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Effects of Passive Limb Movement on Pulmonary Ventilation

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This study was undertaken to determine if the observed increase in ventilation during passive limb movement was a reflex hyperventilation or a response to an increased metabolic need for oxygen. Experiments on human volunteers were designed to test the hypothesis that the rapid increase of ventilation at the onset of exercise was due to stimulation of the joints. Results of these studies showed significant increases in ventilation, oxygen consumption, carbon dioxide production, ventilation/oxygen consumption ratio, and heart rate compared to rest and recovery values. The data lead to the conclusion that the rapid increase of ventilation at the onset of exercise is a true hyperventilation and that stimulation of the joints can be a significant contributor to increased pulmonary ventilation.

INTRODUCTION

Geppert and Zuntz [1] in 1888 and Krogh and Lindhard in 1913 [2] were the first to describe a rapid increase in pulmonary ventilation ($\dot{V}E$) at the onset of exercise. Since their pioneering work, other investigators have used a variety of techniques to confirm these observations and attempt to elucidate the mechanism that provides for the response. Because the increase in ventilation at the onset of exercise is apparently too fast for central chemoreceptors to be activated, most investigators have assumed that the increase in ventilation is mediated neurally and is associated with exercise itself [3,4,5,6,7]. Two mechanisms have been proposed. Krogh and Lindhard [2] were the first to hypothesize the "cortical-radiation" theory, which postulates that at the onset of exercise the brain directs an increase in respiratory muscle activity while simultaneously directing contraction of skeletal muscles. The other prominent theory proposes the existence of joint receptors which initiate increased respiration upon mechanical stimulation [8,9]. A third proposal, based on receptors sensitive to change in pulmonary artery pressure or P_aCO_2 has been proposed by Wasserman's group [10,11] and others [12]. These hypotheses have not, however, been confirmed [13] by other investigators. Furthermore, little support has been found for the existence of chemoreceptors in the joints [14].

Abbreviations: HR: heart rate P_aCO_2: pulmonary artery pressure $PETCO_2$: end tidal CO_2 $PETO_2$: end tidal O_2 PLM: passive limb movement R: respiratory exchange ratio $\dot{V}_E$: volume of expired air $\dot{V}CO_2$: carbon dioxide production $\dot{V}CO_2/\dot{V}O_2$: respiratory exchange ratio $\dot{V}E$: pulmonary ventilation $\dot{V}E/\dot{V}O_2$: hyperventilation $\dot{V}O_{max2}$: aerobic capacity $\dot{V}O_2$: oxygen uptake

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The cortical radiation theory was based upon the observation of a very rapid (within 20–30 seconds) change of $\dot{V}E$ at the onset and cessation of moderate to heavy exercise. The joint receptor activation theory depended upon data from passive limb movement (PLM) experiments. Pulmonary ventilation increased when the joints were flexed by external (passive) physical means. During these experiments, however, neither oxygen uptake ($\dot{V}O_2$) nor heart rate (HR) were generally measured. Without continuous measurement of $\dot{V}O_2$, it cannot be determined whether the increased pulmonary ventilation during PLM is a reflex hyperventilation or the response to an increased metabolic need for oxygen.

By measuring $\dot{V}_E$ and $\dot{V}O_2$ continuously and using PLM as a means to eliminate voluntary muscle activation, we were able to test the hypothesis that the rapid increase in $\dot{V}E$ at the onset of exercise is the consequence of peripheral mechanoreceptor (joint) stimulation.

MATERIALS AND METHODS

Nine healthy young men, ages 21 through 25, volunteered to serve as subjects. After physical examinations, all volunteers provided informed consent.

We used a modified cycle ergometer with a motor attached to the flywheel. The subjects sat behind the ergometer with their feet strapped on to platform pedals. This ergometer has been described thoroughly by Bigland-Ritchie et al. [15].

Subjects breathed continuously through a low-resistance three-way valve. Partial pressures of expired oxygen and carbon dioxide were measured, using electronic O_2 and CO_2 analyzers, and the volume of air breathed was continuously measured, using a dry gas meter. Oxygen uptake, carbon dioxide production ($\dot{V}CO_2$), and pulmonary ventilation were computed during each minute. In addition, the heart rate of each subject was determined every 30 seconds from a cardiotachometer.

The passive leg movement experiment was performed three times on each subject, and the results of each replicate were averaged to determine the arithmetic mean. Following attachment of probes, each subject's ventilation and composition of expired air was measured for five minutes of rest, during a five-minute period in which their legs were spun at 60 rpm on the ergometer, and during a three-minute recovery period. Subjects were not made aware of the instant that PLM would begin in order to prevent a conditioned or anticipatory response [16].

