

Sleep and Respiration in Microgravity

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ABSTRACT

Sleep is often reported to be of poor quality in microgravity, and studies on the ground have shown a strong relationship between sleep-disordered breathing and sleep disruption. During the 16-day Neurolab mission, we studied the influence of possible changes in respiratory function on sleep by performing comprehensive sleep recordings on the payload crew on four nights during the mission. In addition, we measured the changes in the ventilatory response to low oxygen and high carbon dioxide in the same subjects during the day, hypothesizing that changes in ventilatory control might affect respiration during sleep. Microgravity caused a large reduction in the ventilatory response to reduced oxygen. This is likely the result of an increase in blood pressure at the peripheral chemoreceptors in the neck that occurs when the normally present hydrostatic pressure gradient between the heart and upper body is abolished. This reduction was similar to that seen when the subjects were placed acutely in the supine position in one-G. In sharp contrast to low oxygen, the ventilatory response to elevated carbon dioxide was unaltered by microgravity or the supine position. Because of the similarities of the findings in microgravity and the supine position, it is unlikely that changes in ventilatory control alter respiration during sleep in microgravity. During sleep on the ground, there were a small number of apneas (cessation of breathing) and hypopneas (reduced breathing) in these normal subjects. During sleep in microgravity, there was a reduction in the number of apneas and hypopneas per hour compared to preflight. Obstructive apneas virtually disappeared in microgravity, suggesting that the removal of gravity prevents the collapse of upper airways during sleep. Arousals from sleep were reduced in microgravity compared to preflight, and virtually all of this reduction was as a result of a reduction in the number of arousals from apneas and hypopneas. We conclude that any sleep disruption in microgravity is not the result of respiratory factors.

INTRODUCTION

There are many reasons to expect that the lung will behave quite differently in the microgravity environment of spaceflight than it does here on the Earth. The lung is an unusual organ in that it comprises little actual tissue mass in a relatively large volume. It is an expanded network of air spaces and blood vessels designed to bring gas and blood into close proximity to facilitate efficient gas exchange. As a direct consequence of this architecture, the lung is highly compliant and is markedly deformed by its own weight.

Although there is little, if any, structural difference between the top and bottom of the normal human lung, there are marked functional differences, caused by the effects of gravity. For example, the air spaces at the top of the lung are relatively over-expanded compared to those at the bottom of the lung. As a consequence of this, ventilation (the amount of fresh gas reaching the gas-exchanging region) is higher at the bottom of the lung, because the initial smaller volume there makes the lung more readily able to expand in response to a given breathing effort. There are even larger differences in pulmonary blood flow (perfusion) between the top and bottom of the lung—most of the blood flow goes to the base (bottom) of the upright lung. While both ventilation and pulmonary perfusion increase towards the lower regions of the lung, the differences in perfusion are larger than those in ventilation. As a result, the ventilation-perfusion ratio is higher at the top than at the bottom of the lung. Since it is the ventilation-perfusion ratio that determines gas exchange, regional differences in exhaled gas and effluent blood composition will occur. We have extensively studied the effects of gravity on the lung in previous Space Shuttle missions stretching back to 1991, and on numerous occasions in the NASA KC-135 Microgravity Research Aircraft. While many of the effects of gravity on the lung were predictable, there have been a large number of surprising observations (West, 1997; Prisk, 2000a).

Ventilatory responses

On Neurolab, we turned our attention to a previously unexplored area of pulmonary physiology in microgravity, namely the possible changes in the neural control of ventilation, and the effects of such changes on sleep. Humans have two, largely independent mechanisms that control breathing. The primary control mechanism is a change in the amount of carbon dioxide (CO₂) in the blood. If CO₂ rises (hypercapnia), chemoreceptors in the brain stem cause a marked increase in ventilation. The result of this is to eliminate more CO₂ and return blood CO₂ levels to normal. A separate feedback control system senses a low partial pressure of oxygen (O₂) in the blood (hypoxia) via chemoreceptors located in the carotid bodies in the neck. This also stimulates respiration. Not only are the control paths for O₂ and CO₂ different, the sensors are located in different places. The O₂ sensors are solely peripheral (primarily in the carotid bodies in the neck, with a small component from the aortic bodies in the aortic arch), and the CO₂ sensors are primarily central (brain stem), with only a small peripheral component.

Potential mechanisms of changes in the ventilatory response

It has long been known that cardiovascular changes directly affect respiration. In his 1945 Nobel Prize lecture, Corneille Heymans noted that "... variations in arterial blood pressure exert an effect on the respiratory center ... by a reflex mechanism involving the aortic and carotid sinus receptors." In cats, hypotension increased the firing rate of aortic chemoreceptors markedly, and slightly increased the neural output from carotid chemoreceptors. Hypoxia markedly increased the carotid body firing rate. Similarly, in dogs, hypotension increases carotid body activity. This is known to occur via a central pathway through changes in peripheral chemoreceptor activation, as opposed to a direct effect on the peripheral chemoreceptors themselves, because unilateral changes in baroreceptor pressure altered chemoreceptor response on the opposite side (see Prisk, 2000b, for further details). In humans there is less direct evidence for a strong coupling. An increase in blood pressure inhibits the ventilatory response to hypoxia when CO₂ levels are kept constant.

