EFFECTS OF BODY POSITION ON THE VENTILATORY RESPONSE FOLLOWING AN

IMPULSE EXERCISE IN HUMANS

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ABSTRACT

The aim of this study was to identify some of the mechanisms which could be involved in the blunted ventilatory response (VE) to exercise in the supine (S) position. The contribution of 1- the recruitment of different muscle groups  2- the activity of the cardiac mechanoreceptors , 3- the level of arterial baroreceptor stimulation and 4- the hemodynamic effects of gravity on the exercising muscles, was analyzed during upright (U) and S exercise. The delayed rise in VE and pulmonary gas exchange following an impulse like change in work rate (supra-maximal leg cycling at 240 W for 12 seconds) was measured in seven healthy subjects and six heart transplant patients both in the U and S positions. This approach allows the study of the relationship between the rise in VE and oxygen uptake without the confounding effects of the contractions of different muscle groups. These responses were compared to those triggered by an impulse like change in work rate produced by the arms which were positioned at the same level of the heart in the S position and in the U position to separate the effects of gravity on the post exercising muscles from those on the rest of the body. Despite superimposable VO2 and VCO2 responses, the delayed VE response following the leg exercise was significantly lower in the S posture than in the U position for each control subject and cardiac transplant patient (- 2.58 ± 0.44 l/min and - 3.52 ± 1.11 l/min respectively). In contrast, when the impulse exercise was performed with the arms, the reduction of the ventilatory response in the S posture reached at best one third of the deficit following the leg exercise and was always associated with a reduction in VO2 of similar magnitude. It is concluded that the reduction in the VE response to exercise in the S position is independent of the types (groups) of muscles recruited and is not critically dependent on afferent signal originating from the heart, but seems to rely on some of the effects of gravity on the post-exercising muscles.
It has already been recognized that the ventilatory response to a constant work rate exercise is affected by the position of the body in humans. For instance, Weiler Ravel et al. (38) have shown that the VE phase I and phase II responses to a constant work rate exercise are reduced in the supine (S) position compared to an upright (U) exercise of similar intensity. Based on the observation that the cardiovascular (cardiac output) changes are also blunted in the supine position exercise (3, 27, 36), it was proposed (38) that a circulatory mechanism related to the magnitude of the cardiovascular response to exercise could account for the reduced exercise hyperpnea in the S position (or exaggerated response in the U position). It remains unclear however through which receptors such a mechanism of circulatory origin can affect the control of breathing in exercise.

This study was therefore intended to determine the possible mechanisms which alter the ventilatory response to exercise according to body position. More specifically two questions were addressed. Since different groups (types) of muscles are recruited in the U position and in the S position it was firstly necessary to determine whether the reduced VE response in the supine position does not simply reflect a different muscular efficiency – and thus muscle afferent recruitment or central command involvement- (see 8 or 11 for discussion and review) as a slower and lower VO₂ response in the S position (38) suggests. This was achieved by analyzing the relationship between the delayed rise in VE, VO₂ and VCO₂ triggered by an “impulse” change in work rate both in the S and U positions. The rational for using such an approach was the following : if a short burst (10-15 seconds) of a supra-maximal exercise is imposed on a subject, the rise in VO₂, VCO₂ and VE triggered by this "impulse forcing" occurs well after cessation of the contractions (12, 13, 40). Based on the principle of linearity, an "impulse forcing", which can be regarded as the first derivative of a constant work rate (WR) exercise, is expected to trigger a
delayed ventilatory and metabolic responses which follow the temporal profile of the first derivative of the response to a step exercise (12). Indeed, the traditional $\text{VE}$ phases I and II (6) are replaced by a sudden and transient increase in $\text{VE}$ for a few breaths followed by a clearly delayed rise in pulmonary gas exchange and $\text{VE}$ which subside exponentially (12, 13, 14, 40). The second phase of the $\text{VE}$ response therefore occurs at a time (more than 20 seconds into recovery) when neither the cortical and sub cortical drive to the spinal motoneurons nor muscular contraction-related information of a mechanical nature is operating (see 11 for discussion). Yet the $\text{VE}$ response is that expected of a step exercise, and follows the change in pulmonary gas exchange (39). Figure 1 gives an example of the responses of one subject. In other words, an impulse like change in work rate offers the opportunity to study the ventilatory response to exercise while the body is in the peculiar situation of being at rest but behaving as if exercising from a metabolic and circulatory point of view. If changing the body position affects the ventilatory control system during exercise independently of the type of muscle recruited, the delayed rise in $\text{VE}$ which follows that in $\text{VO}_2$ and $\text{VCO}_2$ after the cessation of the muscular contractions is still expected to be reduced in the S position at any given level of pulmonary gas exchange when compared to an upright exercise.

