Vital capacity, respiratory muscle strength, and pulmonary gas exchange during long-duration exposure to microgravity

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Submitted 8 November 2005; accepted in final form 29 March 2006

Prisk, G. Kim, Janelle M. Fine, Trevor K. Cooper, and John B. West. Vital capacity, respiratory muscle strength, and pulmonary gas exchange during long-duration exposure to microgravity. J Appl Physiol 101: 439–447, 2006. First published April 6, 2006; doi:10.1152/japplphysiol.01419.2005.—Extended exposure to microgravity (μG) is known to reduce strength in weight-bearing muscles and was also reported to reduce respiratory muscle strength. Short-duration exposure to μG reduces vital capacity (VC), a surrogate measure for respiratory muscle strength, for the first few days, with little change in O₂ uptake, ventilation, or end-tidal partial pressures. Accordingly we measured VC, maximum inspiratory and expiratory pressures, and indexes of pulmonary gas exchange in 10 normal subjects (9 men, 1 woman, 39–52 yr) who lived on the International Space Station for 130–196 days in a normoxic, normobaric atmosphere. Subjects were studied four times in the standing and supine postures preflight at sea level at 1 G, approximately monthly in μG, and multiple times postflight. VC in μG was essentially unchanged compared with preflight standing [5.28 ± 0.08 liters (mean ± SE), n = 187; 5.24 ± 0.09, n = 117, respectively; P = 0.03] and considerably greater than that measured supine in 1G [4.96 ± 0.10, n = 114, P < 0.001]. There was a trend for VC to decrease after the first 2 mo of μG, but there were no changes postflight. Maximum respiratory pressures in μG were generally intermediate to those standing and supine in 1G, and importantly they showed no decrease with time spent in μG. O₂ uptake and CO₂ production were reduced (~12%) in extended μG, but inhomogeneity in the lung was not different compared with short-duration exposure to μG. The results show that VC is essentially unchanged and respiratory muscle strength is maintained during extended exposure to μG, and metabolic rate is reduced.

In contrast to Skylab, Spacelab, the Russian Mir space station, and the International Space Station (ISS) operated or operate with a normobaric 21% O₂-balance N₂ atmosphere. Baranov et al. (4) reported a reduction in postflight forced vital capacity (FVC) of between 5 and 25%, with an apparent increase in the magnitude of the effect as flight durations increased over the range of 7–366 days. There were concomitant reductions in peak flow and other indexes of forced expiration. A study of two cosmonauts who lived on Mir for 180 days showed a reduction in VC (~31%) 1 day after return, primarily because of a reduction in both expiratory reserve volume and inspiratory capacity (43). Measurements made ~10 days after return showed a persisting reduction in VC. These reductions were attributed to a marked weakening of the respiratory muscles during flight. However, it should be noted that in-flight measurements made in these two subjects 9 days and 175 days into flight were not significantly different from those measured supine preflight, although they were lower than those measured seated preflight.

Pulmonary ventilation has been shown to be largely unaltered by exposure to μG for 1–2 wk, with only a small reduction in tidal volume and a compensatory increase in breathing frequency, likely as a result of an altered mechanical configuration of the chest wall and abdomen in μG (33). There were only small changes in O₂ uptake (VO₂), CO₂ output (VCO₂), and end-tidal P O₂ and P CO₂. The matching of ventilation to perfusion has been reported to remain unaltered in long-duration μG (44). However, long-duration bed rest of 113 days showed a reduction VC and diffusing capacity of the lung for CO immediately after bed rest that appeared to persist for up to 2 wk into the recovery period (29). Thus there is some question as to what effect, if any, an extended period in μG might have on pulmonary gas exchange and its determinants.

The present study reports VC, respiratory muscle strength, and pulmonary gas exchange and its determinants in 10 subjects who lived on the ISS for between 4 and 6 mo. In contrast to other studies, we performed extensive in-flight measurements in addition to the preflight and postflight measurements and directly assessed respiratory muscle strength through the use of maximum inspiratory and expiratory pressures (MIP and MEP, respectively). Given the inconsistent nature of previous reports of VC in and after μG exposure, and on the basis of our previous studies of gas exchange in short-duration μG, we hypothesized that VC would be essentially unchanged by sustained exposure to μG, that respiratory muscle strength would be maintained, and that pulmonary gas exchange would be unaltered beyond those changes associated with the initial adaptation to μG.

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METHODS

Subjects

We studied 10 subjects (9 male, 1 female) all of whom were long-term residents of the ISS. All subjects were healthy on the basis of physical examination by flight surgeons, had a good level of physical fitness, and had normal pulmonary function as evidenced by preflight pulmonary function tests performed by us. All subjects self-reported as nonsmokers. Average age (at the beginning of flight) was 45 yr (range 39–52) and average height was 174 cm (range 164–183).