Respiration and sleep

Respiration and sleep are strongly coupled here on Earth, with respiratory disorders being a common cause of sleep disruption. Sleep disruption results from various mechanisms, among them sleep-disordered breathing. Probably the best-known form of sleep-disordered breathing is obstructive sleep apnea (OSA) (Strohl, 1984). In OSA, as the subject is sleeping, the muscles in the upper airway at the back of the throat relax, and in some subjects the result is a closing of the airway. Respiratory effort continues, but is ineffective, so that there is a period in which no fresh air reaches the lungs, lowering O₂ and raising CO₂. Eventually, the changes in O₂ and CO₂ cause an arousal from sleep (although the patient with OSA may not be aware of this) and the airway opens, often accompanied by loud snoring or snorting. The subject then falls asleep again and the cycle repeats. OSA is thought to have potentially serious health consequences, including raised blood pressure and a suspected increase in the risk of heart attack. In addition, the disruption to sleep can result in excessive daytime drowsiness, which can have serious consequences in situations such as driving a car. There are also other forms of sleep-disordered breathing such as central apnea (a cessation of breathing effort altogether) and hypopneas (a reduction in breathing effort that may at times be cyclical).

In spaceflight, sleep disruption is common, and sleeping medications are often used. We hypothesized that alterations in the control of ventilation might be a contributory factor in the sleep disruption seen in spaceflight. The experiment we performed on Neurolab measured the ventilatory responses both to lowered O₂ and increased CO₂ during the day, and, in conjunction with our colleagues from Brigham and Women's Hospital, performed a comprehensive study of sleep quality, quantity, and disruption (see science report by Dijk et al., in this publication).

METHODS

Control of ventilation studies

We used the experimental system that we had previously developed for studying lung function in spaceflight. The astronaut lung function experiment (ALFE) hardware is an automated system that allows the subject to perform numerous lung function tests without the assistance of another crewmember. Gas flow is measured using a flowmeter that is part of the ALFE hardware, and gas concentrations are measured by sampling the gas at the lips of the subject using a mass spectrometer as the subject breathes on the mouthpiece.

The ventilatory response to elevated CO_2 was measured using a rebreathing method (Read, 1967). A bag in the system was filled with a gas mixture of 7% CO_2 , 60% O_2 , balance nitrogen (N_2) and the subject breathed normally in and out of the bag. Metabolic production by the subject raised the CO_2 in the bag and stimulated breathing until the PCO_2 reached 70 mmHg (~10%), or until four minutes had elapsed, or until the subject was unable to continue. While metabolic consumption lowered the O_2 in the bag, the O_2 never decreased below that in air, eliminating the possibility of any hypoxic stimulus.

The hypoxic response was measured in a similar fashion (Rebuck, 1974). In this case, the bag was filled with a gas mixture of 17% O_2 , 7% CO_2 , and the balance N_2 and again the subject breathed normally in and out of the bag. Metabolic consumption lowered the O_2 in the bag, stimulating breathing until the inspired PO_2 reached 43 mmHg (~6%), or until four minutes had elapsed, or until the subject was unable to continue. To avoid metabolic production increasing CO_2 in the bag and thereby stimulating breathing, a computer-controlled variable speed fan withdrew some of the gas from the bag and passed the gas through a canister filled with soda lime, which absorbed the CO_2 and thus kept its concentration constant.

The ventilatory responses were calculated from a plot of ventilation against either end-tidal PCO_2 for the hypercapnic response or arterial oxygen saturation (SaO_2) for the hypoxic response. Arterial oxygen saturation was measured with a pulse oximeter on the subject's finger. After a threshold level has been reached, both of these plots show an approximately linear increase in ventilation as CO_2 rises or as SaO_2 falls. The slope and intercept of the fitted lines, as well as ventilation at predetermined levels of CO_2 or SaO_2 , provide measures of the ventilatory responses. Figures 1 and 2 show examples of the hypoxic and hypercapnic responses in one of the subjects studied.

As another measure of ventilatory drive, we measured the inspiratory occlusion pressure during air breathing during the early part of the ventilatory response tests described above. The inspiratory occlusion pressure is the pressure generated when the subject begins to inspire against an unexpectedly occluded breathing path. The pressure measured is that 100 milliseconds after the valve is closed, since this is before the subject has time to consciously react to the obstruction. Because the sudden closure of the breathing path was obtrusive when ventilation was stimulated, the occlusion pressure was only measured during the beginning of the ventilatory response tests.

Sleep and Respiration in Microgravity

Sleep studies

The sleep system that was developed for this spaceflight experiment consisted of a portable digital sleep recorder, a custom-fitted sleep cap, a body suit with sensors to measure rib cage and abdominal motion, a cable harness, an impedance meter, and a signal quality assessment computer system. This system is fully described in a chapter in this volume by Dijk et al. Briefly, the sleep recordings included four channels of brainwave activity (EEG), two channels of eye motion (EOG), two channels of muscle tone (EMG), the electrocardiogram (ECG), nasal airflow (thermistor), snoring sounds, light levels (on/off), arterial oxygen saturation SaO_2 , and motion of the rib cage and abdomen. Figure 3 shows a subject fully instrumented for sleep during Neurolab.