Our second objective was to determine if receptors located in the circulatory system could, due to certain effects of gravity, depress the $\text{VE}$ response to exercise in the supine position as suggested by Weiler-Ravell et al. (38). The hydrostatic effects of gravity can affect many compartments of the circulatory system which might in turn modify the ventilatory response to exercise. For instance, the blunted rise in cardiac output at the onset of exercise in the S position has been suggested to account for the accompanying relative hypopnea (38). A higher pressure at the level of the arterial baroreceptors in the S than in the U position may also reduce the $\text{VE}$
response (4, 18, 32). On the other hand, the mechanical load applied by the venous return from the exercising limbs in the U position, together with a higher perfusion pressure, might represent an additional stimulus to breath when compared to the S position, through the stimulation of muscle slow conducting afferent fibers (15, 18, 24). To clarify the putative role of 1- the cardiac mechanoreceptors , 2- the arterial baroreceptors and –3 the muscle circulation, the delayed ventilatory responses to an impulse change in work rate in the S and U position were also studied in heart transplant patients and in a condition where the effects of gravity on the post-exercising muscles could be dissociated from those on the rest of the body by using a group of muscles positioned at the same distance of the heart in both positions.

METHODS

Subjects. Seven healthy male subjects and six patients with heart transplants were studied. They were informed about the general purpose of the study and an informed consent was obtained after the agreement of our local ethical committee. The age, height and weight were 36 years old (30-48), 1.75 m (1.65-1.90) and 72 kg (69-92) respectively (median and range) for the control subjects and 45 years old (27-51), 1.74 m(1.70 –1.85) and 71 kg (62-86) for the heart transplant patients. The patients were studied 30 ±16 months (2 –108 months) after the transplantation when in a stable condition and none of them had symptoms of cardiac or respiratory insufficiency. One patient had had a heart and lung transplantation.

Equipment. The subjects exercised on a table-mounted electromagnetically braked ergometer and breathed room air through a low dead space face mask (small or medium size Hans Rudolph mask, Hans Rudolph inc., Kansas city, USA) connected to a pneumotachograph (MediGraphics Prevent pneumotachograph, Medical Graphics Corporation, St. Paul, Minnesota,
USA). The ergometer could be tilted from the vertical to horizontal position and was modified to allow the subjects to pedal with their arms which could be positioned at any desired level from the heart in either posture. The inspiratory and expiratory flows were measured and the respiratory gas was continuously sampled from the pneumotachograph. The $O_2$ and $CO_2$ concentrations were determined by rapidly responding $O_2$ and $CO_2$ analyzers (Datex Analyzers, Medical Graphics System, Medical Graphics Corporation, St. Paul, Minnesota, USA). Respiratory flow, $P_{O_2}$ and $P_{CO_2}$ were digitized at 100 Hz for breath-by-breath calculation of $VE$ and pulmonary gas exchange. All the data were processed on line and stored on disk for further analysis. The systemic arterial blood pressure was estimated non invasively from the measurement of the finger arterial pressure (Finapres System, Ohmeda, Louisville USA). A Finapres cuff was placed around the index and connected to a Finapres Monitor (Ohmeda 2300, Ohmeda, Louisville, USA). This approach allows uninterrupted recording of the BP signal, which, at least for the mean blood pressure, is a very reliable estimate of intra-arterial BP (see 19 for review). The finger with the cuff was positioned at a level corresponding to that of the carotid bifurcation (upper part of the neck). The electrocardiogram was monitored from a three-lead configuration. The output signals from the Finapres were fed to an analogue to digital converter (Mac Lab System) and displayed on line on a microcomputer screen. The frequency of numerization was set at 200 Hz.

Protocol.