Experiment Timing

Subjects performed a short battery of pulmonary function tests (described in Tests of Pulmonary Function) several times preflight, at approximately monthly intervals throughout their 4- to 6-mo sojourn on the ISS, and multiple times postflight. The first in-flight measurement was typically ~1 mo after arrival on the ISS. As a part of the overall study, we also examined the effects of space walk on pulmonary function by taking measurements on the day after space walk. These data are reported elsewhere (35) and were excluded from the present analysis.

Preflight and postflight measurements were performed both in the upright posture (standing) and supine (within ~10 min of assuming the supine posture). Preflight measurements were made on four occasions typically in the 4 mo preceding flight, although for some subjects this interval was slightly longer. Subjects underwent extensive training on the maneuvers before the start of data collection to minimize any training effects. All preflight sessions were performed at sea level.

Postflight data were collected wherever possible on the day of landing (R+0) in the supine posture only, and on the after day (R+1) in the upright posture. Not all subjects were able to participate in R+0 testing. Some subjects had testing delayed by ~1 day either because of the use of alternative landing sites or because of inability to participate in testing because of vestibular disturbances. With the exception of two subjects who landed at Dryden Flight Research Facility in Edwards, CA (barometric pressure ~690 mmHg), all postflight testing was at sea level. Subsequent postflight testing occurred at R+4 or R+5, at R+10–13, at ~R+45 (6 subjects only), and finally at ~R+ mission length.

Equipment

We used the Human Research Facility, Rack-1 equipment in the laboratory of the ISS coupled to a small amount of equipment specific to this experiment. For all tests except forced spirometry, subjects breathed on a flanged mouthpiece assembly consisting of a pulmonary function test filter (Pall type PF-30S), a Fleisch no. 2 pneumotachograph (OEM Medical), and a modified Hans Rudolph sliding valve (type 2810B). Total dead space of the breathing assembly was 125 ml. The pneumotachograph was coupled to a Validyne MP-45 differential pressure transducer (~±2 cmH2O) via Viton tubes of ~80 cm in length. The box holding the pressure transducer and demodulator had a LED bar-graph meter to provide feedback to the subject for expiratory flow control. For forced spirometry a Fleisch no. 4 pneumotachograph coupled to a 30-cm-long tapered cylinder of volume ~150 ml was used as in previous spaceflight studies (18). This was coupled to the same Validyne pressure transducer in place of the Fleisch no. 2 pneumotachograph and was calibrated separately as described below.

For measurement of maximum inspiratory and expiratory pressure, a separate Validyne MP-45 differential pressure transducer (~±200 cmH2O) was used with its own demodulator. At a predetermined lung volume (see below), subjects actuated the sliding valve connecting them to a path that was closed except for a small ~1-mm-diameter hole ~20 mm long, providing a flow resistance of ~150 cmH2O·L−1·s. This allowed a small air leak, preventing any contribution of the buccal muscles to the maximum expiratory pressure and eliminating glottal closure during the maximum inspiratory pressure test (9). Pressure was measured as the average over a 1-s period (2, 12).

Gas concentration was measured at the distal end of the pneumotachograph, proximal to the sliding valve (~98 ml from the mouth), by a quadrupole mass spectrometer specially built for spaceflight (GASMAP, Marquette, Milwaukee, WI). The mass spectrometer sampled gas at 60 ml/min and had a dynamic response (10–90%) of ~100 ms, which was sufficiently fast so that no dynamic response correction was required for these resting studies (5). In addition, subjects were instrumented with a three-lead ECG using a battery powered amplifier [National Aeronautics and Space Administration (NASA)], which approximated a lead II configuration providing heart rate (HR).

All signals were sampled by the GASMAP by use of a 12-bit analog-to-digital converter at 100 Hz, and the data were stored on a personal computer (IBM ThinkPad 760XD) using specially written software. This software also provided real-time prompting of subject actions and data display. Data were transmitted to the ground for monitoring in real time and in batch mode at the completion of the experiment day for subsequent analyses.

Calibration was performed at the beginning and end of each day by having the GASMAP sample three gas mixtures of known composition. Flow was calibrated by integration of strokes from a 3-liter calibration syringe (Hans Rudolph model 5530) separately for each pneumotachograph. The calibration strategy allowed for separate calibration factors for inspiratory and expiratory flow. GASMAP transit time was determined by the measured delay between the flow resulting from a sharp puff of CO2-containing gas into the pneumotachograph and the 50% point in the subsequent rise of the CO2 signal (5), and this delay was accounted for in subsequent analyses.

Tests of Pulmonary Function

Because of the limited experimental facilities on board the ISS at the time of this study, we were unable to perform any pulmonary function tests that required the use of specialized gas mixtures. Thus all tests performed used only cabin air. In all cases subjects were extensively trained in the maneuvers, coached through them numerous times in the preflight period, provided with graphical feedback of data to permit data quality assessment (supplemented with extensive online help), and encouraged to reject and repeat maneuvers not meeting predefined standards for data quality. At times throughout the flight, the investigators on the ground provided feedback on the quality of the data.