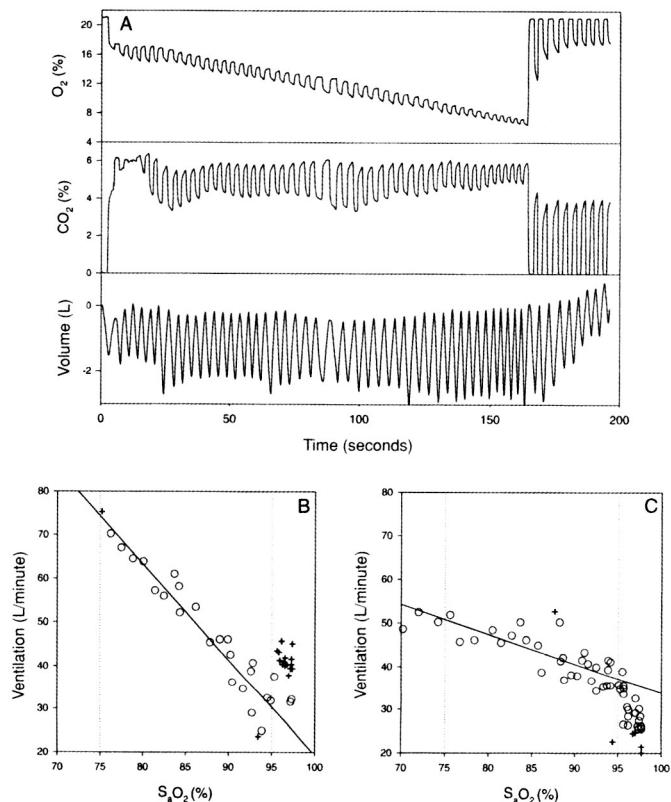


Figure 1. Example of a tracing showing the measurement of the hypoxic ventilatory response (HVR) in one subject standing in one-G (A, B) and in microgravity (C). Subjects rebreathed from a bag for up to four minutes during which time the O_2 in the bag fell and the CO_2 was held constant by a computer-controlled CO_2 removal circuit (A). As O_2 falls, there is a small increase in the respiratory frequency and a substantial increase in the volume of each breath, both of which serve to increase overall ventilation. Also shown is the analysis (B, C) in which breath-by-breath ventilation is plotted as a function of SaO_2 . The line is the least-squares best fit to the points lying between 75% and 95% SaO_2 , and within two SD of the best fit to all data points in that range. Points lying outside this range are marked by a cross. (From Prisk, 2000b, with permission; reproduced from *Journal of Applied Physiology*.)

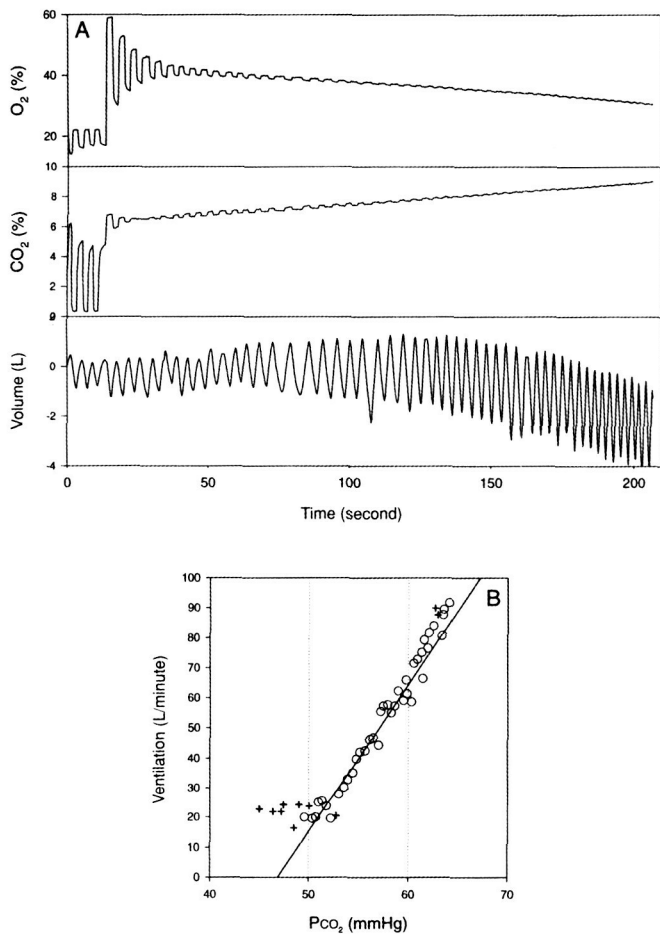


Figure 2. Example of a tracing showing the measurement of the hypercapnic ventilatory response (HCVR) in one subject in microgravity (A). Subjects rebreathed from a bag for up to four minutes during which time the CO₂ in the bag rose. Although O₂ falls, it always remains above 30%, eliminating any contribution from a hypoxic stimulus. The increase in ventilation is more marked than that in the HVR test (Figure 1). Also shown is the analysis in which breath-by-breath ventilation is plotted as a function of PCO₂. The line is the least-squares best fit to the points lying between 50 and 60 mmHg, and within two SD of the best fit to all data points in that range. Points lying outside this are marked by a cross. Note that ventilation only begins to increase above a threshold level of PCO₂, in this case about 50 mmHg.

For the sleep studies, we combined data from Neurolab with data from a fifth subject studied on a later flight, STS-95. A total of 77 polysomnographic recordings were collected preflight, inflight, and postflight on one female and four male subjects (64 on the Neurolab crew, and 13 on STS-95). On each Neurolab subject, there were nine recordings preflight, four inflight, and three postflight. On STS-95, there were six preflight, four inflight, and three postflight recordings. The details of the sleep sessions may be found in the chapter on sleep by Dijk et al. in this publication. This chapter also describes the administration of melatonin, which formed part of the overall Sleep Team experiment design.

