Effects of gravity and blood volume shifts on cardiogenic oscillations in respired gas

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Montmerle, Stéphanie, and Dag Linnarsson. Effects of gravity and blood volume shifts on cardiogenic oscillations in respired gas. J Appl Physiol 99: 931–936, 2005. First published April 21, 2005; doi:10.1152/japplphysiol.00252.2005.—During the cardiac cycle, cardiogenic oscillations of expired gas (COSflow) are generated. At the same time, there are heart-synchronous cardiogenic oscillations of airway flow (COSflow), where inflow occurs during systole. We hypothesized that both phenomena, although primarily generated by the heartbeat, would react differently to the cephalad blood shift caused by inflation of an anti-gravity (anti-G) suit and to changes in gravity. Twelve seated subjects performed a rebreathing-breath-holding-expiration maneuver with a gas mixture containing O2 and He at normal (1 G) and moderately increased gravity (2 G); an anti-G suit was inflated to 85 mmHg in each condition. When the anti-G suit was inflated, COSflow amplitude increased (P = 0.0028) at 1 G to 186% of the control value without inflation (1-G control) and at 2 G to 205% of the control value without inflation (2-G control). In contrast, the amplitude of COS of the concentration of the blood-soluble gas O2 (COS[O2/He]), an index of the differences in pulmonary perfusion between lung units, declined to 75% of the 1-G control value and to 74% of the 2-G control value (P = 0.0030). There were no significant changes in COSflow, or COS[O2/He] amplitudes with gravity. We conclude that the heart-synchronous mechanical agitation of the lungs, as expressed by COSflow, is highly dependent on peripheral-to-central blood shifts. In contrast, COS[blood-soluble gas] appears relatively independent of this mechanical agitation and seems to be determined mainly by differences in intrapulmonary perfusion.

Cardiogenic oscillations are heart-synchronous variations in the concentration of a specific gas component x (COSx) in the airways.

COSx has been used to study intrapulmonary gas mixing and perfusion heterogeneity. Several investigations have studied COSx to assess the effects of gravity on the distribution of ventilation and perfusion in the lungs (14, 21, 23, 24, 27). COSx is generated from a combination of concomitant gas composition differences and heart-synchronous sequential emptying between units with different gas compositions. In many studies, COSx values are compared between different conditions of gravity, which may induce differences in the distribution of ventilation, perfusion, central blood volume, and stroke volume (SV). Gravity-induced changes in these hemodynamic variables may modify the mechanical agitation caused by cardiac action on the lungs, thereby altering COSx amplitude without necessarily reflecting a change in intrapulmonary gas concentration differences. Rohdin et al. (26, 27) addressed this issue by normalizing COSx amplitudes for SV. In an alternative approach, Montmerle et al. (23) compared conditions where central hemodynamics were likely to be similar.

This experiment was designed to study the effects of moderate hypergravity and changes in blood volume distribution imposed by use of an anti-G suit on COSx. In particular, we wanted to compare conditions where we knew from a parallel study (22) that SV was the same but, at the same time, there were differences in gravity and blood volume distribution. We assessed the mechanical action of cardiac pumping on the lung tissue from COSflow, because COSx is generated from a combination of heart-synchronous sequential emptying of pulmonary units and gas composition differences between these units.

We hypothesized that relatively small cardiogenic blood volume pulsations would suffice to cause sequential emptying and, thus, produce COSx because of the compliant nature of the lung tissue. As a consequence, we reasoned that COSx would reflect primarily the concentration differences between sequentially emptying lung units and would be modulated to only a small extent by the size of the intrathoracic blood volume pulsations.

METHODS

Subjects

We studied 12 subjects (6 men and 6 women) recruited by an advertisement. All were healthy nonsmokers. Their mean ± SD ages, heights, and weights were 25.6 ± 4.5 yr, 1.78 ± 0.08 m, and 70.0 ± 10.9 kg, respectively. They received written information before the start of the experiment and provided verbal consent in accordance with the national Swedish ethical guidelines. The protocol adhered to the principles of the Declaration of Helsinki and had been approved by the Regional Research Ethics Committee of Karolinska Institutet, Stockholm, Sweden.