Forced spirometry. Subjects performed a FVC expiration with effort maintained for a minimum of 8 s, followed immediately by a FVC inspiration. At least three blows judged to be “good” by the subject (on the basis of reproducibility of the tracings) were recorded in each session. Data were analyzed as in previous spaceflight studies (18) and met American Thoracic Society requirements for the performance of spirometry (1, 3).

Slow VC. This was determined either from a controlled exhalation from total lung capacity (TLC) to residual volume (RV) at a flow rate of 0.5 L/s or from a short period of resting breathing followed by an inhalation to TLC and subsequent exhalation to RV in an uncontrolled (but not forced) manner. There were no differences in the value of VC from individual tests, and so the data from both maneuvers were used in reporting the VC. The volume was converted to BTPS conditions.

MIP and MEP. Subjects performed maximal inhalation and exhalation efforts against the occluded valve position (see above) twice within each experimental session. In a single sequence lasting ~90 s, subjects breathed quietly for ~15 s and then went to a predetermined lung volume and performed a MIP or MEP maneuver against the closed valve for a maximum of 5 s. The process was repeated to cover each lung volume-pressure combination. In all cases the order was MIP at functional residual capacity (FRC), MIP at RV, MEP at FRC, MEP at TLC.
Intrabreath inequality of ventilation-perfusion ratio. The intrabreath ventilation-perfusion (iV/Q) technique allows calculation of the degree of V˙A/Q˙ inequality from a single, controlled VC expiration. This concept, originally used by West and associates (45), has been shown to reflect the degree of V˙A/Q˙ inequality determined using the multiple inert-gas elimination technique in dogs exposed to methacholine challenge (37). It has also been used to examine V˙A/Q˙ inequality in both divers (13) and astronauts (33).

The technique is fully described in prior publications (22, 37). Briefly, the subject breathed quietly for ~60 s allowing the determination of the resting VO₂ and VCO₂. VO₂ and VCO₂ were calculated by the N₂ balance method (6), and expired ventilation, tidal volume, breathing frequency, and other variables were calculated as the average over the ~60-s period of quiet breathing. The subject then inhaled to TLC and without delay exhaled to RV at a controlled flow rate of 0.5 l/s while watching the flowmeter on the pressure transducer box. In subsequent analysis the instantaneous respiratory exchange ratio (intrabreath-R) that result from a computerized model of gas exchange was then compared with calculated values of the V˙A/Q˙ inequality in both divers (13) and astronauts (33).

The resultant value of this V˙A/Q˙ inequality is the slope of the iV/Q over the course of the expiration was then calculated by interpolation between adjacent intrabreath-R isopleths, each with differing values for Q˙ (and thus for V˙A/Q˙). A prior study has shown that the most sensitive index for VO₂ and VCO₂ is the slope of the iV/Q as a function of expired volume over the first half of the expiration (37). This and other indicators of V˙A/Q˙ inequality (33) were calculated from the iV/Q-vs.-exhaled volume plot.

Distribution of pulmonary perfusion. We used the hyperventilation-breath-hold maneuver previously employed in studies of pulmonary perfusion in μG (27, 36). In brief, the subject vigorously hyperventilated for 20 s, reducing PCO₂ in all areas of the lung to ~20 Torr. The subject then rapidly inhaled to TLC and performed a 15-s breath hold. During the breath hold, CO₂ was added to the lung units at a rate proportional to the local blood flow-to-lung volume ratio. Because at TLC regional lung volume is largely uniform (28), the regional PCO₂ at the end of the breath hold is a marker of regional pulmonary perfusion. The subject then exhaled at 0.5 l/s, and CO₂ concentration was plotted as a function of expired volume. The size of the cardiogenic oscillations and the height of the terminal change in CO₂ concentration after the onset of airway closure provide indications of the degree of inhomogeneity of pulmonary perfusion (36).

Statistical Methods

We used the same techniques employed in our previous spaceflight studies. We used a two-way ANOVA (categorical variables were subject and time in μG) in a randomized block design. In cases in which there was a significant F-ratio, post hoc testing using the Bonferroni adjustment was used to test for resulting differences. Significance was accepted at the P < 0.05 level and noted at the P < 0.10 level. To examine any effects of duration of exposure to μG, or reexposure to 1G, upon return we additionally separated in-flight data into early in-flight (within the first 2 mo of flight) and late in-flight (data collected beyond 2 mo in orbit), and early return (data collected after the first 3 days of return) and late return (data collected after the first 3 days of return to 1G).

