Pulmonary gas exchange is not impaired 24 h after extravehicular activity

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Prisk, G. Kim, Janelle M. Fine, Trevor K. Cooper, and John B. West. Pulmonary gas exchange is not impaired 24 h after extravehicular activity. J Appl Physiol 99: 2233–2238, 2005. First published August 25, 2005; doi:10.1152/japplphysiol.00847.2005.—Extravehicular activity (EVA) during spaceflight involves a significant decompression stress. Previous studies have shown an increase in the inhomogeneity of ventilation-perfusion ratio (VA/Q) after some underwater dives, presumably through the embolic effects of venous gas microemboli in the lung. Ground-based chamber studies simulating EVA have shown that venous gas microemboli occur in a large percentage of the subjects undergoing decompression, despite the use of prebreathe protocols to reduce dissolved N2 in the tissues. We studied eight crewmembers (7 male, 1 female) of the International Space Station who performed 15 EVAs (initial cabin pressure 745 mmHg, final suit pressure either ~295 or ~220 mmHg depending on the suit used) and who followed the denitrogenation procedures approved for EVA from the International Space Station. The intrabreath VA/Q slope was calculated from the alveolar Po2 and PCO2 in a prolonged exhalation maneuver on the day after EVA and compared with measurements made in microgravity on days well separated from the EVA. There were no significant changes in intrabreath VA/Q slope as a result of EVA, although there was a slight increase in metabolic rate and ventilation (~9%) on the day after EVA. Vital capacity and other measures of pulmonary function were largely unaltered by EVA. Because measurements could only be performed on the day after EVA because of logistical constraints, we were unable to determine an acute effect of EVA on VA/Q inequality. The results suggest that current denitrogenation protocols do not result in any major lasting alteration to gas exchange in the lung.

Decompression; ventilation-perfusion ratio; venous gas emboli

EVA Involves Decompression Stress

EXTRAVEHICULAR ACTIVITY (EVA, space walk) necessitates space suits that operate at a low absolute pressure. The space suits in common use today are the US-built Extravehicular Mobility Unit (EMU), which operates at ~220 mmHg (~4.3 psia), and the Russian-built Orlan, which operates at a slightly higher pressure of ~295 mmHg (~5.7 psia). At the present time suits that operate at a higher pressure than these are not available because they limit astronaut/cosmonaut mobility. To have a simple and robust environmental control system both suit types use a 100% O2 atmosphere, resulting in a hyperoxic environment for the wearer.

In contrast to the suits themselves, the current generation of spacecraft [the US Space Shuttle, the Russian Soyuz, and the International Space Station (ISS)] all normally operate with a sea-level atmosphere (21% O2, balance N2, total pressure ~760 mmHg). Thus the transition from the cabin atmosphere to the suit atmosphere is associated with a significant decompression stress. The ratio of the initial partial pressure of N2 in the tissues to the final absolute pressure resulting from this pressure change is ~2.5:1 for the US suit, which is sufficiently large that, without the use of preventative measures, frank decompression sickness (DCS) would be expected to result in almost all cases (18). As a consequence, there are elaborate and time-consuming denitrogenation protocols that must be performed as part of the EVA preparation. These span several hours and typically involve long periods of O2 breathing, coupled with moderate-intensity whole-body exercise and a staged pressure reduction (15, 34).

Despite these procedures, some studies have shown a considerable incidence of N2 bubbles [venous gas microemboli (VGE)] in the blood, ~50%, as measured by Doppler ultrasound (33), and a sizeable incidence of clinical DCS, ~25%, in test subjects (10, 33). Despite these ground observations, there are no confirmed cases of DCS resulting from EVA (9, 16, 24), although there is at least one unconfirmed report of possible DCS in an Apollo-era flight (8, 23). There are, however, confounding factors that might limit such reports. These factors include the higher metabolic rate typically seen in EVA compared with ground simulations (15); the suit design itself, which may mask joint pain; recompression at the completion of EVA, prophylactic analgesic use; and possible underreporting by EVA crewmembers (5). It has also been suggested that N2 elimination rates in microgravity (μG) may be different from those in normogravity (1G), lowering the incidence of DCS, although these have never been measured.

