td>94 ± 3</td>
<td>0.94 ± 0.10†</td>
</tr>
<tr>
<td>-40 mmHg</td>
<td>74 ± 3</td>
<td>91 ± 4</td>
<td>0.86 ± 0.13†</td>
<td>75 ± 3</td>
<td>94 ± 3</td>
<td>0.88 ± 0.09†</td>
</tr>
<tr>
<td>-50 mmHg</td>
<td>74 ± 3</td>
<td>90 ± 3</td>
<td>0.78 ± 0.11†</td>
<td>75 ± 3</td>
<td>93 ± 2</td>
<td>0.77 ± 0.09†</td>
</tr>
<tr>
<td>-60 mmHg</td>
<td>69 ± 4</td>
<td>82 ± 5</td>
<td>0.62 ± 0.10†</td>
<td>76 ± 2</td>
<td>92 ± 2</td>
<td>0.74 ± 0.09†</td>
</tr>
<tr>
<td>Last 30 s</td>
<td>61 ± 3</td>
<td>73 ± 4†</td>
<td>0.71 ± 0.11†</td>
<td>68 ± 4</td>
<td>82 ± 4*</td>
<td>0.59 ± 0.05†</td>
</tr>
<tr>
<td>Recovery</td>
<td>69 ± 2</td>
<td>86 ± 3</td>
<td>1.12 ± 0.17</td>
<td>71 ± 3</td>
<td>91 ± 3</td>
<td>1.17 ± 0.12</td>
</tr>
</tbody>
</table>

Values are means ± SE. A trend for slightly greater (P > 0.12) diastolic (DBP) and mean arterial pressure (MAP) after sleep restriction becomes apparent at more severe levels of lower body negative pressure (LBNP). FBF, forearm blood flow. Significantly less than baseline within a sleep restriction condition: *P < 0.05; †P < 0.01.
forearm blood flow, which decreased continually during LBNP until −60 mmHg, at which time it increased slightly (Table 1). After sleep restriction, however, forearm vascular resistance remained above baseline levels throughout LBNP, exhibiting only a slight decline at the end of tolerance.

Heart Rate Variability

Sleep restriction did not affect heart rate variability, as shown in Fig. 1 (P = 0.82). LBNP, on the other hand, significantly reduced heart rate variability within both sleep conditions (P = 0.02). Specifically, heart rate variability was reduced from a baseline of 61 ± 9 ms to 37 ± 3 ms during −60-mmHg LBNP before sleep restriction (P = 0.046), whereas heart rate variability decreased from a baseline of 60 ± 9 ms to 36 ± 3 ms during −60-mmHg LBNP after sleep restriction (P = 0.021). There was no interaction between LBNP and sleep condition (P = 0.98). One subject was omitted from heart rate variability analyses because of a wandering pacemaker, so only nine subjects make up the data pool.

DISCUSSION

The effect of sleep restriction on sleep architecture was consistent with the known effects of sleep restriction (1, 2). Although sleep restriction of 4 h/night for 4 consecutive nights did not affect orthostatic tolerance, the ability to maintain blood pressure in the face of an LBNP challenge appears to be equal to or augmented slightly after sleep restriction, inasmuch as LBNP-induced systolic blood pressure reduction and heart rate elevation at more stressful LBNP levels were each attenuated after sleep restriction. The lesser post-sleep-restriction heart rate response to LBNP may simply be a baroreflex-mediated response to the higher blood pressures maintained after sleep restriction. Sleep restriction also had no effect on arterial-cardiac baroreflex function or heart rate variability; therefore, sleep restriction for 4 nights does not appear to impair reflex control of cardiovascular function.

Arterial-Cardiac Baroreflex Function and Heart Rate Variability

Arterial-cardiac baroreflex function and heart rate variability were unaffected by sleep restriction. The parasympathetic branch of the autonomic nervous system exerts its control on arterial pressure mainly by affecting heart rate (15). Because the arterial-cardiac baroreflex and heart rate variability tests are based on heart rate or R–R interval data, these results indicate that vagal control of heart rate has not been significantly altered by sleep restriction. These tests do not directly assess cardiac sympathetic nerve activity, and one must therefore exercise caution in drawing conclusions regarding SNA. Ewing et al. (8) measured 24-h heart rate variability and found that healthy men lost their diurnal variation in heart rate variability during a period of sleep deprivation (total sleep deprivation for 48 h). This was due to the loss of the increase in heart rate variability that normally occurs with sleep. However, daytime/wakeful heart rate variability was unaffected by the sleep deprivation. Although their subjects underwent sleep deprivation as opposed to sleep restriction, our results agree, inasmuch as we also found no change in wakeful heart rate variability. In addition, our study demonstrated that sleep restriction does not alter the decrease in heart rate variability that occurs in response to an orthostatic stress.

A related study in our laboratory provided some insight into the changes in sympathetic responses to alternative stresses after sleep restriction. It examined the effects of sleep restriction on catecholamine responses to the combined physical and mental stress of handgrip exercise with simultaneous timed tasks employing logical, spatial, and mathematical skills. Results showed a trend toward decreased catecholamine release in response to stress after sleep restriction (unpublished observations). Nevertheless, in the present study the support of arterial pressure (perhaps mediated by increased systemic vascular resistance) was not impaired; therefore, our data suggest that sleep restriction did not adversely affect the control of parasympathetic or sympathetic activity.