Equipment

Human centrifuge. Experiments were conducted in a 7.25-m-radius human centrifuge (ASEA, Västerås, Sweden) at Karolinska Institutet. The floor of the gondola was horizontal when stationary (1-G tests) and was perpendicular to the resultant normal and centrifugal G vectors when the centrifuge was spinning (2-G tests). The back rest of the seat of the gondola reclined at an angle of 28°. Thus the gravitational effect of 1- and 2-G exposures on the subject was 0.88 and 1.77 Gz, respectively (i.e., in the head to foot direction). For convenience, we refer to these Gz gravitational loads as 1 and 2 G.

Slip rings at the center of the centrifuge allowed audiovisual monitoring, power supply, and transmission of the physiological...
signals between the gondola and a control room. We used a dedicated respiratory monitoring system consisting of a quadrupole mass spectrometer for gas analysis (model AMIS 2000, Innovision, Odense, Denmark) located in the center of the centrifuge and coupled to a custom-made valve activated by a pneumatic rotary drive (type DSR-25-180-P, Festo Pneumatic, Esslingen, Germany) placed in the gondola. In turn, the rotary drive was powered by compressed air and an array of solenoid valves. From the rotary valve, the subject could, via a mouthpiece, breathe air or rebreathe from a 4-liter rubber bag. This valve was controlled remotely by an operator in the control room. A flowmeter (type 3719, Hans Rudolph, Kansas City, MO) coupled to a pressure transducer (model CD12, Validynde, Northridge, CA) was attached to the cabin air port of the rotary valve for measurement of expiratory flow. The membrane of the pressure transducer was mounted perpendicular to the direction of rotation to minimize the effects of the normal and centrifugal G vectors on pressure recordings. The volume of the instrumental dead space was 150 ml. Calibration of the flowmeter was performed daily with a 3-liter syringe (series 5530, Hans Rudolph) within the experimental flow range. Gas was sampled from an inlet located between the valve and the mouthpiece. This inlet was coupled to a 10-m sampling tube, connected to the mass spectrometer. The mass spectrometer was calibrated before each session with two mixtures with known compositions of all relevant gas components (Air Liquide, Malmö, Sweden). The delay of response of the mass spectrometer compared with the flowmeter signal was 7.37 ± 0.20 (SD) s. The 10–90% response time for a step change in the gas composition was ~180 ms. Data were recorded with a data-handling system (Biopac, Goleta, CA) at a sampling frequency of 200 Hz and stored digitally.

Anti-G suit. The pneumatic anti-G suit was the full-coverage model used by Swedish military pilots in the 9-G aircraft JAS 39 Gripen [anti-G ensemble 39 (AGE-39), Swedish Defense Materiel Administration, Stockholm, Sweden]. The upper edge of the suit was placed at the level of the iliac crest and the lower edge at ankle level. The suits were fitted snugly on each subject.

The suits were inflated manually with air from a cylinder fixed in the center of the centrifuge. Inflation took ~1 min to complete, and the centrifuge was not started until the pressure was stable (target value ±2 mmHg on the manometer fixed to the suit). Two target pressures were used: 0 (control) and 85 mmHg (inflation). The subject could deflate the suit by opening a valve on the left side of the seat and did so when the test was completed. The total time with the suit inflated ranged from 2 min (1-G tests) to 4 min (2-G tests).

Instrumentation

The subjects sat in the gondola during all tests, with the right arm resting on a support approximately at heart level. Three ECG electrodes were placed on the subject’s chest for monitoring of heart rate (type AS2, Datex, Helsinki, Finland). Arterial beat-by-beat blood pressure was measured with a volume-clamp technique (Portapres, TNO, Amsterdam, The Netherlands).

The operator monitored the subject continuously via voice communication and a video camera. G was measured by an accelerometer mounted in front of the subject approximately at heart level.

Procedures

Subjects were instructed to avoid caffeine intake for 24 h before the experiment and to have a light meal 2 h before the tests.