The sleep staging of each recording was performed using standard criteria. Obstructive apneas were defined as a cessation of airflow for a minimum of 10 seconds with continued respiratory effort as evidenced by movement of the rib cage or abdomen. Central apneas were characterized by the absence of airflow and respiratory movement for a minimum of 10 seconds. Hypopneas were scored according to standard criteria. Apnea-hypopnea indices ((AHIs) (events/hour)) were determined for the sleep period, the total sleep time, and for the rapid eye movement (REM) and non-REM (nREM) times.

Arousals were determined by the standard criteria outlined by the American Sleep Disorders Association based on changes in the EEG. An arousal was considered to be associated with a respiratory event when it occurred within 15 seconds after the event. Snoring was considered as present if the microphone signal was above a 10% threshold for more than half of a 30-second epoch. For each event, the SaO₂ was averaged over the duration of the event.

Regarding respiration, we saw no difference in the sleep data between the results from nights on which subjects took melatonin and from the nights on which they took a placebo. We therefore combined the data without regard to the presence of melatonin or placebo.

RESULTS

Hypoxic ventilatory response

Microgravity markedly decreased the hypoxic ventilatory response (HVR) (Prisk, 2000b). The slope of the HVR (the increase in ventilation with decreasing arterial oxygen saturation) was approximately halved by microgravity, and became the same as that measured when the subjects were acutely placed in the supine position (Figure 4). Microgravity and the supine position resulted in reductions to approximately 46±10% and 53±11%, respectively, of that in preflight standing control data for the slope of the HVR. There were concomitant reductions in the intercept of the ventilation line, with values being 55±7% in microgravity and 59±6% for the supine position. Neither the slope nor the intercept measured standing in the postflight period as significantly different from that measured preflight.

The changes in the slope and the intercept both affect the increase in ventilation as arterial oxygen saturation decreases. Spaceflight reduced the ventilation at an SaO₂ of 75% to approximately 65% of that measured standing in the preflight period ($p < 0.05$) with a similar reduction when subjects were in the supine position.

There were small increases in the HVR when the subjects were standing in the postflight period (Figure 4), but these failed to reach the level of statistical significance. When we examined the day-to-day changes in the ventilation at an SaO₂ of 75%, we found no consistent changes during the 16 days of the flight. Similarly, there was no change in the response with time either standing or supine during the postflight period.



Figure 3. Mission Specialist Dave Williams fully instrumented for sleep during the Neurolab mission. The details of the sleep instrumentation are covered in the report by Dijk et al., in this volume. The CD player is personal equipment. (Photograph NASA 90E5077)

Response to increased CO₂

In sharp contrast to the HVR, microgravity did not significantly alter the hypercapnic ventilatory response (HCVR) (Prisk, 2000b). Figure 5 shows the changes in ventilation resulting from elevated CO₂ by plotting the ventilation calculated from the measured response at a PCO₂ of 60 mmHg. This measurement combines any change in slope with any change in set point for CO₂ above which ventilation begins to increase. As was the case with the HVR, there was no difference in the ventilatory response to CO₂ as the length of time in microgravity increased. Supine, the CO₂ response was slightly reduced, but this did not reach the level of statistical significance preflight.

Overall, the changes we saw in the HCVR suggest a slight steepening of the response with a concomitant shift of the line to the right. The end expiratory PCO₂ measured during quiet breathing rose from 36 mmHg standing preflight to 39 mmHg inflight, and to 41 mmHg supine.

Inspiratory occlusion pressures

The changes in inspiratory occlusion pressures are similar to the overall changes in control of ventilation (above). Figure 6 shows the inspiratory occlusion pressures measured during air breathing and those measured during the early stages of both the HVR

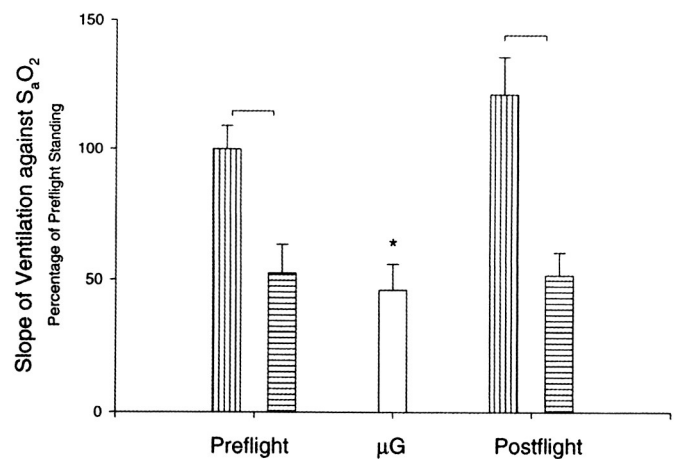


Figure 4. Slope of the hypoxic ventilatory response (HVR) measured standing and supine in one-G, and in microgravity. Both microgravity and the supine position approximately halve the HVR. Markers between adjacent bars indicate $p < 0.05$. An * indicates $p < 0.05$ compared to preflight standing control. Vertical shading, standing; horizontal shading, supine; open bars, microgravity. (From Prisk, 2000b, with permission; reproduced from *Journal of Applied Physiology*.)