1 - Control measurements

The impulse load consisted of a 240 W exercise for the legs and a 175 W exercise for the arms applied for 12 seconds. This level of work rate was selected so that each subjects could pedal in both positions without too much unnecessary movement of the trunk.
Following a visual signal, the subjects were asked to pedal at a frequency between 85-95 RPM. At this frequency, the torque applied to the pedals was reduced and the test could be performed by each subject with no difficulties. The subjects were familiar with this protocol, since they had all carried out the various tests of the protocol on at least three occasions in the days preceding the experimentation. Sixteen tests were performed by each subject in a random order:

A - On eight occasions, the subjects exercised with their legs. The exercise was performed either in the supine position (4 tests) or in the upright position (4 tests).

B – The responses to the impulse change in WR performed with the legs were compared to the responses triggered by an exercise performed with the arms which were placed in the same position and at a similar level from the heart in both the S and the U positions (the pedal axis was placed at about 40-45 cm from the heart level in both positions, depending on the height of the subject). Following the period of contractions, the arms of the subjects could rest passively at the same level as during the contractions. During and following the arm exercise, the arterial baroreceptors were exposed to the effect of gravity as they were during the leg exercise but the degree of distension of the venous and venular system and the perfusion pressure in the post exercising muscles were no longer dependent on the direct effects of gravity. Also worthy of note is that this approach can dissociate the possible contribution of receptors located in the post-exercise limbs from that of all the receptors of the rest of the body (see discussion). On eight occasions, each subject performed an exercise with the arms either in the S or in the U position.

2- Heart transplant patients
The patients performed the initial part of the protocol, i.e. the leg exercise both in the supine and in the upright position.

Data analysis

All the data were processed on line and stored on disk for further analysis. The breath-by-breath data were transformed into second-by-second files that could be temporally aligned then averaged for each condition. Mean blood pressure was computed from the raw data (Mac Lab), converted in a second-by-second file and temporally aligned to the ventilatory data.

The second phase of the VE, VO₂, and VCO₂ responses was compared between the S and the U position and between the arm and leg exercise by comparing the peak response of VE, VO₂, VCO₂, PETCO₂, VE/VO₂, HR and BP (computed over 15 seconds, paired t test). The VE versus VO₂ relationship was established by regression analysis for the 90 second-period following the peak of the delayed response.

RESULTS

1- Control tests with the leg exercise.

Figure 2 illustrates the averaged temporal profile of the VE, VO₂ and BP responses to the twelve-second bout of leg exercise for all subjects in the upright and in the supine position.

Exercise in the upright position.

The responses consisted in two different phases for both the ventilatory and gas exchange responses: an initial increase in VE occurred as soon as the contractions started. Minute ventilation increased from the resting values of 9.47 ± 0.391/min to 21.6 ± 3.1 l/min. This initial
rise in VE was associated with an increase in VO$_2$ and VCO$_2$, both of which subsided and reached their nadir within 15-25 seconds following the end of the contraction. Minute ventilation started to increase again 17-27 seconds into recovery and reached its maximum (17.59 ± 1.08 l/min) thirty seconds later. The second rise in VE followed that in VO$_2$ (752 ± 55 ml/min), VCO$_2$ (602 ± 42 ml/min) and PETCO2 (46 ± 0.9 Torr). The mean blood pressure changes had a very similar pattern of response: after an initial increase in BP (from 95 ± 10 mmHg to 108 ± 6 mmHg), mean BP decreased then increased again to 106 ± 4 mmHg (Figure 2). Finally, HR increased abruptly during the contracting phase then subsided toward resting values (Figure 3).

**Exercise in the supine position.**

Resting ventilation was lower in the S position than in the U position (8.73 ± 0.22 l/min), but without reaching significance. The impulse exercise triggered a delayed increase in VO$_2$ and VCO$_2$ which was similar to that in the U position (Figure 2), but the peak of the second component of the ventilatory response was significantly lower in every subject by an average of 2.58 ± 0.44 l/min (Δ = -17.2 ± 9 %, p<0.001). The level of PETCO$_2$ associated with the second rise in ventilation was significantly higher in the S position than in the U position (48.3 ± 0.8 Torr, P<0.01, Figure 2). Since the VO$_2$ peak response was similar in both positions, the VE/VO$_2$ ratio was significantly lower in the S position than in the U position (20.3 ± 0.7 versus 23.6 ± 1.0, P< 0.001). Finally, the mean BP (at the neck level) was significantly higher in the S than in the U position at rest (by 7 ± 3 Torr) and remained higher during and following the impulse exercise by about 7 Torr (Figure 2), while HR was significantly reduced in the S position by 13-15 b/min (p<0.001, Figure 3) both at rest and during the impulse exercise.
2- Cardiac transplant patients.