Decompression Causes VGE and Can Alter the Distribution of the Ventilation-Perfusion Ratio

The formation of N2 bubbles in the blood is a common consequence of decompression (18). Such bubble formation is most common in the venous circulation, and, as a consequence, VGE are filtered from the circulation by the pulmonary capillary network (7, 19). Studies in deep-saturation divers have shown that VGE filtration by the lungs results in measurable alteration to pulmonary gas exchange as evidenced by reductions in lung CO-diffusing capacity (DLCO) (31, 32) and by an increase in forced vital capacity (12, 32), possibly through changes in lung recoil. Similar changes have also been seen after nonsaturation dives (13, 30). Similarly, there are reports that VGE can alter ventilation-perfusion ratio (VA/Q) in the lung. Hlastala et al. (20) infused bubbles into the lungs of dogs under normobaric conditions and showed widening of the VA/Q distribution determined from the multiple inert-gas elimination technique (MIGET). In addition, there is at least one report of alteration to VA/Q using the intrabreath VA/Q (IV/Q) technique (17, 28) after saturation dives (11), as well as anecdotal evidence to support this.

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We hypothesized that the decompression stress associated with EVA in μG may result in the formation of VGE that are filtered by the lungs and that this would in turn result in a measurable alteration to pulmonary gas exchange. To test this hypothesis, we measured several aspects of pulmonary function in astronauts and cosmonauts resident on the ISS before and after EVA.

**METHODS**

**Subjects**

We studied eight subjects (7 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 44 yr (range 39–47), height 174 cm (range 164–183), and body mass (measured preflight) 77 kg (range 63–95 kg).

**Experiment Timing**

As part of a study of long-duration exposure to μG (reported elsewhere), subjects performed a short battery of pulmonary function tests (described below) at approximately monthly intervals throughout their 4- to 6-mo sojourn on the ISS. Before an EVA the regular sessions were scheduled to occur within the week preceding. It should be emphasized that all data reported here were collected in μG.

On the day after EVA (less than 24 h after recompression), subjects performed the same battery of pulmonary function tests. Our original experimental design called for the post-EVA tests to be performed as soon as possible after recompression on the day of EVA. However, the combined length of the EVA preparation and the EVA itself was so great that this proved impractical. In one instance an atmospheric contamination incident in the laboratory of the ISS resulted in a postponement of the post-EVA testing to the second day after EVA (within 48 h of recompression).

The eight subjects performed a total of 15 EVAs from the ISS. Of those, nine were performed using the Russian Orlan suits and six were performed using the US EMU. Because of the small number of measurements involved, we have not further distinguished between the suit type used.

**EVA Preparation and Length**

All subjects followed the current operational EVA preparation procedures. These differed depending on the suit used. EVAs averaged 344 min in length (range 298–411), and repressurization (still in suit breathing 100% O₂) occurred in 10–15 min.

For the US suit, the major components of the EVA preparation procedure included whole body exercise at up to 75% maximal O₂ uptake (maximal VO₂) for ~10 min while breathing 100% O₂ at 760 mmHg for a ~50-min period. This was followed by a decompression while still breathing O₂ to ~530 mmHg to a total elapsed time of 80 min of 100% O₂ breathing. Suit-up (doming) lasting 30–90 min followed, while subjects breathed O₂-enriched air (26.5% O₂, balance N₂ at 530 mmHg total pressure). The suit was then purged and sealed, and the total pressure then rose to slightly above sea level (~810 mmHg) while subjects breathed >95% O₂ for ~40 min. The decompression for EVA then occurred with a 25-min stop at ~480 mmHg on the way to a final absolute suit pressure of ~220 mmHg, which was maintained for the duration of the EVA.

For the Russian Orlan suit, EVA preparation involved doming and purging the suit while at 760 mmHg (~10 min), after which point only O₂ at >95% was breathed. After the suit was sealed, it was pressurized to its standard working pressure of 5.7 psi, or 295 mmHg above ambient pressure, giving an in-suit pressure of 1,055 mmHg that was maintained for ~30 min. The airlock was then depressurized over a ~10 min period, lowering suit pressure to ~295 mmHg, and this final suit pressure was maintained for the duration of the EVA.