The subject sat in the centrifuge and was restrained by a seat belt. A rebreathing bag was filled with 2.5–4 liters of a gas mixture containing 21% O2 and 5% He (an inert blood-insoluble gas). The bag volume corresponded initially to 50% of the subject’s estimated total lung capacity at normal gravity and was then adapted slightly according to the subject’s preference. The subject donned a nose clip and took a few normal breaths with the valve in the nonbreathing mode. After expiring to residual volume, the subject switched the valve to rebreathe the full bag volume back and forth five times starting from residual volume within ~5 s, ending with a full inspiration from the bag, and then held his/her breath for 10 s with glottis open if possible. The subject then expired to residual volume at an individually adapted flow rate that corresponded to the volume of the rebreathing bag exhaled in 10 s. Expiratory flow was controlled by the subject viewing a screen in real time.

The experimental procedure was rehearsed on two or more occasions before the first recording. The rebreathing-breath-holding-expiration sequence was performed at 1 and 2 G, with and without anti-G suit inflation (1-G control, 1 G + inflation, 2-G control, and 2 G + inflation). Tests were randomized with regard to the G level and inflation pressure (IP). During the 1-G tests, the centrifuge was stationary. During the 2-G tests, the maneuver started at the onset of 2 G. The average time to reach 2 G was 8.5 ± 1.3 (SD) s. When the maneuver was completed, which took ~30 s, the centrifuge returned slowly to 1 G. The mean time at 2 G was 50 s.

Subjects rested while sitting between tests. The tests were repeated until three usable maneuvers were obtained per combination of G level and IP. At least 9 min were allowed between tests to clear foreign gases from the lungs.

Data Analysis

Traces were studied with a proprietary interactive graphic analysis program developed with LabVIEW software (National Instruments, Austin, TX). Airflow oscillations were analyzed on the recordings when breath holding was performed with an open glottis (7 subjects). The software defined the oscillations as cardiogenic when they occurred between two R peaks of the simultaneous ECG recording, and nadir-to-peak amplitudes were determined to obtain the COS amplitude. A flow baseline was established as the mean value over that period and was approximately zero. The flow signal was integrated to compute the volume of air moved into or out of the thorax per cardiac cycle [pulsatile gas volume (PGV)].

Expirograms for O2 and He were plotted as a function of expired volume. Traces were then normalized, the mean concentration of O2 and He at the fifth inspiration of rebreathing being defined as 100%, to correct for the variability of lung volume-dependent inert gas dilution between subjects and to allow comparison of expirogram parameters obtained with O2 and He. To correct for incomplete gas mixing after rebreathing, traces of the normalized blood-soluble gas O2 were divided by the normalized nonsoluble gas He. Thus the normalized O2-to-normalized He ratio (O2/He) was computed sample by sample and plotted as an expirogram. Henceforth, the terms O2, He, and O2/He refer to normalized values. We focus on the O2/He data, although we also report the parameters from the O2 and He expirograms for completeness. In the three types of expirograms (normalized traces and ratios), the start and end of the alveolar plateau (phase III) were visually identified and marked using a cursor. The slope of phase III was identified on each plotted curve using linear regression and subtracted from the curve. COS(O2), COS(He), and COS(O2/He) were defined, and their amplitudes were computed in an analog manner as for COSampl. All COS amplitudes and PGV values measured in each file were used.

Finally, system gas volume (Vsyst) was computed from the equilibration of He between the rebreathing bag and the lungs. Median values were calculated for each subject and each G level and IP. We choose medians, instead of means, because of the large number of COS values obtained per test and condition (~10 values per test, thus ~30 per subject and condition); a median is more representative of the distribution of the values within a sample. Moreover, this enabled us to eliminate some random noise at the end of phase III, when there is no more COS; this random noise was computed as COS by the software, because it was part of phase III. For consistency, medians were computed also for the other parameters.
#### RESULTS

IP when the suit was inflated was 85 ± 4 mmHg at 1 G (equal to the target pressure) and 96 ± 5 mmHg at 2 G (target pressure +13%). This drift can be explained by the inability of the operator to manually control IP during the 2-G runs. However, we believe that this is unlikely to have influenced our results, because we showed in a previous study that the increase in SV caused by inflation of the anti-G suit is maximal at 85 mmHg and does not change further at higher IP (22).

Figure 1 shows a typical recording of COSflow during breath holding. COSflow amplitude did not change with gravity but increased when the anti-G suit was inflated (Table 1). Values were 86% higher at 1 G + inflation than at 1-G control. In contrast with COSflow amplitude, PGV (Table 1) showed overall differences with G level and with IP in the Greenhouse-Geisser and Huyn-Feldt analyses, but these differences were small, and the post hoc test showed no differences between any of the four combinations of G level and IP.