The second phase of the $\dot{V}E$ response was significantly higher in the U position than in the S position ($22.52 \pm 1.21$ vs. $18.83 \pm 0.421$ l/min, $p<0.01$) with a rise in $\dot{V}O_2$ of similar magnitude (Figure 4). In addition, although a relative hyperventilation was consistently observed in the patients, the effects of body position were, if anything, larger than in the control group, despite lower $PETCO_2$ in the transplant patients (Figure 2 and 4). The reduced ventilatory response in the supine position was however always associated with a significantly higher $PETCO_2$ ($39 \pm 2$ vs. $36 \pm 2$ Torr). It is worth noting that the blunted ventilatory response in the S position was observed in the patient who had had a heart-lung transplantation as illustrated in Figure 5.

Except for the mean BP levels which were higher and more variable than in the control group, the BP responses were similar to those observed in the control subjects. The pressure at carotid level was higher by about $4.8 \pm 3$ Torr in the S posture than in the U posture. At rest, all the subjects displayed a tachycardia, with a slight difference between the S and U position ($97 \pm 4$ vs. $102 \pm 5$ b/min). The HR response to exercise was virtually abolished in both positions (Figure 3).

3-Arm exercise.

The effects of body position on the response to the arm exercise was both qualitatively and quantitatively different than during the leg exercise (Figure 5). First, the oxygen uptake response to the arm exercise was significantly higher in the U than in the S position ($650 \pm 32$ Vs. $700 \pm 31$ ml/min, $p<0.01$, $-7.6 \pm 1.6\%$). On averaged, ventilation was higher in the U position ($17.79 \pm 0.84$ l/min vs. $16.90 \pm 0.94$ l/min, $p<0.05$) but in the same proportion as $\dot{V}O_2$ ($-5.9 \pm 2.2\%$). This ventilatory reduction represented less than one third of the difference observed
following the leg exercise (Figure 7). Subject-by-subject analysis revealed that in contrast to the leg exercise, three subjects had a virtually identical level of ventilation with the arm exercise whether in the S or the U position. Since \( \text{VE} \) was depressed when \( \text{VO}_2 \) was low in the S position, \( \text{VE}/\text{VO}_2 \) ratio was similar in both positions (25.6 ± 0.7 vs. 25.9 ± 0.6, NS). Finally, during the 90 s following the peak response of the second phase, the slope and the intercept of the \( \text{VE} \) vs. \( \text{VO}_2 \) regression were similar in either position (Figure 8). In contrast, following the leg exercise, the slopes of the \( \text{VE} \) vs. \( \text{VO}_2 \) regression lines were significantly lower in the S than in the U posture (10.4 ± 1.3 vs. 16.1 ± 2.5, p<0.01), but with no difference in the intercepts (Figure 8).

The difference in the \( \text{PETCO}_2 \) peak response between S and U position (-1.3 ± 1 Torr) did not reach significance (Figure 6). Finally, the mean BP could not be accurately measured during and following the arm exercise, but the mean BP prior to the boot of exercise was 6.9 ± 4 Torr higher in the S position.

**DISCUSSION**

We used an impulse-like change in work rate to study the control of breathing in a situation where the rise in pulmonary gas exchange and ventilation can be dissociated from the muscle contractions. As in previous reports (12, 13, 14, 40), we found that 20 seconds after the end of the exercise bout, a second rise in \( \text{VE} \) occurs, which closely follows the increase in \( \text{VO}_2 \) and \( \text{VCO}_2 \) by a few seconds. This second phase of the ventilatory response has already been shown to have the characteristics expected from the response to a constant work rate exercise, despite no contractions being performed (39, 40 for discussion).
The major finding of the present study was that the delayed VE response to an impulse change in WR was significantly reduced in the supine position, despite a similar magnitude of pulmonary gas exchange. Furthermore, this effect was still observable in patients who lack afferent information from the heart, but was virtually abolished when the impulse exercise was performed with the arms positioned at a similar level from the heart in both the S and U positions. Indeed, the difference between the two postures in response to the arm exercise was 1-dramatically less than following the leg exercise and 2- proportional to the change in pulmonary gas exchange (Figures 7), leading, unlike after the leg exercise, to a similar VE/VO₂ ratio in both positions.