**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 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 Validyne pressure transducer and demodulator had a LED bar-graph meter displaying flow to allow the subject to control expiratory flow. 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 (14). This was coupled to the same Validyne pressure transducer in place of the Fleisch no. 2 pneumotachograph and was calibrated separately as described below.

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 that no dynamic response correction was required for these resting studies (3). In addition, subjects were instrumented with a three-lead ECG using a battery powered amplifier [National Aeronautics and Space Administration (NASA)] that approximated a lead II configuration providing heart rate.

All signals were sampled by the GASMAP using 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 experimental day for subsequent analysis.

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). 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 (3), and this delay was accounted for in subsequent analyses.

**Tests of Pulmonary Function**

Because of limited experimental facilities on board the ISS at the time of this study, we were precluded from performing any pulmonary function tests that required the use of specialized gas mixtures. Thus all tests performed used only cabin air. For the purposes of this portion of the overall study, three tests performed as part of the test battery are relevant.

**Forced spirometry.** Subjects performed a forced vital capacity expiration with effort maintained for a minimum of 8 s, followed immediately by a forced vital capacity inspiration. At least three blows judged to be “good” by the subject were recorded in each session. Data were analyzed as in previous spaceflight studies (14) and met American Thoracic Society requirements for the performance of spirometry (1, 2).

**Intrabreath inequality of V˙A/Q˙.** The V˙A/Q˙ technique allows calculation of the degree of V˙A/Q˙ inequality from a single, controlled,
Table 1. Resting gas exchange

<table>
<thead>
<tr>
<th></th>
<th>Pre-EVA</th>
<th>Post-EVA</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Cabin pressure, mmHg</td>
<td>749±1</td>
<td>751±2</td>
<td>NS</td>
</tr>
<tr>
<td>VT, ml</td>
<td>807±30</td>
<td>811±43</td>
<td>NS</td>
</tr>
<tr>
<td>fB, min⁻¹</td>
<td>12.2±0.5</td>
<td>13.1±1.3</td>
<td>0.003</td>
</tr>
<tr>
<td>VE, ml/min</td>
<td>9,350±298</td>
<td>10,200±873</td>
<td>NS</td>
</tr>
<tr>
<td>V̇A, ml/min</td>
<td>7,744±260</td>
<td>8,436±725</td>
<td>NS</td>
</tr>
<tr>
<td>Ti/TOT, %</td>
<td>41.5±0.5</td>
<td>41.3±0.9</td>
<td>NS</td>
</tr>
<tr>
<td>V̇R/VTI, ml/min</td>
<td>380±12</td>
<td>409±31</td>
<td>0.061</td>
</tr>
<tr>
<td>Alveolar dead space, ml</td>
<td>35.3±1.7</td>
<td>34.7±2.8</td>
<td>0.042</td>
</tr>
<tr>
<td>PETCO₂, Torr</td>
<td>107.5±1.2</td>
<td>109.3±2.9</td>
<td>NS</td>
</tr>
<tr>
<td>PETCO₂, Torr</td>
<td>40.0±0.5</td>
<td>41.6±0.8</td>
<td>0.004</td>
</tr>
<tr>
<td>V̇CO₂, ml/min</td>
<td>297±6</td>
<td>323±12</td>
<td>0.078</td>
</tr>
<tr>
<td>V̇CO₂, ml/min</td>
<td>242±8</td>
<td>268±20</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, ml/min</td>
<td>60.3±1.2</td>
<td>64.5±1.7</td>
<td>(0.092)</td>
</tr>
</tbody>
</table>

Values are means ± SE. EVA, extravehicular activity; VT, tidal volume; fB, breathing frequency; VE, minute ventilation; V̇A, alveolar ventilation; Ti/TOT, percent time spent inspiriting; V̇R/VTI, average inspiratory flow rate; PETCO₂, and PETCO₂, end-tidal partial pressures of oxygen and carbon dioxide; V̇O₂, oxygen consumption; V̇CO₂, carbon dioxide production; NS, not significant. P values between 0.50–0.10 are in parentheses.

Results

We initially examined the effect of EVA taking into account suit type (Russian Orlan vs. US EMU). There was no significant difference based on suit type, and so all post-EVA data have been treated as equivalent. There were no statistical differences between data collected at different time points of the subjects’ stay on the ISS. We therefore chose to treat all µG data that were not collected as part of the post-EVA sessions as our control data to maximize the statistical power of our study.