It should be pointed out that a study such as this with only 10 subjects is inadequately powered to confirm the null hypothesis (i.e., the hypothesis that there is no change in a particular variable). Confirming the null hypothesis with the effect sizes present in much of the data would require subject populations >50, something impractical for a spaceflight experiment. However, in many of the variables that were observed to apparently not change in this study, it could be argued that even if the data reflect an underlying alteration that cannot be confirmed statistically, the magnitude of the change is sufficiently small as to be physiologically insignificant.

RESULTS

Slow VC

Table 1 and Fig. 1 show the results for the measurements of VC over the course of the study. As expected, VC was lower supine than standing in 1G as seen previously (19). Postflight

<table>
<thead>
<tr>
<th></th>
<th>VC, liters</th>
<th>FVC, liters</th>
<th>FEV₁, liters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing preflight</td>
<td>5.24±0.09 (117)</td>
<td>4.89±0.15 (40)</td>
<td>3.69±0.15 (40)</td>
</tr>
<tr>
<td>Early in-flight</td>
<td>5.41±0.14 (57)†</td>
<td>5.18±0.26 (18)†</td>
<td>3.91±0.20 (18)†</td>
</tr>
<tr>
<td>Late in-flight</td>
<td>5.22±0.10 (130)‡(1)</td>
<td>4.25±0.17 (35)‡</td>
<td>3.68±0.13 (35)‡</td>
</tr>
<tr>
<td>Standing early postflight</td>
<td>5.19±0.20 (30)</td>
<td>5.27±0.35 (9)†</td>
<td>3.40±0.29 (9)†</td>
</tr>
<tr>
<td>Standing late postflight</td>
<td>5.14±0.11 (85)</td>
<td>4.85±0.18 (26)</td>
<td>3.60±0.13 (26)‡</td>
</tr>
<tr>
<td>Supine preflight</td>
<td>4.96±0.10 (114)*</td>
<td>4.60±0.15 (39)*</td>
<td>3.42±0.11 (39)*</td>
</tr>
<tr>
<td>Supine early postflight</td>
<td>4.57±0.20 (27)†</td>
<td>4.63±0.31 (10)</td>
<td>3.48±0.24 (10)</td>
</tr>
<tr>
<td>Supine late postflight</td>
<td>4.86±0.11 (81)‡</td>
<td>4.60±0.18 (26)</td>
<td>3.33±0.14 (26)</td>
</tr>
</tbody>
</table>

Values are means ± SE with number of measurements in parentheses. VC, vital capacity; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s. *P < 0.05 compared with preflight standing. †P < 0.05 compared with preflight supine ‡P < 0.05 comparing early and late. Significance marks in parentheses indicate 0.05 < P < 0.10.
VC was not different from that measured preflight in either posture. When early and late in-flight periods were compared, there was a trend ($P < 0.10$) for VC to be lower late in-flight, with late in-flight VC being the same as that measured in the standing posture preflight (Fig. 1 and Table 1). The absolute magnitude of this difference was a decrease in VC of 1.80 liters ($P = 0.06$) compared with that measured preflight supine in 1G. The absolute magnitude of this difference was a decrease in VC of 1.80 liters ($P = 0.06$) compared with that measured preflight supine in 1G. There were no changes in ERV comparing preflight and late in-flight. Importantly, there was no suggestion of disproportionate changes in FEV1 or midexpiratory flows that might be associated with alterations in airway caliber.

Flows during a FVC inspiration (Table 2) were unchanged compared with those measured in the upright posture in 1G. As was the case for the expiratory flows, inspiratory flows measured supine in 1G were lower than those in both the upright posture and in μG.

### Maximum Respiratory Pressures

At FRC, MIP in μG was similar to those measured in the upright posture in 1G, or very slightly reduced (Fig. 3A, Table 3). There were no differences in either pressure between measurements made early in flight and those made later in flight. In the postflight period there was an initial reduction in inspiratory pressures measured upright, although this was small (−5 mmHg). Inspiratory pressure increased in the later postflight period compared with those measured immediately postflight. At RV, MIP in μG was not different from that measured supine in 1G, and there were no trends for a change with time (Fig. 3B, Table 3). Postflight there was trend (non-significant) for maximum inspiratory pressure to increase.

Early in flight, MEP at TLC was reduced compared with that measured either standing or supine in 1G (which were not different, Fig. 4B, Table 3). By later in flight, the magnitude of this difference had been reduced (from ~6.8 mmHg, compared with upright, to ~3.6 mmHg), although the difference remained significant. There were nonsignificant trends for an increase in maximum expiratory pressure in the postflight period. MEP measured at FRC (Fig. 4A, Table 3) showed essentially similar trends, but the changes did not reach the level of significance.