The effect of posture on the level of ventilation has already been investigated both at rest (1) and during a constant work rate exercise (38). Alveolar ventilation has been found to be lower at rest in the S position than in the U position (1), but with no clear explanation for this finding. During exercise (38), the ventilatory phase I and II have also been reported to be reduced and slowed. In addition, Weiler-Ravell et al. (38) found that the O₂ uptake response was always blunted. Whereas a reduced VO₂ phase I reflected the limited increase in cardiac output at the onset of a constant WR exercise in the S posture (3, 27, 36), the lower steady state VO₂ reported in that study (38) makes it difficult to interpret the resulting ventilatory outcome, since a low VO₂ may simply have reflected a better mechanical muscular efficiency – and therefore a reduced ventilatory stimulation from central or muscular origin (8 for discussion) - in the S position. The recruitment of different groups (types) of muscles during the contractions (muscles from the back for instance) could thus account for part of the difference in ventilation reported by Weiler-Ravell et al. (38). Nevertheless, the present finding that an intense leg exercise of short
duration in the S position triggers a lower VE response than in the U position, despite similar O₂ uptake, still supports the conclusion of that study: the VE response to exercise is reduced in the S position, independently of (or in addition to) the effects of recruitment of different types of muscles. The position therefore affects the control of breathing in exercise by altering the coupling between ventilation and pulmonary gas exchange, a fundamental tenet of blood gas homeostasis. It becomes relevant for our understanding of the regulation of exercise hyperpnea to determine the nature of the afferent signal that is depressed in the S position.

Contribution of the chemical control of respiration

The ventilatory response to CO₂ sensitivity has consistently been shown to be similar in the supine and the sitting position (1, 28, 29), whereas the response to hypoxia has been reported to be either diminished or unchanged in the S position. The levels of hypoxia at which such a difference is observable (28) have no equivalent with the changes in PaO₂ that may occur following the impulse exercise. One should therefore not expect that the larger VE response to exercise in the U position can be accounted for by a change in the chemical regulation of breathing, at least through a change in CO₂ sensitivity. This is of importance since the delayed rise in ventilation occurs after a rise PETCO₂ by several Torr, as has already been reported (12, 14). Such a rise in PETCO₂ (Figure 1 and 2) could be accounted for by at least two mechanisms: 1- the phase lag between the rise in VCO₂ and in ventilation could transiently have disrupted the alveolar gas composition and thus arterial blood gas homeostasis, and 2- perhaps more importantly, the abrupt increase in CO₂ output to the lungs following the impulse should increase the slope of the expired PCO₂ “plateau” and thus PETCO₂ out of proportion of the changes in
mean PACO$_2$. The exact magnitude of the change in arterial PCO$_2$, and its contribution to the ensuing hyperpnea, is therefore hard to predict, but even if the level of PETCO$_2$ may differ from that of PACO$_2$, the VE-PETCO$_2$ relationship obtained in the control subjects in both positions clearly shows that PETCO$_2$ is dictated by the level of ventilation rather than the opposite, i.e. PETCO$_2$ being lower in the U position when minute ventilation was higher.

**Role of cardiac receptors.**

Although distension of the right heart or the pulmonary arteries can experimentally stimulate ventilation (21, 23), their role in adjusting the level of ventilation to the rate of incoming blood has never been confirmed (2, 17). The hypothesis that the blunted increase in cardiac output may contribute to the blunted increase in ventilation in the S posture (38) could offer a rather unifying explanation for the present observations. However, the blunted increase in the delayed VE response in the S posture in the cardiac transplant patients, does show that information originating from the right or the left heart are not a prerequisite for a reduced VE response in the S posture to occur. Indeed, although a limited functional sympathetic reinnervation has been demonstrated in humans several years after a cardiac transplantation (5), no clear anatomical evidence has been forthcoming to suggest that this was associated with a reconnection of the cardiac afferent system which follows both the sympathetic and parasympathetic pathways. The almost totally abolished heart rate response to the short burst of heavy exercise in our patients, even in those who were studied several years after the transplantation, also support the contention that these patients do lack significant afferent innervation from the heart.
Other effects of gravity of respiratory control

The lack of specific reduction in the VE response when the exercise was performed in the S position with a group of muscles positioned in such a way that the hydrostatic effect of gravity on their circulation was minimized may help us to distinguish between several other putative mechanisms.