COS(O2/He) amplitude did not change with G level but decreased when the anti-G suit was inflated (Table 1, Fig. 2).

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### Table 1. COSflow amplitude and PGV measured during breath holding with an open glottis

<table>
<thead>
<tr>
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<th>1 G</th>
<th>2 G</th>
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<tr>
<td></td>
<td>Control</td>
<td>Inflation</td>
<td>G level IP</td>
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<tr>
<td>COS</td>
<td>105±56* (53, 156)</td>
<td>184±89† (102, 267)</td>
<td>89±45‡ (48, 131) 188±93 (103, 274)</td>
</tr>
<tr>
<td>O2, %</td>
<td>2.9±1.1‡ (2.4, 3.6)</td>
<td>1.6±0.3§ (1.3, 1.8)</td>
<td>3.3±1.3† (2.4, 4.1) 2.0±0.5 (1.6, 2.3)</td>
</tr>
<tr>
<td>He, %</td>
<td>2.5±0.3 (2.2, 2.7)</td>
<td>2.4±0.3 (2.2, 2.5)</td>
<td>2.3±0.3 (2.1, 2.5) 2.3±0.3 (2.1, 2.5)</td>
</tr>
<tr>
<td>O2/He, %</td>
<td>3.5±1.3* (2.7, 4.3)</td>
<td>2.5±0.5† (2.2, 2.8)</td>
<td>3.9±1.2† (3.2, 4.7) 2.7±0.5 (2.4, 3.0)</td>
</tr>
<tr>
<td>PGV, ml BTPS</td>
<td>24±13* (13, 36)</td>
<td>46±19† (28, 63)</td>
<td>22±12 (11, 33) 38±17 (22, 54)</td>
</tr>
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Values are means ± SD, with 95% confidence intervals in parentheses; n = 7. COS flow, cardiogenic oscillation (COS) of flow; PGV, pulsatile gas volume (i.e., volume of a moved into and out of the thorax during each cardiac cycle). A breath holding-expiration maneuver was performed, and COS for the normalized gases O2, He, and the O2-to-He ratio were measured on the expirograms (n = 12). The maneuver was performed at 1 and 2 G and at 0 (control) and 85 mmHg (inflation) of inflation pressure (IP). Significant P values (<0.05) are depicted in bold. Results of post hoc tests are as follows *Different from 1 G + inflation; †different from 2-G control; ‡different from 2 G + inflation.
Values at 1 G + inflation were 25% lower than at 1-G control. Moreover, COS\(_{O_2/He}\) amplitudes at 2 G + inflation were 18% lower than at 1-G control, a difference that approached significance (\(P = 0.053\)).

Table 1 presents the data for COS\(_{O_2}\) amplitude and COS\(_{He}\) amplitude.

\(V_{sys}\) did not change with G level but decreased when the anti-G suit was inflated (\(P = 0.023\)), and there was an interaction between G level and IP (\(P = 0.028\)). Mean values were 4.84 ± 0.88 liters at 1-G control, 4.84 ± 0.94 liters at 1 G + inflation, 4.90 ± 0.83 liters at 2-G control, and 4.79 ± 0.85 liters at 2 G + inflation.

**DISCUSSION**

Our main finding is the dissociated response of COS\(_{flow}\) and COS\(_{O_2/He}\) to inflation of the anti-G suit at 1 and 2 G. Although cardiac pumping nearly doubled COS\(_{flow}\) when the anti-G suit was inflated, suggesting a marked increase of the heart-synchronous mechanical agitation of the lungs, COS\(_{O_2/He}\) decreased by 25–30%. We discuss these findings in the context of the possible mechanisms underlying the responses of COS\(_{flow}\) and COS\(_{O_2/He}\).

**Cardiogenic Flow Oscillations**

We observed a mean COS\(_{flow}\) amplitude of 105 ml/s at 1-G control, which agrees with the value of 120 ml/s previously measured in seated humans (9) and with similar values obtained in supine subjects (7). Similar to previous studies in humans and animals (9, 33), we found large interindividual variability in COS\(_{flow}\) and PGV.