Standardized ventilatory values for $\dot{V}E$, $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E/\dot{V}O_2$, and the respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$) were calculated. We defined hyperventilation as $\dot{V}E/\dot{V}O_2$ and respiratory exchange ratio (R) values significantly greater than baseline values [17].

Aerobic capacity, $\dot{V}O_{max2}$, was determined using a cycle ergometer. Following a three-to-five minute warm-up period, subjects were instructed to maintain a constant pedaling rate of 60 rpm, while the resistance on the flywheel was increased incrementally at two-minute intervals. The experiment was terminated when the subjects could no longer maintain pedaling rate. Oxygen consumption was measured throughout the experiment. Aerobic capacity was expressed as maximum oxygen consumption per kilogram of body weight.

The re-breathing test of Read [18] was used to measure metabolic sensitivity to CO_2. A five-liter anesthesia bag was filled from a cylinder containing a mixture of 7 percent CO_2, 50 percent O_2, and 43 percent N_2. This bag was placed in a ten-liter Nalgene bottle equipped with a series of valves. The first one-way valve was an inlet for room air

TABLE 1
Cardiopulmonary Responses to Passive Limb Movement

	Rest	PLM	Recovery
$\dot{V}E$ (liters/minute)	4.9 ± 0.7	8.2 ± 1.1	4.9 ± 0.8
$\dot{V}O_2$ (liters/minute)	0.21 ± 0.03	0.31 ± 0.07	0.21 ± 0.04
$\dot{V}CO_2$ (liters/minute)	0.16 ± 0.03	0.27 ± 0.05	0.16 ± 0.03
$\dot{V}E/\dot{V}O_2$ (liters air/liters O_2)	24.3 ± 2.4	27.1 ± 3.7	24.8 ± 1.9
R (dimensionless)	0.79 ± 0.09	0.88 ± 0.06	0.78 ± 0.08
HR (beats/minute)	60.3 ± 1.2	69.3 ± 3.8	59.2 ± 1.3

Mean (± standard deviation) values, in BTPS, of nine subjects of volume of expired air, $\dot{V}E$; volume of oxygen consumed, $\dot{V}O_2$; volume of expired carbon dioxide, $\dot{V}CO_2$; respiratory exchange ratio, R; and heart rate, HR; during rest, passive limb movement, and recovery periods. All PLM values are significantly different, $p < .05$, from resting and recovery values.

to enter the Nalgene bottle. The second valve controlled the outflow from the bottle and directed exhaust air to a flow meter which measured $\dot{V}E$. Throughout the five-minute experiment, carbon dioxide concentration in the bag was continually measured. In addition, O_2 content was ascertained to ensure subject safety. Metabolic CO_2 sensitivity was expressed as $(L/minute)/(\%CO_2/100)$.

A repeated measures analysis of variance was used to determine significance of differences among variables in the three phases (rest, PLM, recovery) of the experiment. Scheffe's multiple comparison procedure was used to isolate the mean value(s) contributing to any significant F value found. The paired t-test was used to determine significant differences between resting and PLM values for each subject. Differences were considered significant at $p < 0.05$.

RESULTS

Table 1 shows mean volumes, in BTPS, for $\dot{V}E$, $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E/\dot{V}O_2$, R, and heart rate for each of the three conditions of rest, PLM, and recovery. All of the mean values of these variables obtained during the PLM phase of the experiment were significantly ($p < 0.05$) greater than those obtained during the rest and recovery periods.

Figure 1 shows the mean changes in per-minute ventilation throughout each phase of the experiment. The mean $\dot{V}E$ during PLM averaged 8.2 ± 1.1 L/minute, a value that was significantly greater than rest or recovery values. Figure 2 shows the $\dot{V}O_2$ and $\dot{V}CO_2$ increases during PLM compared to rest and recovery. Generally, the greatest

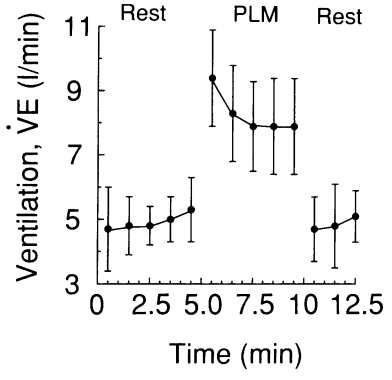

FIG. 1. Graph of ventilation ±SD (liters/minute) versus time (minute). Ventilation was significantly greater during PLM than during rest or recovery periods. The ventilatory increase became less pronounced as the PLM period progressed.