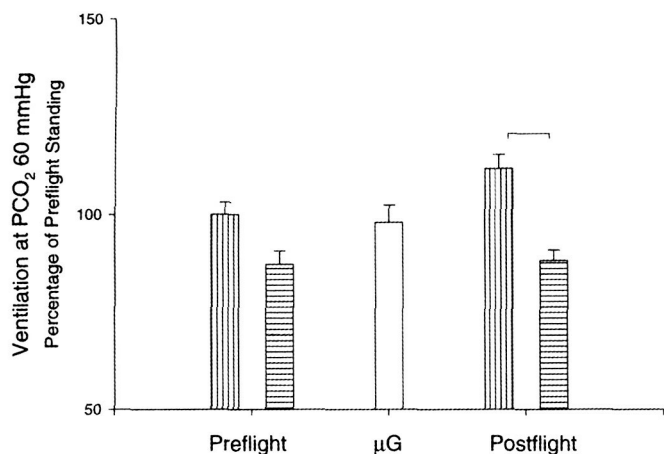


Figure 5. Ventilation measured at a PCO₂ of 60 mmHg during the hypercapnic ventilatory response (HVCr) test. Format same as Figure 4. (From Prisk, 2000b, with permission; reproduced from *Journal of Applied Physiology*.)

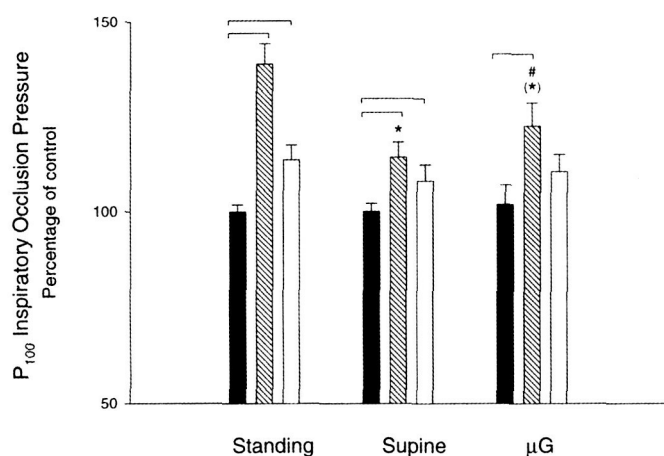


Figure 6. The inspiratory occlusion pressure measured 100 milliseconds after the closure of a valve at the beginning of inspiration (P₁₀₀). The black bars show the P₁₀₀ values breathing air. The shaded bars show the P₁₀₀ measured during the HVCr test when the PO₂ was between 75 and 85 mmHg. The open bars show the P₁₀₀ measured during the HVCr test when the PCO₂ was between 43 and 50 mmHg.

A marker between adjacent bars indicates $p < 0.05$.

* indicates $p < 0.05$ compared to preflight standing.

indicates $p < 0.05$ compared to preflight supine.

Parentheses indicate $0.10 < p < 0.05$.

(From Prisk, 2000b, with permission; reproduced from *Journal of Applied Physiology*.)

and HCVR tests. Occlusion pressures during the hypoxic test (measured during breaths in which the end tidal O₂ was between 75 and 85 mmHg) showed a marked increase above air breathing in all cases. However, the increase was significantly less in both the supine position and in microgravity than it was standing. In contrast, occlusion pressures during the measurement of the HCVR (when the PCO₂ was between 43 and 50 mmHg) showed a modest increase above air breathing that was not different among the three conditions studied.

Respiration and sleep apneas and hypopneas in microgravity

On the ground, this group of young, normal subjects had a low apnea-hypopnea index (AHI) of only 7.6 ± 1.4 events/hour. Three of the subjects had an AHI below 5.0, one 6.0, and only one had an AHI in the mildly abnormal range at 19.9 ± 2.9 . Almost all of these events resulted from hypopneas with an average apnea index of only 0.9 ± 0.3 , and a hypopnea index of 6.7 ± 1.2 (Figure 7). The AHI decreased dramatically during microgravity by 52% to 3.4 ± 0.8 events/hour, and almost all of these were hypopneas (3.1 ± 0.8), with almost no apneas (0.3 ± 0.1). Postflight, the AHI increased to 9.4 ± 2.3 , which was not statistically different from the preflight values. The AHI preflight was approximately the same in both rapid eye movement (REM) and non-rapid eye movement (nREM) sleep. Inflight, there was a slight increase in the AHI during REM; and postflight, the AHI was higher during REM sleep and was ~50% greater than that preflight (see Elliott, 2001, for details).

Preflight, obstructive apneas accounted for ~21% of the total number of apneas that occurred during a sleep period (1.6 ± 0.7), the rest being central or mixed in origin. Inflight, the number of obstructive apneas decreased to essentially zero (0.1 ± 0.1).

Snoring and arousals associated with respiratory events

Snoring essentially disappeared in microgravity. The percentage of time spent snoring during the preflight sleep periods was $16.8 \pm 3.0\%$, and this was reduced to $0.7 \pm 0.5\%$. Postflight, the snoring returned to preflight levels (Figure 8).

The number of arousals associated with a respiratory event (an apnea or a hypopnea) during the preflight sleep periods was on average 5.5 ± 1.2 arousals/hour within the context of a total number of arousals of 18.0 ± 1.8 arousals/hour (Figure 9). Inflight, the number of respiratory arousals/hour decreased markedly by 70% to 1.8 ± 0.6 arousals/hour while the total number of arousals/hour decreased by only 19% to 13.4 ± 1.5 arousals/hour. Thus, almost all of the decrease in the arousal index was as a result of the reduction in the respiratory arousal index (Figure 9). Postflight, the arousal indices were not different to preflight levels.