### Pulmonary Gas Exchange

Pulmonary ventilation (Table 4) was reduced in μG compared with both preflight standing and supine as a result of a reduction in tidal volume (of ~0.1 liter compared with standing). There was a concomitant reduction in alveolar ventilation of ~1.1 l/min (−11%) that was accompanied by an increase in

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**Table 2. Forced spirometry**

<table>
<thead>
<tr>
<th></th>
<th>Expiratory</th>
<th>Inspiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FEV1/FVC, %</td>
<td>FEF25, 1/s</td>
</tr>
<tr>
<td>Standing preflight (n = 40)</td>
<td>75.7±0.7</td>
<td>3.82±0.16</td>
</tr>
<tr>
<td>Early in-flight (n = 18)</td>
<td>75.3±0.9</td>
<td>3.93±0.27†</td>
</tr>
<tr>
<td>Late in-flight (n = 35)</td>
<td>75.7±0.7†</td>
<td>3.78±0.18**†</td>
</tr>
<tr>
<td>Standing early postflight (n = 9)</td>
<td>75.4±1.5</td>
<td>4.16±0.46</td>
</tr>
<tr>
<td>Standing late postflight (n = 26)</td>
<td>74.5±1.0</td>
<td>3.61±0.21</td>
</tr>
<tr>
<td>Supine preflight (n = 39)</td>
<td>74.4±0.7</td>
<td>3.40±0.15*</td>
</tr>
<tr>
<td>Supine early postflight (n = 10)</td>
<td>72.9±1.5</td>
<td>3.24±0.34</td>
</tr>
<tr>
<td>Supine late postflight (n = 26)</td>
<td>72.7±1.0†</td>
<td>3.19±0.20</td>
</tr>
</tbody>
</table>

Values are means ± SE with number of measurements in parentheses. FEF50, forced expiratory flow after exhalation of 50% VC; PEFR, peak expiratory flow rate; FIF50, forced expiratory flow rate at 50% of inspired volume; FIF25–75, forced inspiratory flow at 25–75% VC; PIFR, peak inspiratory flow rate. *P < 0.05 compared with preflight standing. †P < 0.05 compared with preflight supine. ⋆P < 0.05 comparing early and late. Significance marks in parentheses indicate 0.05 < P < 0.10.
end-tidal Pco2 of ~2.3 Torr above that seen in the standing posture in 1G but similar to the values in the supine posture both pre- and postflight.

Metabolic rate (as indicated by VO2 and VCO2) was significantly lower in μG by ~12% and 16%, respectively, compared with standing in 1G, leaving respiratory exchange ratio unaltered (Fig. 5, Table 4). HR was reduced by 9 beats/min compared with standing in 1G but remained slightly above that in the supine posture. There were trends (nonsignificant) for VO2, VCO2, and HR to fall with longer duration exposure to μG.

The inhomogeneity of gas exchange was only slightly altered by μG. The most sensitive marker of V̇A/Q̇ inhomogeneity that was measured, that is the slope of iV/Q over the first half of phase III, was actually higher in μG than that standing in 1G (Table 4). The range of iV/Q seen over phase III was unaltered compared with standing in 1G, and both were higher in the supine posture. Other markers of inhomogeneity of both

Table 3. Maximum respiratory pressures

<table>
<thead>
<tr>
<th>Condition</th>
<th>MIP FRC, mmHg</th>
<th>MIP RV, mmHg</th>
<th>MEP FRC, mmHg</th>
<th>MEP TLC, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing preflight</td>
<td>51.6±1.4 (76)</td>
<td>54.3±1.3 (74)</td>
<td>43.8±1.3 (71)</td>
<td>56.0±1.4 (72)</td>
</tr>
<tr>
<td>Early in-flight</td>
<td>49.3±1.3 (35)+</td>
<td>47.1±1.5 (37)*</td>
<td>40.3±1.9 (34)</td>
<td>49.2±1.4 (37)+</td>
</tr>
<tr>
<td>Late in-flight</td>
<td>49.5±1.3 (85)+</td>
<td>47.0±1.3 (78)*</td>
<td>43.1±1.2 (80)</td>
<td>52.4±1.0 (82)*</td>
</tr>
<tr>
<td>Standing early postflight</td>
<td>46.8±2.9 (18) (×)</td>
<td>52.1±2.3 (18)</td>
<td>43.7±2.5 (18)</td>
<td>53.3±3.0 (18)</td>
</tr>
<tr>
<td>Standing late postflight</td>
<td>53.6±1.7 (52) (×)</td>
<td>56.2±1.4 (52) (×)</td>
<td>47.0±1.3 (51)</td>
<td>58.5±1.6 (52)</td>
</tr>
<tr>
<td>Supine preflight</td>
<td>44.4±1.2 (78)*</td>
<td>45.2±1.2 (78)*</td>
<td>41.0±1.3 (76)*</td>
<td>53.9±1.4 (78)</td>
</tr>
<tr>
<td>Supine early postflight</td>
<td>39.6±1.9 (16)</td>
<td>42.0±2.3 (16)</td>
<td>40.3±2.5 (15)</td>
<td>54.0±2.2 (16)</td>
</tr>
<tr>
<td>Supine late postflight</td>
<td>44.6±1.6 (50)</td>
<td>45.1±1.5 (51)</td>
<td>40.1±1.3 (49)</td>
<td>52.4±1.5 (51)</td>
</tr>
</tbody>
</table>