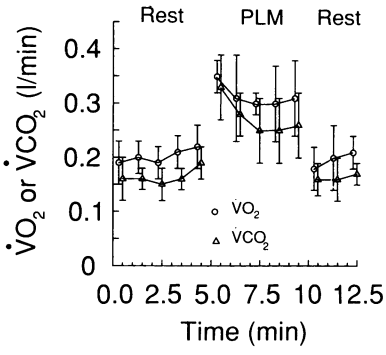

FIG. 2. Graph of $\dot{V}O_2$ ±SD and $\dot{V}CO_2$ ±SD (liters/minute) versus time. The pattern is similar to that seen with ventilation.

values occurred at the onset of PLM, with latter values consistently lower. Figure 3, which shows the changes in $\dot{V}E/\dot{V}O_2$, follows this same pattern. The rest and recovery $\dot{V}E/\dot{V}O_2$ values of 24–25 liters per liter are similar to those reported in the literature [19]; however, the $\dot{V}E/\dot{V}O_2$ increased rapidly to 28 liters per liter at the onset of PLM, significantly higher than those observed during rest or recovery. Also, $\dot{V}E/\dot{V}O_2$ was significantly greater during the first two minutes of PLM compared to the last minute. The respiratory exchange ratio (R) changes followed this same pattern (Fig. 4). The sharp increase in R from resting values indicates that body stores of CO_2 were reduced during PLM. Both of these sets of data indicate significant hyperventilation during PLM, particularly at its onset. Likewise, as shown in Fig. 5, the heart rate increased an average of 17 BPM at the onset of PLM and gradually declined to a value 7 BPM above baseline as PLM continued. The HR increase is consistent with an increase in sympathetic discharge and an increase in venous return to the heart from movement of the muscles during PLM.

Table 2 shows the large variation among individual subjects in the change in $\dot{V}E/\dot{V}O_2$ during PLM from rest and recovery levels. The range of values extended from 0.4 percent decrease in the ratio to a 36.3 percent increase during the transition from rest to PLM. Similarly, during the transition from PLM to recovery, the variation in $\dot{V}E/\dot{V}O_2$ ranged from −4.9 percent to 27.6 percent. The ventilatory response to PLM showed no correlation to metabolic CO_2 sensitivity.

DISCUSSION

Our results showing a sharp increase in pulmonary ventilation with the onset of passive limb movement are consistent with the findings of others who used different

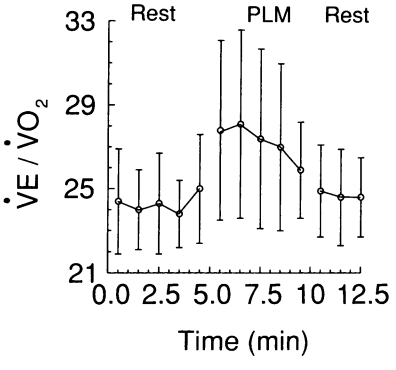

FIG. 3. Graph of $\dot{V}E/\dot{V}O_2$ ±SD (liters/liter) versus time (minute). The figure indicates a hyperventilation occurring during PLM. Due to the experimental design of each subject serving as his own control, the paired analysis at the data shows a significant increase in hyperventilation during PLM.

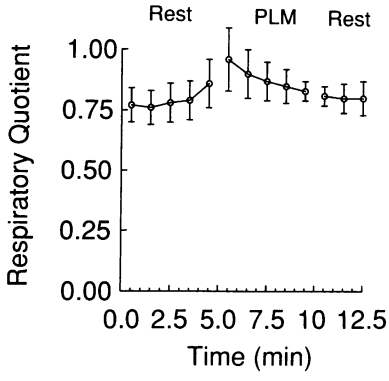

FIG. 4. Graph of respiratory exchange ratio ± SD (dimensionless) versus time (minute). The graph shows a significant increase in R during PLM. This increase in R during PLM is consistent with hyperventilation and the $\dot{V}E/\dot{V}O_2$ data.