Table 1 reports the results from the 60-s period of resting breathing that preceded the iV/Q test. EVA resulted in a trend for an increase in ventilation resulting from an increase in breathing frequency, with an accompanying increase in metabolic rate, although in physiological terms the changes were small. Heart rate was slightly elevated post-EVA, and there was a reduction in alveolar dead space. End-tidal PCO₂ was elevated (by ~2 mmHg) post-EVA.

There were no significant changes in the distribution of V̇A/Q in the lungs caused by EVA as measured using the intubation technique (Table 2; Fig. 1) with the exception of a trend (P = 0.093) for an increase in the range of iV/Q seen over phase IV of the expiration (after airway closure). There was no corresponding change in closing volume (data not shown). Similarly, there were no changes in the degree of inhomogeneity of pulmonary perfusion measured using the hyperventilation breath-hold maneuver (Fig. 1).

There were small but significant changes in forced spirometry after EVA (Table 3). These were principally a slight increase in forced expiratory volume in 1 s, but there were other changes in midexpiratory flows that were contradictory in

Table 2. Intra breath inhomogeneity of V̇A/Q and pulmonary perfusion

<table>
<thead>
<tr>
<th></th>
<th>Pre-EVA</th>
<th>Post-EVA</th>
<th>P</th>
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<tbody>
<tr>
<td>iV/Q slope, ml⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Phase III</td>
<td>0.011±0.003</td>
<td>0.018±0.008</td>
<td>NS</td>
</tr>
<tr>
<td>1st half</td>
<td>0.046±0.006</td>
<td>0.062±0.020</td>
<td>NS</td>
</tr>
<tr>
<td>2nd half</td>
<td>−0.022±0.003</td>
<td>−0.028±0.008</td>
<td>NS</td>
</tr>
<tr>
<td>iV/Q range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase III</td>
<td>0.145±0.013</td>
<td>0.202±0.055</td>
<td>NS</td>
</tr>
<tr>
<td>Phase IV</td>
<td>0.035±0.004</td>
<td>0.050±0.009</td>
<td>(0.093)</td>
</tr>
<tr>
<td>Pulmonary perfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO-Height, % CO₂</td>
<td>0.035±0.005</td>
<td>0.038±0.008</td>
<td>NS</td>
</tr>
<tr>
<td>PV Height, % CO₂</td>
<td>−0.084±0.018</td>
<td>−0.114±0.036</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE. iV/Q slope, slope of intubation V̇A/Q(iV/Q) as a function of expired volume over the indicated range; iV/Q range, vertical range of iV/Q over the indicated range; CO-height, cardiogenic oscillation height; PV height, height of terminal deflection following airway closure.

Statistical Methods

We used the same techniques employed in our previous spaceflight studies. We used a two-way ANOVA (categorical variables subject and EVA) 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 differences resulting from EVA. Significance was accepted at the P < 0.05 level and noted at the P < 0.10 level. Note that all data in this study were collected in µG and there was no comparison made with tests performed in 1G in support of other scientific objectives.
Anticipated Changes

Our hypothesis was that VGE are almost certainly caused by the decompression stress associated with EVA and that these would cause an alteration in gas exchange in the lung. The likely effect could be either through a direct embolic effect (the plugging of pulmonary capillaries) or through inflammatory changes secondary to the emboli.

A single deep air dive (to 5.5 bar) has been shown to decrease DLCO, which was seen to occur in parallel with the presence of VGE (13). Previous studies of saturation divers after ascent have shown significant alterations to gas exchange and pulmonary function, thought to be due to the effects of VGE. A single 300-m saturation dive for 12 days increased vital capacity by ~0.5 liters and decreased DLCO by ~10% (12). Similar dives have also been shown to alter iV/Q (11). Saturation dives of varying severity have been shown to decrease DLCO, increase lung volume, increase closing volume, and decrease midexpiratory forced expiratory flows (31, 32). These studies implicated both direct alterations to gas exchange due to the direct embolic effect and longer term changes attributable to inflammation that might result from the effects of VGE. However, the possible confounding effects of pulmonary O2 toxicity associated with deep dives are difficult to separate out. Unfortunately the equipment necessary to perform measurements of DLCO was not available on the ISS at the time these studies were performed.