**Cardiovascular factors in COS\(_{flow}\) generation.** During the cardiac cycle, the heart exerts a mechanical action on the emptying and filling of the lung alveoli (7, 10, 20). During breath holding with an open glottis, one can observe an outward movement of gas with each cardiac diastole and an inward movement of gas with each systole (10), which starts ~100 ms after the R wave on the ECG (7, 9). Our recordings clearly showed an inflow during systole and an outflow during diastole (Fig. 1).

Two experiments in dogs have suggested that PGV is correlated with SV (15) and that PGV is equivalent to about one-third of SV (33). The present finding of a mean PGV of 24 ml at 1-G control is compatible with these studies, inasmuch as the SV of a seated human adult is ~60−70 ml (8). However, the only other studies performed in humans found much lower PGV values, ~7 ml (7, 9). An explanation for this discrepancy is that these subjects were not specifically instructed to keep their glottis open, as ours were; therefore, these subjects probably had a larger upper airway resistance than those of the present study (for discussion of the influence of airflow resistance on COS\(_{flow}\), see Pulmonary factors in COS\(_{flow}\) generation).

Rather than being a direct function of SV, COS\(_{flow}\) is more likely to be initiated by cyclic changes in the overall intrathoracic blood volume (7, 10, 15), which are in turn related to SV: During systole, there is a temporary systolic negative blood balance in the thorax. The volume of blood ejected from the left ventricle (i.e., SV) is only partly simultaneously compensated for by the effects of right ventricular systolic suction on thoracic inflow, and the remainder enters the thorax during diastole (8). This causes a transient volume reduction in the thoracic cavity, which in turn results in an inflow of air if the airways are open (7). The extent to which the intrathoracic parts of the large systemic vessels, the lung vessels, or the heart contribute to overall heart-synchronous blood volume changes is not known, and we will refer to such changes as intrathoracic blood volume pulsations.

**Pulmonary factors in COS\(_{flow}\) generation.** The effect of thoracic blood volume movements on the parenchyma could be damped by stiffness of the lung tissue. This hypothesis is consistent with the results of Lichtwarck-Aschoff et al. (18), who observed that PGV decreases when lung compliance decreases in ventilated pigs. These authors also observed a decrease in compliance of the chest wall in a representative experimental animal (M. Lichtwarck-Aschoff, personal communication). Decreased compliance of the chest wall should augment COS\(_{flow}\) amplitude for the following reasons: The blood leaving the thorax during systole tends to decrease intrathoracic pressure, and if the chest and diaphragm are flaccid enough, they will move inward, thereby reducing the need for air influx into the chest. Heckman and co-workers (15) reported lower COS\(_{flow}\) amplitudes when the chest was open, an extreme case of low chest wall compliance. Opening the chest exposes the heart and the lungs to ambient air, radically diminishing the mechanical influence of cyclic thoracic blood volume changes on the pulmonary parenchyma. Thus, in the experiment performed by Lichtwarck-Aschoff et al., it appears that the potentially augmenting effects of decreased chest wall compliance on COS\(_{flow}\) were masked by the damping effects of decreased lung compliance.

Differences in compliance between lung regions are probably also important; in their bronchoscopic experiments in supine humans, West and Hugh-Jones (34) observed that pulsatile flow variations were not present in each bronchus studied. However, this could also reflect differences in airway resistance between lung regions.

Colebatch et al. (9) found that COS\(_{flow}\) amplitude decreases as airway resistance increases. In the closed upper airway, heart-synchronous compression rarefaction of the intrathoracic gas must be a major factor; accordingly, using a body plethysmograph, Bosman and Lee (7) found heart-synchronous volume variations with a closed airway in the external chest.

It is unclear from which alveolar populations COS\(_{flow}\) originate, and our data do not give any topographical information. West and Hugh-Jones (34) studied this issue by using an argon-dilution technique to estimate variations in pulsatile gas flow in the bronchi of supine sedated patients. They found that “appreciable cardiac pulsations occur in all five lobar bronchi and, as might be expected, the largest pulsations are found in the left lung. However, the consistency with which large pulsations can be detected in the right middle-lobe bronchi is interesting.” Our interpretation of these observations is that proximity to the heart is one, but not the only, factor that determines the extent of heart-synchronous airway flow oscillations.