Values are means ± SE with number of measurements in parentheses. MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity. *P < 0.05 compared with preflight standing. †P < 0.05 compared with preflight supine. ‡P < 0.05 comparing early and late. Significance marks in parentheses indicate 0.05 < P < 0.10.
**DISCUSSION**

The important result from these studies is that long-duration exposure to μG in a normoxic, normobaric environment results in no significant change in VC, respiratory muscle strength, or most indexes of pulmonary gas exchange beyond that seen in the initial transition to μG. This result is in sharp contrast to the limited number of previous studies that have all reported a reduction in VC (4, 39, 43), a possible reduction in respiratory muscle strength (43), and a possible detriment to gas exchange evidenced by changes in gas exchange after long-duration bed rest (29), and to one report of lowered arterialized O₂ levels (24). There was, however, an overall reduction in total metabolic rate.

**VC**

In contrast to previous studies, we saw little in the way of change in VC either in-flight or postflight. There was in fact a small increase in VC (of ~170 ml or ~3%) in measurements made in the first 2 mo of exposure to μG, and in measurements made in the subsequent portion of the flight there was no difference compared with standing in 1G (Fig. 1). There were comparable changes in FVC (Fig. 2).

VC has long been used as an indicator (albeit nonspecific) of changes in pulmonary function that might result from environmental stresses. For example, VC has been shown to be increased after ascent from saturation dives (14, 42). Reductions in VC are also considered to be an indicator of the degree of lung damage that results from pulmonary O₂ toxicity (10, 11, 25).

In the context of spaceflight, the earliest reports of VC in μG are from the Skylab missions in the 1970s (39), which showed a ~10% reduction in the VC measured in subjects exposed to μG for up to 84 days. However, these observations are confounded by the hypobaric, O₂-enriched atmosphere in the Skylab vehicle which was a 70% O₂-balance N₂ atmosphere at an absolute pressure of 258 mmHg. Although the atmosphere was slightly hyperoxic (measured inspired P O₂ of ~170 Torr), it seems unlikely that this was sufficient to have resulted in

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**Table 4. Ventilation, pulmonary gas exchange, V̇A/Q, and pulmonary perfusion**

<table>
<thead>
<tr>
<th></th>
<th>Standing</th>
<th>In-flight</th>
<th>Postflight</th>
<th>Supine</th>
<th>Postflight</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRCO₂</td>
<td>1.9 mL</td>
<td>2.0 mL</td>
<td>2.1 mL</td>
<td>2.0 mL</td>
<td>2.0 mL</td>
</tr>
<tr>
<td>HR</td>
<td>70 bpm</td>
<td>68 bpm</td>
<td>70 bpm</td>
<td>72 bpm</td>
<td>70 bpm</td>
</tr>
<tr>
<td>V̇A</td>
<td>341 mL/min</td>
<td>341 mL/min</td>
<td>341 mL/min</td>
<td>341 mL/min</td>
<td>341 mL/min</td>
</tr>
<tr>
<td>iV/Q 1st half</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>iV/Q P3</td>
<td>0.51</td>
<td>0.51</td>
<td>0.51</td>
<td>0.51</td>
<td>0.51</td>
</tr>
<tr>
<td>CO2 P4</td>
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<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Values are means ± SE with number of measurements in parentheses. V̇A, tidal volume; V̇E, total ventilation; PR, respiratory exchange ratio; HR, heart rate; V̇O2, alveolar dead space; V̇CO2, alveolar breath-hold end-tidal P CO2 level; % CO2, VC, V̇A/Q, and pulmonary perfusion.
pulmonary O₂ toxicity, which is known to reduce VC (10, 11, 25). However, the high fractional concentration of O₂ in the Skylab atmosphere may have compromised alveolar stability, as areas of high Vₐ/Q will rapidly absorb O₂ and have their regional lung volume greatly reduced because of the lack of the normally present insoluble inert gas component present in air (78% N₂) (15, 31, 32). This, combined with airway closure that still occurs in μG (23), could have contributed to the reduction in VC seen in Skylab (39). This conjecture is supported by the results from ground studies performed before the Skylab flights, which showed a ~5% reduction in VC in subjects exposed to 56 days of a comparable atmosphere (68% O₂, balance He, total pressure 258 mmHg) (38).

In short-duration spaceflight (up to ~2 wk) in Spacelab (a normoxic, normobaric environment), we showed that VC was essentially unchanged compared with that measured with subjects standing on the ground (19). There was an initial decrease in VC seen after ~24 h of exposure to μG, attributed to the translocation of blood into the thorax, but subsequent measurements were indistinguishable from those made standing in 1G in the preflight period.