The most dramatic decrease in the arousal index was seen in the subject with the highest AHI preflight. That subject's inflight respiratory arousal index dropped from a preflight value of 16.3 ± 2.3 to 6.3 ± 1.1 events/hour. This was within the context of a total arousal index preflight of 35.7 arousals/hour, which was reduced to 23.5 ± 1.5 inflight, again almost completely as a result of the reduction in respiratory arousals.

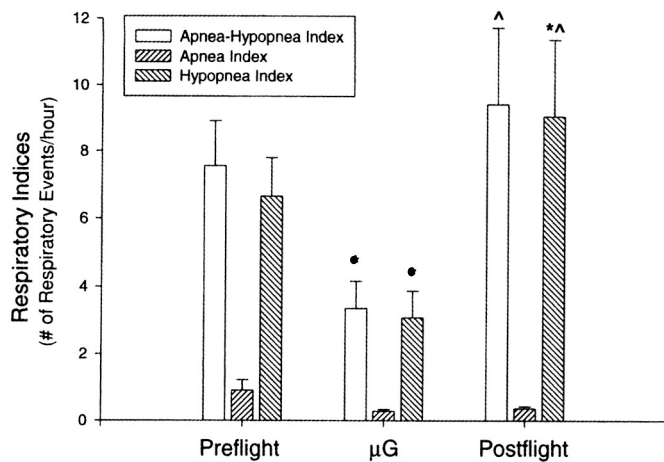


Figure 7. The apnea-hypopnea index and its subdivisions. An * indicates $p < 0.05$ compared to preflight and a ^ indicates $p < 0.05$ compared to inflight. (From Elliott, 2001, with permission; reproduced from *American Journal of Respiratory and Critical Care Medicine*.)

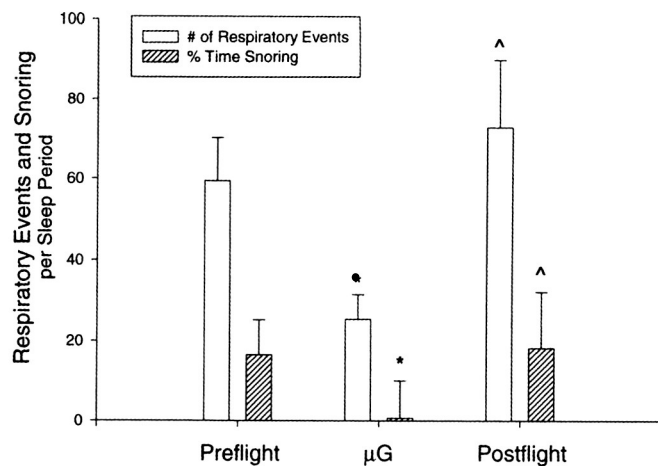


Figure 8. The total number of respiratory events in a sleep period and the percentage of time spent snoring in a sleep period. Significance markings same as Figure 7. (From Elliott, 2001, with permission; reproduced from *American Journal of Respiratory and Critical Care Medicine*.)

DISCUSSION

Changes in control of ventilation in microgravity

The principal finding of this portion of the study is that the hypoxic response in microgravity is only about half of that measured standing in one-G (Figure 4). This is essentially unaltered by the amount of time spent in microgravity up to the 15 days over which we were able to make measurements. Upon return to one-G, the hypoxic response was slightly elevated compared to preflight control data, and this elevation persisted for at least one week. In sharp contrast to this, exposure to microgravity left the ventilatory response to hypercapnia unaltered.

The reduction in the hypoxic ventilatory response resulted from changes in both the slope and the intercept of the ventilatory response, with the slope being reduced slightly more than the intercept. The degree of reduction seen in microgravity in the hypoxic response closely matched that seen in the response measured after the subjects acutely assumed the supine position. Those measurements were generally made within five to 40 minutes of becoming supine.

To a large extent, the differences seen in ventilation at an SaO_2 of 75% result from differences in the increase in the tidal volume, and not from alterations in frequency. Only postflight were there changes in respiratory frequency (a slight increase) that reached the level of significance. These changes match the strategy used to produce a lower ventilation under resting breathing conditions in microgravity (West, 1997; Prisk, 2000) where frequency was largely unaltered and tidal volume decreased to reduce total ventilation compared to standing in one-G.

There was no overall change in the hypercapnic response as measured by the ventilation at a PCO_2 of 60 mmHg caused

by exposure to microgravity. However, there was some indication that the slope of the response steepened somewhat both in microgravity and supine, and that this was accompanied by a concomitant increase in the PCO_2 at a calculated ventilation of zero. However, only the zero intercept showed a statistically significant increase. There was also an increase in the end expiratory PCO_2 measured during quiet breathing. The increase from 36 mmHg to 39 mmHg was smaller than that seen between standing and supine (36 to 41 mmHg), but raises the possibility of a shift in the set point of the PCO_2 . Measurements made in an environmental chamber study in which the PCO_2