**Effects of anti-G suit inflation on COS\(_{flow}\).** When the anti-G suit was inflated, COS\(_{flow}\) amplitudes were 186% and PGV values were 255% of their 1-G control values; these responses were similar at the two gravity levels (Table 1, Fig. 2). When an anti-G suit is inflated, increases in central blood volume (32) may become large enough for systolic suction into the right heart to be accounted for to a larger extent by blood already in
the thoracic cavity, which would attenuate the impact of systolic suction on the rate of influx of blood to the thorax. Acting in a similar direction, the venous blood volumes in the legs and abdomen decrease, dramatically reducing the blood volume accessible for systolic suction into the thorax. This would in turn increase the systolic negative blood balance in the thorax and, together with a 10–30% increase in SV (22), would increase CO$_{\text{flow}}$ amplitude and PGV. Such changes are consistent with previous data showing that CO$_{\text{flow}}$ amplitude increases in subjects moving from the seated to the supine posture, which increases SV and central blood volume (9).

Anti-G suits also affect the lungs: lung compliance decreases (6), probably because of the increased blood content in the lungs, which tends to decrease CO$_{\text{flow}}$ amplitude and PGV (18). We found no reports on the effect of anti-G suit inflation on chest wall compliance, but it seems logical that the chest wall would become stiffer because of the upward movement of the diaphragm (13). Consequently, CO$_{\text{flow}}$ amplitude and PGV should increase (7). The net outcome of these opposing actions of the lower lung compliance and the lower chest wall compliance on CO$_{\text{flow}}$ during anti-G suit inflation is uncertain.

**Effects of increased gravity on CO$_{\text{flow}}$.** SV and central blood volume are lower at 2 G than at 1 G (4, 19). At 2 G, the compliance of the respiratory system is lower, the diaphragm moves downward (5, 12, 13), and the lung is distorted, leading to an increase in pleural pressure gradients. However, in the present study, CO$_{\text{flow}}$ amplitude and PGV did not differ between 1-G control and 2-G control or between 1 G + inflation and 2 G + inflation. Thus any effect of an increase to 2 G on the generation of CO$_{\text{flow}}$, if it exists, is small, probably because the pulmonary effects of increased gravity compensate each other: decreased lung compliance decreases CO$_{\text{flow}}$ amplitude, whereas decreased chest wall compliance increases CO$_{\text{flow}}$ amplitude.

SV is similar at 1-G control and 2 G + inflation (22). In contrast, CO$_{\text{flow}}$ values were almost twice as large during 2 G + inflation as during 1-G control. This observation suggests that effects of anti-G suit inflation other than SV per se have a much greater impact on the outcome of CO$_{\text{flow}}$.

**Cardiogenic oscillations of O$_2$/He**

We present the mechanisms generating CO$_{\text{[O$_2$/He]}}$ only briefly here, because these have been discussed extensively elsewhere (10, 23). Laviolette and Cormier (17) showed that CO$_{\text{[O$_2$/He]}}$ represents intraregional (i.e., small-scale) differences in gas content. Whether these differences are caused by ventilation or perfusion differences depends on the maneuver performed before the slow expiration, which enables one to record COS: Laviolette and Cormier (17) focused on ventilation distribution. In the present experiment, we wanted to study perfusion distribution. Thus we used the blood-soluble gas O$_2$, which was first distributed in the lungs as homogeneously as possible. In addition, we computed O$_2$/He to correct for any incomplete homogenization. During the subsequent breath holding, O$_2$ was taken up by the blood at a rate proportional to local perfusion. Thus changes in the concentrations of O$_2$ observed subsequently, during the final expiration, represented perfusion differences that were primarily of intraregional origin.

Cardiovascular and pulmonary factors in CO$_{\text{[O$_2$/He]}}$ generation.** Studies in dogs have suggested that cardiac wall movements during the cardiac cycle act on the surrounding parenchyma (31), creating CO$_{\text{[O$_2$/He]}}$ (11, 15). It is likely that only a small part of CO$_{\text{[O$_2$/He]}}$ is generated by the direct mechanical action of the heart on lung units, because the changes in heart volume and cardiac rotation movements during the cardiac cycle are small (16, 31). The main mechanism probably relates to the sequential emptying of lung units during expiration as a result of differences in the time constants between lung units in their response to pressure waves generated by the heart (1) or the different locations of these lung units in relation to a pulsating vessel (3, 10).