There are only limited reports available from long-duration flight aboard the Russian Mir, a vehicle with a normoxic, normobaric atmosphere. Baranov et al. (4) reported a reduction in VC of up to ~20% in postflight measurements, with the magnitude of the effect being dependent on the duration of μG exposure (up to ~1 year). Venturoli et al. (43) made very limited in-flight measurements of 2 subjects aboard Mir for 180 days in 1995. In-flight measurements were made on days 9 and 175 of flight and showed a small ~5% reduction in VC compared with sitting in 1G. However, in measurements performed 1 day after return to 1G, VC was reduced by ~31% both in the sitting and supine postures. Repeat measurements on days 10–12 after return to 1G remained reduced by (~15%) and remained so by ~6% up to 120 days after return to 1G. These reductions were attributed to a reduction in respiratory muscle strength, although no explanation was given for the maintenance of VC during flight in the face of such an abrupt decline immediately postflight.

Postflight we saw almost no difference in VC compared with preflight, in sharp contrast to previous studies (4, 43). In the standing posture, VC was unaltered in either the early- or late-postflight periods compared with that measured preflight (Table 1, Fig. 1). However, in the supine posture, VC in the early postflight periods was reduced compared with that measured preflight and that measured in the late-postflight period. However, in marked contrast to other studies (4, 43), this reduction was very much smaller (~572 ml or ~11%) than the large reductions they reported [31% in the case of Venturoli et al. (43)]. In particular, there was no apparent change in VC comparing the first day of measurement in the postflight period with any other postflight day. In the implementation of our study, we were only able to measure VC in the supine posture on R+0 (the day of landing) and then only in a subset of the subjects, either because subjects were unavailable because of landing at alternative sites or because some subjects were too unwell to participate in testing because of vestibular disturbances. In some cases these may have limited subject effort in the early postflight data. Furthermore, it was apparent that all subjects tested on R+0 were tired and it is not clear that maximal effort VC maneuvers were achieved. We therefore consider the reduction of VC in the supine posture in the immediate postflight period to be of little physiological significance (and in fact it may be spurious).

The results from forced spirometry support this conjecture. We saw no change in FVC, FEV₁, or midexpiratory flows comparing postflight and preflight data (Tables 1 and 2, Fig. 2). Similarly, inspiratory flows (changes that depend almost exclusively on muscle performance and effort, as opposed to changes in expiratory flow limitation) were unchanged by long-duration exposure to μG.

Respiratory Muscle Strength

Taken overall, long-duration exposure to μG did not appear to alter respiratory muscle strength to any significant degree. Although MIP and MEP measured in μG generally differed from those measured preflight, there are reasons why this might be expected. But, importantly, there were no cases in which either MIP or MEP at any lung volume was altered between the early-in-flight and late-in-flight measurement periods (Table 3 and Figs. 3–4). Had μG resulted in a progressive reduction in respiratory muscle strength, we would have expected to see reductions in MIP or MEP as the exposure time increased.

From postural studies and studies in μG (7, 8, 17, 20), gravity is known to influence the configuration of the chest wall, particularly that of the abdominal compartment, and static lung volumes. Although ERV in-flight was not different from that measured standing in 1G, the lack of gravity decreases FRC and RV (19) and makes the abdominal contents and the diaphragm dome move cranially. These alterations are expected to impact on both MIP and MEP. The test sequence we used did not include a direct measurement of FRC as this was not possible in-flight because of the lack of compressed breathing gas mixtures; in addition, changes in chest wall configuration were not measured.

In the absence of such measures, interpretation of differences in MIP and MEP between preflight and in-flight (Table 3, Figs. 3–4) is speculative at best. In 1G, MIP (and to a lesser extent MEP) were lower in the supine posture than standing. This reduction, which is consistent with previous studies (26), has been attributed to suboptimal activation, recruitment, and coordination of the diaphragm and nondiaphragmatic muscles. This mechanism may contribute to the lower values of MIP and MEP at FRC and to the lower values of MIP at RV, in-flight compared with 1G standing. At TLC, MEP (Table 3, Fig. 4) was reduced in μG compared with both standing and supine in 1G. In this case, the lack of any stable platform against which to push may have limited MEP. In this context it is notable that late-in-flight measurements showed a trend toward being higher, perhaps because subjects became more adept at the maneuver as time in μG progressed.