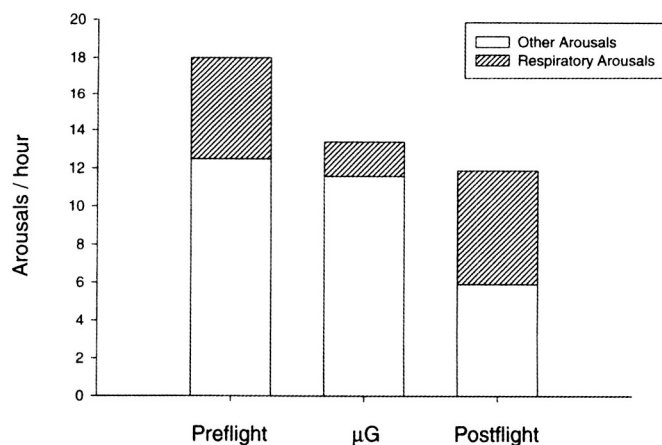


Figure 9. Arousals from respiratory causes (shaded) and non-respiratory causes (open bars). Note that inflight, virtually all of the reduction in arousals is a result of the fewer number of arousals resulting from respiratory causes. (From Elliott, 2001, with permission; reproduced from *American Journal of Respiratory and Critical Care Medicine*.)

was elevated to 1.2% (8.6 mmHg) showed an early increase in the set point (Elliott, 1998) that gradually abated. However, that study failed to show any significant alterations when the environmental PCO₂ was controlled at 5.0 mmHg. In the case of Neurolab, environmental PCO₂ averaged ~2.3 mmHg, a level below that in the chamber studies.

The changes in the ventilatory responses can be explained by changes in neural drive to the respiratory muscles. This conclusion is supported by the inspiratory occlusion pressure measurements (Figure 6). Hypoxia resulted in a substantial rise in the inspiratory occlusion pressure in all cases, although there were marked differences in the magnitude of the increase between the different conditions tested. The greatest response was measured with the subjects standing, where there was an increase of ~40% above that measured breathing air. While there was no change in the inspiratory occlusion pressure measured during air breathing in either the supine position or in microgravity, the increase seen during hypoxia in the supine position and in microgravity was significantly less than the increase measured standing. The reductions suggest that the hypoxic drive is approximately halved by either the supine position or by microgravity, an observation consistent with the ~50% reduction seen in the slope of the ventilatory response (Figure 4). In contrast, hypercapnia (a PCO₂ between 43 and 50 mmHg) resulted in the same increase in occlusion pressures regardless of the condition in which it was measured, consistent with the lack of a significant change in the response to inhaled CO₂.

Changes in the hypoxic ventilatory response resulting from blood pressure changes have been seen before. For example, an increase in carotid level blood pressure of ~10 mmHg results in a 33% smaller increase in ventilation elicited by a hypoxic challenge of breathing 10% O₂. Other studies have shown that the hypoxic response is reduced in the supine position by ~43% compared to the upright, a reduction of similar magnitude to that which we observed in our preflight control data (Figure 4). It therefore seems likely that the changes we observed in the HVR result from changes in blood pressure at the carotid chemoreceptors.

The blood pressure measured at the level of the heart changes only slightly between standing and supine rising only ~3mm Hg. However, the transition from the standing position to supine in one-G abolishes the hydrostatic difference in pressure between heart level and carotid level. Thus, when lying down we would expect an increase in carotid level blood pressure of 15–20 mmHg due to hydrostatic effects. Adding these two effects suggests that overall there is an increase in carotid level pressure of ~20 mmHg. This increase in pressure likely explains the decrease in hypoxic ventilatory response we observed in the supine position.

Microgravity results in only modest changes in heart level blood pressure, with a decrease of ~4 mmHg. However, in the absence of gravity, the hydrostatic gradient between heart level and the carotid region is also absent. Thus, despite the slight decrease in heart level blood pressure, it is likely that carotid level blood pressure in microgravity is considerably above that in the standing posture in one-G. Such an increase is consistent with the physical changes such as facial puffiness

associated with the early period in microgravity. Again, this increase in pressure likely explains the decrease in hypoxic ventilatory response we observed in microgravity.

Blood pressure falls in the upright position in the period immediately following flight to a variable degree. Certainly in these subjects, there was a persisting reduction in cardiac stroke volume of ~10% for the week immediately following flight, although a concomitant tachycardia maintained cardiac output. This suggests that carotid systolic pressure was slightly reduced compared to preflight, and this may have contributed to the increase in HVR we observed in the standing posture postflight (Figure 4).

Most of the hypercapnic ventilatory response can be ascribed to the central chemoreceptors. However, a significant component of the response comes from the carotid chemoreceptors. We reasoned that while there might be no change in the central chemoreceptor response to CO₂ as a result of exposure to microgravity, there may well be some change in the peripheral component of this response. Our data show that this is not the case. These results are consistent with those of other studies that show a reduction in the HVR, but not the HCVR in the supine position compared to the upright position (see Prisk, 2000b, for details).

It might be argued that the reduction in HVR was as a result of some mechanical disadvantage of the respiratory muscles supine and in microgravity. However, our data do not support a reduction in the HVR due to mechanical factors. As Figure 6 shows, inspiratory occlusion pressure breathing air was unaltered by the supine posture in one-G or by microgravity, and was similar in the three conditions during hypercapnia. Similarly, there was no significant change in the HCVR caused by microgravity (Figure 5). These results would not be expected if the cause of the reduced HVR supine and in microgravity was mechanical in origin.