The experiments of Wei et al. (31) in dogs suggested that the amplitude of CO$_{\text{[O$_2$/He]}}$ is related to SV, although these authors did not demonstrate significant correlations between these variables. SV probably influences the generation of CO$_{\text{[O$_2$/He]}}$ in two entirely opposite ways: 1) SV induces intrathoracic blood volume pulsations, which mechanically influence the emptying of compliant lung units. Thus, if all other factors remain constant, an increase in SV tends to increase CO$_{\text{[O$_2$/He]}}$. 2) An increase in SV and, thereby, pulmonary blood flow increases capillary recruitment, which decreases the differences in pulmonary perfusion and lowers the amplitude of CO$_{\text{[O$_2$/He]}}$ of the blood-soluble gas studied.

**Effects of anti-G suit inflation and gravity on CO$_{\text{[O$_2$/He]}}$.** As for CO$_{\text{flow}}$, the effects of anti-G suit inflation and gravity on CO$_{\text{[O$_2$/He]}}$ were similar at the two gravity levels (Table 1, Fig. 2). Because CO$_{\text{[O$_2$/He]}}$ represents a product of concomitant sequential emptying of lung units and gas composition differences between such units, there was a striking dissociation between the responses of CO$_{\text{[O$_2$/He]}}$ and those of CO$_{\text{flow}}$. Anti-G suit inflation resulted in a ~30% reduction in CO$_{\text{[O$_2$/He]}}$ amplitudes at both gravity levels, whereas CO$_{\text{flow}}$ amplitudes nearly doubled. In contrast, inflation to 85 mmHg increased SV only by ~10% at 1 G and by 30% at 2 G (22). Taken together, these findings show that the dominating factor behind CO$_{\text{[O$_2$/He]}}$ amplitudes must be differences in gas composition between asynchrnonously emptying lung units, rather than the mechanical agitation of the lung tissue. It is of special interest to compare the data between 2-G control and 2 G + inflation: our previous study (22) showed that SV increased with inflation, but not with cardiac output, because of a concomitant bradycardia. Thus the tendency toward a reduction in CO$_{\text{[O$_2$/He]}}$ in the present study (P = 0.053) cannot be explained by increased pulmonary blood flow. Instead, this trend might be explained by the generally elevated vascular pressures in the lung circulation (29, 30), which should improve capillary recruitment and cause less perfusion heterogeneity in the lungs, as reflected in the decreased CO$_{\text{[O$_2$/He]}}$ amplitudes. Moreover, the decrease in lung compliance (6) and upward movement of the diaphragm (13) should reduce the number of compliant alveoli and, thus, further contribute to the decrease in CO$_{\text{[O$_2$/He]}}$ amplitude.

We found no difference in CO$_{\text{[O$_2$/He]}}$ between the 1- and 2-G conditions. This result agrees with the data reported by Rohdin et al. after 1 min of exposure to 2 G (27) and with previous experiments performed during parabolic flight (23). Thus any net cardiopulmonary effects of 2 G on CO$_{\text{[O$_2$/He]}}$ must be small.
A likely explanation is that hypergravity has opposing influences on the generation of COS$_{O_2/He}$. On one hand, it reduces SV (19, 25, 28), which tends to reduce the mechanical impact of cardiac activity on the lungs. On the other hand, hypergravity tends to increase the differences in O$_2$/He between sequentially emptying lung units by causing larger perfusion differences between these units.

**Potential effect of lung volume changes.** In the present experiment, $V_{sys}$ changed with IP. However, the variations in $V_{sys}$ measured when the anti-G suit was inflated compared with no inflation were +4 ml at 1 G and −115 ml at 2 G. Although statistically significant, such small changes are likely not biologically significant. Thus the present changes in $V_{sys}$, between conditions are unlikely to have influenced our results.

**Conclusions**

SV is, by definition, the prime mover of the generation of any heart-synchronous event but does not appear to be the main factor influencing COS$_{flow}$ and COS$_{O_2/He}$. Instead, we found that COS$_{flow}$ depends primarily on intrathoracic blood volume, whereas COS$_{O_2/He}$ reflects differences in intraregional pulmonary perfusion.

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