Certainly, decompression can produce bubbles that are sufficiently large to occlude the pulmonary circulation. Bubble diameters of 19–700 μm have been observed in experimental decompressions in animals, with the majority of the bubbles in the 20- to 30-μm size range (19). Bubbles of between 14 and 189 μm in size have been shown to be filtered by the lungs, with a lower size cutoff of ~22 μm for bubbles that can transit the pulmonary circulation (7). Bubbles introduced intravenously under normobaric conditions alter pulmonary gas exchange as determined by MIGET (20). These infused bubbles resulted in the development of regions of high V˙A/Q in the lungs of dogs, although in these nondecompression studies the effects were short lived (~30 min).

Despite these previous studies, we saw no significant changes in any measure pertaining to either the distribution of V˙A/Q or the distribution of pulmonary perfusion. There are at least three potential explanations for this. First, for logistical reasons we were precluded from performing post-EVA measurements until the day after EVA. Second, it may be that there were some changes in the parameters of forced spirometry that reached the level of statistical significance (Table 3). However, these changes were somewhat contradictory in nature (e.g., an increase in forced expiratory flow after exhalation of 50% forced vital capacity with a concomitant decrease in forced maximal midexpiratory flow) and were universally small in magnitude, suggesting that they were physiologically insignificant.

Table 3. Lung volumes and forced spirometry

<table>
<thead>
<tr>
<th></th>
<th>Pre-EVA</th>
<th>Post-EVA</th>
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<tbody>
<tr>
<td>Slow VC, ml</td>
<td>5.624±160</td>
<td>5.679±248</td>
</tr>
<tr>
<td>Forced VC, ml</td>
<td>5.199±162</td>
<td>5.361±252</td>
</tr>
<tr>
<td>FEV1, ml</td>
<td>3.955±120</td>
<td>4.037±179</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>76.2±0.6</td>
<td>75.5±0.9</td>
</tr>
<tr>
<td>PEFR, 1/sec</td>
<td>10.57±0.24</td>
<td>10.50±0.34</td>
</tr>
<tr>
<td>FEF500, ml/s</td>
<td>4.116±155</td>
<td>4.210±235</td>
</tr>
<tr>
<td>FEF25–75, ml/s</td>
<td>3.321±121</td>
<td>3.309±163</td>
</tr>
</tbody>
</table>

Values are means ± SE. VC, vital capacity; FEV1, forced expiratory volume in 1 s; PEFR, peak expiratory flow rate; FEF500, forced expiratory flow rate at 50% VC; FEF25–75, forced expiratory flow rate between 25 and 75% VC.
were no significant changes occasioned by EVA. Third, it may be that the methods available to us were insufficiently sensitive to detect any changes that occurred as a consequence of EVA.

Effect of a 24-h Delay

The logistics of performing an EVA require more than 6 h of preparation before exiting the airlock and the EVA itself lasting ~5–6 h. This coupled with the post-EVA requirements precluded us from making any post-EVA measurements until the day after EVA. Thus the post-EVA measurements occurred 18–24 h after the EVA itself.

It is possible that even if VGE had a direct embolic effect on the lung during EVA, altering the V\textsubscript{A}/Q\textsubscript{a} distribution, this effect may have resolved by the day after. Certainly, the study using infused bubbles showed only a transient effect on the V\textsubscript{A}/Q\textsubscript{a} distribution that resolved within ~30 min (20). However, saturation dive studies have shown longer lasting effects (2–7 days) on measures such as DL\textsubscript{CO} (12, 31, 32). If the embolic effect on gas exchange was not associated with inflammatory changes, then it might be reasonable to expect that there would be no residual effect 24 h after EVA, because any VGE would likely have been resorbed by the gases dissolving into the surrounding blood and tissue. Bubble longevity of infused bubbles has been shown to be generally less than 1 h, supporting this conjecture (6). This effect is even more likely considering the fact that terminating the EVA involves a recompression to sea level from the much lower suit pressure. On the basis of the limitations imposed on this study by the logistics associated with EVA, it is not possible to do more than speculate as to an effect of EVA on lung function either during the EVA or immediately following.