Respiration and sleep in microgravity

Sleep studies during spaceflight have shown a decrease in the total amount of sleep obtained by the astronauts and a reduction in deep restorative (delta) sleep (see science report by Dijk et al. in this publication). However, the important message from this portion of the studies is that not only are respiratory events not increased in microgravity, they are significantly decreased, and they are clearly not the cause of the sleep disruption in microgravity. This is evidenced by the dramatic reduction in the number of sleep-disordered breathing events, amount of time spent snoring, and the number of arousals associated with these respiratory-related events during microgravity (Figures 8 and 9).

The respiratory system is greatly influenced by the force of gravity. The changes the system goes through by just moving from the standing to the supine posture are significant. In the supine posture, functional residual capacity (the normal resting volume of the lung), expiratory reserve, and tidal volumes are all reduced. Functional residual capacity and expiratory reserve volumes are reduced in space, but to a lesser degree when compared to the supine posture; and tidal volume is reduced to a greater extent in space when compared to supine (West, 1997).

In the supine posture, gravity also works to reduce upper airway size and increase upper airway resistance by causing the tongue, soft palate, uvula, and epiglottis to move back toward the posterior pharyngeal wall. The tongue cross-sectional area, uvular width, and soft palate thickness all increase in the supine position resulting in a reduction in the oropharyngeal cross-sectional area. All these anatomical changes caused by moving from the upright to supine posture result in an increase in upper airway resistance. It is widely believed that it is the gravitational forces acting on the upper airway structures that cause an increase in upper airway resistance that results in an increased probability that snoring, hypopneas, and frank obstructive sleep apnea will occur during sleep.

All five subjects in this study showed some degree of snoring from mild to moderate ranging from 8.7 to 32.6% of the sleep period. In microgravity, snoring was almost completely eliminated in all subjects. The change in snoring habits correlate with the changes in the number of respiratory events during sleep period (Figure 8).

Even though the majority of the subjects in this study showed respiratory disturbances as determined from the AHI within the normal range (<5.0/hour), four out of the five subjects showed a reduction in their AHI in microgravity. The greatest reduction in the AHI of almost 60% was seen in the subject with the largest AHI preflight (19.9/hour).

On average, the reduction in AHI was greatest in the nREM periods (a 68% reduction) as opposed to during REM (a 30% reduction). During REM sleep, there is an increase in upper airway resistance when compared to nREM sleep attributed to a loss of upper airway dilator muscle tone. There is also an inhibition of other respiratory muscles, including intercostal muscles, which alters the configuration of the rib cage and its contribution to tidal breathing. Both effects are independent of gravity per se. Though these two mechanisms play a role in the generation of upper airway obstruction, our data support the suggestion that gravity is the primary mechanism contributing to upper airway resistance during both the supine posture and sleep, since a larger effect was seen during nREM than during REM sleep.

The brief arousals caused either by apneas or hypopneas cause reduced or fragmented sleep. Overall we saw a significant reduction of ~70% in the number of respiratory-related arousals in these five subjects, accounting for virtually all of the reduction in the total number of all arousals during spaceflight. This suggests that contrary to our initial hypothesis, microgravity may improve sleep quality to some extent, especially for the subjects with positional sleep disordered breathing problems, obstructive sleep apnea, or upper airway resistance syndrome. For example, in the subject with the greatest AHI, the respiratory-related arousal index and arousal index decreased during spaceflight by 60% and 34%, respectively, with a concomitant increase in sleep efficiency.

Despite the improvement in sleep-disordered breathing, upon return to Earth the crew complained of significant fatigue. This likely resulted from a significantly shorter amount of sleep over virtually the entire flight (only ~6.1 hours per night inflight compared to almost eight hours pre-

flight), although clearly this was not from respiratory causes. It seems likely that the changes we observed during the post-flight period result from this fatigue, as opposed to some adaptive effects relating to the return to one-G.

CONCLUSION

Microgravity exposure greatly reduces the number of sleep-related apneas and hypopneas, significantly reduces snoring, and reduces the number of respiratory arousals in normal, healthy individuals. These changes were probably due to the elimination of the gravitationally induced changes in the upper airway anatomical structures. Indeed, the reduction in the total number of arousals in microgravity resulted almost entirely from the large reduction in respiratory-related arousals. From these data, we can infer that gravity plays a dominant role in the increase in upper airway resistance and obstruction that occurs after the transition to the supine posture and during all stages of sleep.

It has long been recognized that gravity might play a role in some forms of sleep-disordered breathing (especially obstructive sleep apnea (OSA)). However, these data provide the first direct evidence that the effect of gravity on the upper airways is dominant in causing obstruction. As such, the results may prove useful, increasing the emphasis on postural treatments for OSA. The simple expedient of decreasing the rearward gravitational effect on the upper airways by encouraging sleep in a semi-upright posture may prove more acceptable to some patients than other treatments, such as continuous positive airway pressure (CPAP).

Microgravity also resulted in a significant reduction in the hypoxic ventilatory response; however, the change that occurred was no different to that seen in the supine position. In contrast to the hypoxic response, there was no change in the response to inhaled CO₂ caused by either the supine position or by microgravity. Thus, the ventilatory control mechanisms in microgravity in these healthy subjects were much the same as they were in the supine position on the ground. The similarity is borne out by the similar numbers of central apneas and hypopneas observed in microgravity and on the ground, since central events result primarily from the ventilatory control system.

In conclusion, our data suggest that any sleep disruption caused by spaceflight or by microgravity has origins unrelated to the respiratory system.

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