Orthostatic Tolerance

We hypothesized that attenuated vasoconstrictor responses to an orthostatic challenge occur after sleep restriction. Decreased vasoconstrictor responses would compromise the body’s ability to maintain blood pressure, contributing to a decreased orthostatic tolerance, as seen in astronauts after spaceflight (22). Our data indicate, however, that sleep restriction does not compromise tolerance of simulated orthostasis as hypothesized. In fact, although orthostatic tolerance did not change significantly with sleep restriction, subjects maintained arterial blood pressure slightly better during simulated orthostasis after sleep restriction. Arterial pressures tended to be greater with sleep restric-
tion, and this increase over pre-sleep-restriction levels reached statistical significance for systolic pressure at −60-mmHg LBNP.

Mean arterial pressure is determined by heart rate, stroke volume, and systemic vascular resistance, with the product of the former two composing cardiac output. Heart rate tended to be lower during LBNP after sleep restriction, so clearly the tendency for increased blood pressure was not a result of heart rate elevation. Increased systemic vasoconstrictor responses appear to participate in the improved blood pressure maintenance. Before sleep restriction, forearm vascular resistance dropped sharply when LBNP reached −60 mmHg and remained at levels not significantly different from baseline for the remainder of the orthostatic challenge. After sleep restriction, forearm vascular resistance remained above baseline when LBNP reached −60 mmHg and remained significantly greater than baseline levels for the duration of the orthostatic challenge. These changes in forearm vascular resistance responses may represent systemic resistance elevation responsible for the relatively greater systolic pressures observed at severe LBNP levels after sleep restriction.

Lusardi et al. (13) found increases in resting heart rate and systolic blood pressure after 1 night of sleep restriction (4.5 h), so contrary to our study, heart rate elevation may have played a role in the increased systolic pressure they observed. A possible explanation for the discrepancy is that their observed changes in cardiovascular parameters occurred shortly on awakening, and it is unclear whether their subjects were still lying down, sitting, or standing during these measurements. Our heart rate and blood pressure measurements were taken well after the subjects had awakened and while they had been in the supine position for ≥30 min. Another study agreed with our finding of a decreased heart rate, although the decrease occurred under resting as well as stressful conditions, and the stress in their case was dynamic exercise rather than simulated orthostasis (5). Also, that study employed 30 h of sleep deprivation as opposed to sleep restriction, possibly indicating that total sleep deprivation has a more pronounced effect than sleep restriction on heart rate, in that the effect is apparent even at rest.

Stroke volume is another determinant of arterial pressure via its contribution to cardiac output. We can only speculate as to the effect of sleep restriction on stroke volume; we did not measure this parameter. Blood volume, one of the determinants of stroke volume, does not appear to be affected by sleep restriction. Our subjects' weight and hematocrit, both good indicators of changes in body fluid volume over periods of days, were unchanged from before to after sleep restriction (mean weight: 76.4 and 76.5 kg before and after sleep restriction, respectively; mean hematocrit: 38.8 and 38.4% before and after sleep restriction, respectively). The decreased heart rate would increase ventricular filling time and, therefore, stroke volume, but it is doubtful that this increase would be sufficient to overcome the slower heart rate (which has a negative effect on cardiac output) and effectively raise cardiac output and, thus, arterial pressure. Myocardial contractility, a major determinant of stroke volume, was not measured; however, we would expect an increase in contractility to be accompanied by an increase in heart rate, inasmuch as both are stimulated by cardiac SNA. Because of the trend toward a decreased, rather than an increased, heart rate, we are confident that myocardial contractility did not increase. Therefore, it is unlikely that cardiac effects played a role in the trend toward increased arterial pressures observed after sleep restriction. It is important to note that we are drawing conclusions regarding myocardial contractility from heart rate data, yet the sympathetic branch of the autonomic nervous system is more important in the control of the former, whereas the parasympathetic branch is more important in the control of the latter, at least at resting heart rates. Thus our interpretations remain tentative.

It seems plausible that the trend toward better orthostatic blood pressure regulation after sleep restriction may result from a greater proportion of time spent upright during sleep restriction (20 vs. ~16 h/day under normal conditions). Subjects spent more time compensating for the effects of gravity on the circulation during sleep restriction, and perhaps this increased their ability to maintain arterial pressure during orthostatic stress. As mentioned above, a combined physical-mental exercise stress showed a trend toward a decreased release of catecholamines after sleep restriction. This observation, if true for an orthostatic stress as well and combined with the increased vasoconstrictor response at more severe LBNP levels, could suggest an increased sensitivity of the vasculature to sympathetic nerve activation after sleep restriction; however, we did not assess this aspect of vascular function in this study.

If the increased percentage of time spent counterbalancing gravity during sleep restriction does indeed improve blood pressure maintenance during orthostasis, this effect would not occur in sleep-restricted astronauts in space. Therefore, it remains possible that sleep restriction in space could somehow decrease orthostatic tolerance. However, because we saw the opposite trend in this ground-based study, we consider this possibility unlikely.

In conclusion, sleep restriction of 4 h/night for 4 consecutive nights did not affect human orthostatic tolerance, arterial-cardiac baroreflex function, or heart rate variability. Subjects exhibited increased systolic arterial blood pressures and decreased heart rates during simulated orthostatic stress after sleep restriction. This improved maintenance of arterial pressures during LBNP appears to be linked to an increase in peripheral vasoconstriction rather than cardiac output. Thus sleep restriction does produce subtle changes in cardiovascular responses to simulated orthostasis; however, contrary to our hypothesis, these changes do not compromise orthostatic tolerance. Therefore, we conclude that sleep restriction does not decrease orthostatic tolerance, and we offer the possibility that sleep
restriction does not contribute to postspaceflight orthostatic intolerance.

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