Absence of Change With EVA

It may also be that EVA did not result in any significant effect on lung function. On the basis of previous ground studies, it seems likely that VGE did develop during EVA. Previous chamber studies (33) reported a >50% incidence rate for VGE in ground chamber simulations, with ~24% of subjects actually showing symptoms of DCS. Although EVA preparation protocols have evolved and been refined considerably since then, more recent chamber studies still show the presence of VGE (9, 16, 24). Despite these ground studies, there have been no confirmed reports of DCS in flight. Whether this is a consequence of an altered incidence of DCS in \textmu G (and by inference altered incidence of VGE formation) because of more rapid N\textsubscript{2} elimination rates during the prebreath or because of altered reporting (5) is unknown. To our knowledge there are no studies that have been performed in \textmu G examining N\textsubscript{2} elimination rates compared with those in 1G.

Sensitivity of the Methods Employed

Finally, it may be that the methods available to us were not of sufficient sensitivity to detect changes that occur as the result of EVA. Both the iV/Q technique and the hyperventilation-breath hold maneuver have been used by us in the past to examine the effects of \textmu G on lung function (25, 27). In those studies, we were able to show significant changes in lung function occasioned by \textmu G. In the past the iV/Q technique has been used to examine the effects of ascent from saturation dives on lung function (11), and there is anecdotal evidence from nonsaturation dives. Although these studies show a demonstrable effect of ascent on iV/Q, the effects that result from saturation dive ascent may not be reflective of those resulting from decompression before EVA.

On the basis of these prior studies, we conclude that the techniques we were able to employ are sufficiently sensitive to show changes that might be considered to be physiologically significant. The absence of any such changes in this study thus likely implies the absence of physiologically significant changes as opposed to the failure of the techniques to detect such changes.

Changes in Metabolic Rate Post-EVA

Whereas our study did not detect any changes in the distribution of V\textsubscript{A}/Q\textsubscript{a} in the lungs after EVA, there were changes in metabolic rate 24 h after EVA (Table 1). Post-EVA there was a small but statistically significant increase in VO\textsubscript{2} of ~9% and a concomitant trend to an increase in V\textsubscript{CO}\textsubscript{2} of ~9% (not significant). It seems that, to accommodate this increase, there was a slight increase in ventilation via an increase in breathing frequency and a slight rise in end-tidal PC\textsubscript{O}\textsubscript{2}, the latter suggesting an incomplete ventilatory adjustment to the increased metabolic demand.

Post-EVA heart rate was also elevated. We were not able to measure cardiac output because of limited equipment availability, but previous studies performed in \textmu G have shown that once the first week or so of adaptation to the new gravity level is complete, stroke volume is relatively constant (26). Thus an increase in heart rate is likely a reflection of an increase in cardiac output.

The reasons for an increase in overall metabolic rate ~24 h after the completion of EVA are unclear. Although EVA is known to be an energetic activity, it seems surprising that there would be a persisting elevation of metabolic rate on the day after just from the effects of the exercise per se. Intense exercise in 1G has been shown to cause metabolic rate to remain elevated for less than 1 h after the completion of exercise (29). However, EVA involves a long period of exercise at moderately high levels of exertion, and the possibility of some lingering effect involving persisting fatigue cannot be entirely discounted. We imposed constraints on the performance of our studies such that they were performed at least 1 h after eating and at least 2 h after the completion of any routine exercise to minimize such effects. These constraints applied to both pre- and post-EVA studies. If there were other operational factors associated with operations on the day after EVA that might have raised metabolic rate, we have been unable to identify them.

In conclusion, in contrast to our hypothesis, we could detect no significant changes in the distribution of V\textsubscript{A}/Q\textsubscript{a}, or in the distribution of pulmonary perfusion caused by EVA. There was, however, a small but significant increase in overall metabolic rate on the day after EVA, although the origin of this is unclear.

Because we were not able to make measurements immediately after the completion of EVA, the question of whether there is an acute effect of EVA on V\textsubscript{A}/Q\textsubscript{a} distribution remains unanswered. However, the results of this study clearly show that there are no long-term negative consequences of EVA as currently implemented on the distribution of V\textsubscript{A}/Q\textsubscript{a} in the lung.
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