Postflight there were trends (at times significant) for an increase in both MIP and MEP. For the most part this was not solely a result of an early-postflight reduction in maximum pressure generation but a subsequent increase to above that measured preflight. The cause of these increases is unknown; however, we speculate that this may be a reflection of the postflight rehabilitation measures applied to long-duration space travelers, which include numerous strength training exercises that might affect the abdominal muscles.
Numerous studies have shown a marked reduction in the performance of the weight-bearing muscles with impaired force generation and significant atrophy (21, 30). However, this atrophy appears to be due to a lack of activity in the antigravity muscles in μG (the “use it or lose it” model) as opposed to a systemic effect on skeletal muscles per se. Although some respiratory muscles have important postural and antigravity functions (16), the lack of change of respiratory muscle strength seen in these studies suggests that the absence of gravity does not contribute greatly to disuse atrophy in these muscles.

Pulmonary Gas Exchange

The most striking and unexpected observation was that overall there was a decrease in metabolic rate (as evidenced by pulmonary gas exchange) in μG and a trend (not significant) for a reduced VO$_2$ later in flight compared with that measured earlier (Table 4, Fig. 5). This result is in contrast to earlier observations made in short-duration spaceflight (1–2 wk) (33), which showed no change in VO$_2$ or VCO$_2$ compared with that measured standing in 1G. Whether this difference is a result of a higher level of activity in busy, short-duration flights, when the timeline is hectic, or part of the possible trend to a lower metabolic rate does not change as time spent in μG increased is unclear. It may also be that a reduction in body mass contributed to a reduction in metabolic rate. On average our subjects lost ~3% of their body mass over the duration of the flight; however, the reduction in resting V˙O$_2$ (which might be considered as a trend) observed in this study. Importantly, however, the O$_2$ pulse (V˙O$_2$/HR) was unaltered by μG exposure.

Studies in short-duration spaceflight (up to 16 days) and bed rest of 16 days show a slight reduction in energy expenditure (41), although these reductions were smaller than the reductions we saw in VO$_2$ in this study. Importantly, however, athletes have a higher resting metabolic rate than sedentary subjects, even when adjusted for fat-free body mass (40). Thus the reduction in resting VO$_2$ (which might be considered as a surrogate for resting metabolic rate) in long-duration spaceflight might be reflective of a detraining effect during flight of subjects that had a moderately high level of physical activity preflight.

It is likely that the reduced ventilation seen in μG is at least in part a reflection of the reduction in metabolic demand. However, as was the case in short-duration flight, end-tidal Pco$_2$ was elevated in μG (in this case by ~2.3 Torr), suggesting a similar change in the set point of the CO$_2$ control system despite the fact that μG does not seem to alter CO$_2$ response (34).

The distribution of V˙A/Q seen in the lung in μG matched that seen in short-duration flight (Table 4). The range of iV/Q over phase III of a prolonged expiration was virtually identical to that reported before (33) and not different from that seen standing in 1G. This reinforces the previous conclusion drawn from spaceflight studies, namely that, over the range of normal breathing, the major determinant of V˙A/Q inhomogeneity is not gravitational in origin. The iV/Q slope seen over the first half of phase III [the most sensitive indicator of V˙A/Q inhomogeneity from this test (37)] was slightly elevated in μG compared with standing in 1G, lending credence to previous speculation (33) that gravity in fact provides a degree of matching between ventilation and perfusion in the normal upright human lung. The result is also consistent with a previous study in two subjects aboard Mir for ~6 mo, which showed that the matching of ventilation to perfusion was unaltered by the time spent in μG (44).

As was the case with the inhomogeneity of V˙A/Q, the distribution of pulmonary perfusion almost exactly matches that seen in short-duration spaceflight (Table 4) (36). There is a clear influence of gravity on pulmonary perfusion that does not change as time in μG is prolonged. This result is consistent with a strictly mechanical mechanism dominating the distribution of pulmonary perfusion (e.g., the zone 1, 2, 3 model) as opposed to an active control mechanism.

In conclusion, the results of this study show clearly that VC, respiratory muscle strength, and most indexes of pulmonary gas exchange do not suffer physiologically significant degradation when subjects are placed in sustained μG. Our findings are important in the context of future spaceflight missions that may well involve very long exposure to μG (e.g., on a mission to Mars). They show clearly that long-duration exposure to μG does not detrimentally affect the mechanical aspects of lung function, at least in terms of VC and respiratory muscle strength, and does not result in an impairment of pulmonary gas exchange, although there appears to be a reduction in metabolic rate. Taken in the context of previous studies on Skylab (39), the results suggest that, provided that a normoxic, normobaric environment is maintained, it is reasonable to expect no significant degradation in these most basic measures of pulmonary function in long-duration μG.

ACKNOWLEDGMENTS

We gratefully acknowledge the cooperation and efforts of the ISS crew on increments 3, 4, 5, and 6 and the numerous NASA personnel and NASA contractors supporting those increments. In particular we thank Suzanne McCollum, Gwenn Sandoz, and Charlie Williamson for operational support, and John Ludlow for extensive data analysis work.

GRANTS

This study was supported by NASA contract NAS9-98124 and NASA cooperative agreement NCC9-168.

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