First, the arterial baroreceptors, should have been affected by the body position during the arm exercise as in the case of the leg exercise, being exposed to a higher pressure in the S position than in the U position. The arterial baroreflex has a ventilatory component (4, 6, 32), which consists of a depression in VE when the carotid pressure is high. The gain of the relationship between carotid pressure and ventilation has been established in vagotomized dogs and was found to be about 0.5-1 ml/min/kg/mmHg (see also 16, 18 for discussion), but the magnitude of the ventilatory component of the arterial baroreflex is unknown in human beings. We found that BP was 7 Torr higher at carotid level prior to the arm exercise in the S position than in the U position, just as for the leg exercise. Such a difference in baroreceptor stimulation during the arm exercise was associated with HR responses which were to be expected from the involvement of the arterial baroreflex, i.e. higher HR level in the U position, but with little or no effect on ventilation. This suggests therefore that the ventilatory component of the arterial baroreflex can not account for the difference between the S position and the U position during the leg exercise.

Similarly, the lack of specific effect of the body position following the arm exercise suggests that afferent information originating “outside” the exercising muscles, including the lungs and the respiratory muscles can not fully explain the present observation. Incidentally, the fact that changing body position during the arm exercise has little effect on the level of
ventilation, even though this may have affected the mechanics of breathing – change in chest wall compliance or respiratory muscle recruitment (9) – is not unexpected. Indeed, application of an external elastic load or mechanical “unloading” of the respiratory system during a constant work rate exercise, results in an appropriate compensatory increase (or decrease) in respiratory drive, meaning that that total ventilation remains unchanged (see 39 for review). It is worth noting that the patient with a lung and heart transplant who we were able to study also had a lower VE response in the S position than in the U position, suggesting that the lungs which must accommodate a large blood volume in the S position do not participate in this response either.

Finally, the difference in the ventilatory behavior between the leg and the arm exercise according to position also implies that any change in the cerebral or brainstem perfusion induced by the change in posture can not explain the difference between the S position and the U position.

Since structures outside the post exercising muscles seem to contribute little to the reduced ventilatory response to exercise in the S posture during the arm exercise, the possibility that the effect of gravity on the post-exercising muscles themselves could be responsible for part of this effect should be examined. Obviously, the metabolic -or chemical- impact of a lower perfusion pressure in the supine position, with the leg above the heart level, was not strong enough to cause the so-called muscle “chemoreflex” through stimulation of small myelinated or unmyelinated muscle afferent fibers (10, 22, 26, 30, 33). This confirms previous reports on the lack of ventilatory stimulation during vascular occlusion following a dynamic exercise in humans (7, 16, 18, 20, 31). However, the lack of contraction does not necessarily imply that muscle afferent fibers in the post exercising limbs are not involved. A higher perfusion pressure together with greater distension of the venous or venular end of the muscular circulation in the U position than in the S position could have affected the afferent traffic from the hyperemic post-exercising...
muscles. Group IV muscle afferent fibers are located in the adventitia of the vascular structures of the muscle (mostly the venules) (34, 37) and can respond to the mechanical distension of the peripheral vascular network (14, 15) in hyperemic resting muscle. It has already been suggested that the change in the volume of blood in the venular system could be one of the physiological stimuli to these fibers (14, 18, 25). As the load imposed on the venous return was much higher in the U position than in the S position, we could speculate that the degree of distension of the venular side of the muscle circulation could stimulate thin muscle afferent fibers in metabolically active and hyperemic muscles in the U position and reduce this activity in the S position.

Although the present results are consistent with such a mechanism being a contributor to the difference in the VE responses between body positions, testing this hypothesis specifically will require examination of the effects of gravity on the same group of exercising or post-exercising muscles.

It is concluded that the difference in the ventilatory response following an impulse exercise between the S and U positions persists even after the cessation of the contractions and can not be accounted for by the involvement of cardiac mecanoreceptors. The slight difference observed when the exercise was performed with the arms suggests that factors other than those related to the ventilatory component of the arterial baroreflex or to information originating from the respiratory system are responsible for the reduced ventilatory response in the S position during leg exercise.
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**LEGEND TO FIGURES**

**Figure 1:** Temporal profile of the second-by-second ventilatory, pulmonary gas exchange, and PETCO₂ responses to an impulse change in work rate in one subject. Data are the mean of four tests performed in the same condition: leg exercise (240 W) in the upright position. The period of exercise (12 seconds) is indicated by the thick horizontal line. Note that 1- VO₂, VCO₂ and VE start to rise 17-20 sec after the contractions stop 2- ventilation remains elevated for several minutes, despite the fact that PETCO₂ has already returned to control.

**Figure 2:** Averaged response of VE, oxygen uptake (VO₂), PETCO₂ and blood pressure (BP) to an impulse change in WR (240W for 12 seconds) in the upright (U) position (left panels) and in the supine (S) position (right panels) in the seven control subjects. The exercise was performed with the legs. Data are the mean ± sem for all the tests in all the subjects and are shown up to the fourth minute after the end of the exercise bout. The period of exercise is indicated by the thick horizontal line. Note that the VO₂ peak was similar in the supine and upright positions whereas ventilatory response was significantly attenuated and that the PETCO₂ level was higher in the S position than in the U position. The blood pressure at the the carotid baroreceptor level (see method) was found significantly higher in the S position by about 7 mmHg.

**Figure 3:** Averaged HR response to an impulse change in WR in the upright (U) position (left panels) and in the supine (S) position (right panels). Upper panels: leg exercise (240W for 12 seconds) in the seven control subjects. Middle Panels: leg exercise (240W for 12 seconds) in six heart transplant patients. Lower panels: arm exercise (175 W for 12 seconds) in the seven control
subjects. Note that HR was significantly higher in the U position than in the S position and that there was virtually no response in the transplant patients.

**Figure 4:** Averaged response of $\dot{V}E$, oxygen uptake ($\dot{V}O_2$), $\text{PETCO}_2$ to an impulse-like change in WR (240W for 12 seconds) in the upright (U) position (left panels) and in the supine (S) position (right panels) in six heart transplant patients. The exercise was performed with the legs. Data are the mean ± sem of all the tests in all the patients and are shown up to the fourth minute following the exercise bout. The period of exercise is indicated by the thick horizontal line. Note that, like in the control subjects, the $\dot{V}O_2$ peak was similar in the S position and in the U position whereas ventilatory response was significantly attenuated in the S position.

**Figure 5:** Example of the response of $\dot{V}E$, oxygen uptake ($\dot{V}O_2$), $\text{PETCO}_2$ to an impulse-like change in WR (240W for 12 seconds) in the upright (U) position (left panels) and in the supine (S) position (right panels) in one heart-lung transplant patient. The delay between this recording and the transplantation was 6 months. Note that the second phase of the $\dot{V}E$ response was about 4 l/min lower in the S position than in the U position, with a higher $\text{PETCO}_2$ in the former.

**Figure 6:** Averaged response of $\dot{V}E$, oxygen uptake ($\dot{V}O_2$), $\text{PETCO}_2$ to an impulse-like change in WR (175 W for 12 seconds) in the upright (U) position (left panels) and in the supine (S) position (right panels) in the seven control subjects. The exercise was performed with the arms (see methods). Data are the mean ± sem of all the tests in all the subjects and are shown up to the fourth minute following the exercise bout. The period of exercise is indicated by the thick
horizontal line. Note that 1- in contrast to the leg exercise, $\text{VO}_2$ was lower in the S position than in the U position and 2- the reduction in the ventilatory response was at best one third of that observed during the leg exercise.

**Figure 7:** Variation of the peak ventilatory and oxygen uptake response following the arm and the leg exercise expressed in % of change from the upright position. Black bars: arm exercise, hatched bars: leg exercise. Note that ventilation was affected in the same proportion as $\text{VO}_2$ during the arm exercise, whereas the $\dot{\text{VE}}$ response was reduced in the S position out of proportion of the reduced increase in oxygen uptake during the leg exercise. In addition the ventilatory deficit in the supine position following the leg exercise was significantly higher than during the arm exercise (* p<0.01, paired t test)

**Figure 8:** Second-by-second $\dot{\text{VE}}$ vs. $\text{VO}_2$ relationships (mean of all the subjects) during the 90 seconds following the peak of the ventilatory response, in the S position (open symbols) and in the U position (closed symbols). Left panel: response to the arm exercise, right panel: response to the leg exercise The slope of the $\dot{\text{VE}}$ vs. $\text{VO}_2$ relationship was significantly higher in the U position following the leg exercise.
Figure 1. Haouzi et al.
Figure 2. Haouzi et al.
Figure 3. Haouzi et al.
Figure 4. Haouzi et al.
Figure 5. Haouzi et al.
Figure 6. Haouzi et al.
Figure 7. Haouzi et al.
Figure 8. Haouzi et al.