techniques. Bahnson et al. [20] and Dejours [21] had assistants manually flex and extend the limbs of their subjects while $\dot{V}E$ was measured. They reported an increase in ventilation during PLM and assumed a concomitant increase in O_2 consumption; however, they never correlated $\dot{V}E$ to $\dot{V}O_2$. Hence, they were unable to determine whether hyperventilation occurred or whether the increase in $\dot{V}E$ was appropriate to a metabolic increase. Others [22,23] used similar methodologies, but measured O_2 consumption. Otis reported that, in some individuals, an increase in the oxygen consumption was observed, indicating that these maneuvers were not always entirely passive [22]. Otis did not report $\dot{V}E/\dot{V}O_2$ ratios for analysis. Hutt et al. [23] used this same methodology and found that $\dot{V}O_2$ increased in proportion to $\dot{V}E$ only if more than one joint was flexed. Both were unable to explain their observations fully, given the inadequacy of available methods at their disposal. Dixon and his co-workers [24] used a machine that moved the seat, handlebars, and pedals on a bicycle. Although they observed considerable variation among their subjects, they noted an increase in $\dot{V}E$ only with movement of their subjects' bodies. Movement of the legs alone did not produce an increase in $\dot{V}E$. They were unable to explain these differences. Lamb and Tenney [25] reported an increase in ventilation in a third of their subjects whose entire bodies were vibrated in a supine position. They concluded that "there was something about the experience of total-body vibration which was different from vibration of each of the component parts" [25]. They found that those with low resting respiratory minute volumes tended to increase their ventilation, and those with high resting $\dot{V}E$s did not respond to vibration.

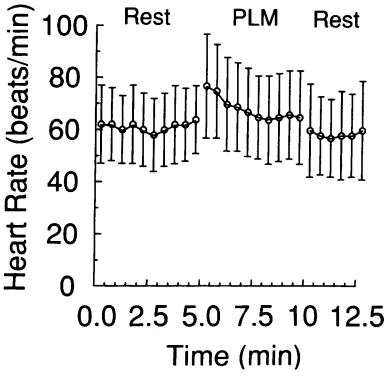

FIG. 5. Graph of heart rate (beats/minute) ±SD versus time (minute). The graph shows a significant increase in heart rate during PLM. The low resting heart rate probably reflects the relative youthfulness of the experimental subjects and the low level of basal sympathetic discharge.

TABLE 2
Individual Responses to Passive Limb Movement

Subject ID	%Δ $\dot{V}E$ from $\dot{V}O_2$ Initial	%Δ $\dot{V}E$ from $\dot{V}O_2$ Recovery	$\dot{V}O_2$ max ml/min Kg	CO_2 Sensitivity $\left(\frac{\text{L/minute}}{\%CO_2\ 100}\right)$
1 DA	36.3	27.6	64.0	548
3 RG	19.2	15.7	56.4	1,242
4 TS	16.5	15.7	60.4	1,198
2 RC	13.2	11.4	46.7	768
8 YK	9.7	3.6	53.0	932
9 DK	4.5	0.8	34.0	1,335
7 BJ	2.7	4.4	51.0	1,023
5 BA	2.0	9.4	64.4	551
6 PD	−0.4	−4.9	36.3	723

The percentage change from resting and recovery values in the $\dot{V}E/\dot{V}O_2$ for each subject. Also listed are each subject's aerobic capacity ($\dot{V}O_2$ max) and sensitivity to increased levels of arterial PCO_2.

An alternative method of investigating the joint-mediated stimulus for ventilation has been to study changes in pulmonary ventilation during the first few seconds of exercise. The theory behind this approach was that these first few breaths were not influenced by a central reflex to chemicals released from the exercising muscles because the response occurred before the possible chemical mediators would be able to travel through the blood stream to the receptors. Proposed mechanisms for this immediate increase in ventilation included stimulation provided by peripheral chemoreceptors or mechanoreceptors in the limbs [26], direct stimulation of the respiratory centers by nerves which originate in the brain [27], or by a pulmonary receptor sensitive to changes in cardiac output [10]. Since $\dot{V}O_2$ was not measured in most of these studies, it is impossible to determine whether hyperventilation or hyperpnea occurred in response to leg movement. One notable exception is the work of Fordyce and his colleagues [7]. They defined "hyperventilation" as a decrease in end tidal CO_2 ($PETCO_2$) and a somewhat larger increase in end tidal O_2 ($PETO_2$) from an air breathing baseline. Although they did not define exactly how much of a change in $PETCO_2$ or $PETO_2$ was necessary to establish hyperventilation, they concluded that they found hyperventilation at the onset of exercise.

Another method of examining the ventilatory response to joint stimulation was to stimulate mechanically or electrically an anesthetized animal's muscles and measure the changes in $\dot{V}E$ [28,29,30]. Although Ponte and Purves [31] noted an increase in $\dot{V}E$ upon stimulation, they, too, did not measure $\dot{V}O_2$. Others blocked nerve transmission from the joint and either found an absence of hyperpnea or no change in the response. The results of the chordotomy experiments, however, may have been influenced by the trauma caused by these procedures [30].

Our data support the existence of joint receptors that stimulate increased pulmonary ventilation at the onset of leg movement. Because ventilation was increased without any command for muscle work, our data limit the importance of the cortical radiation theory. Furthermore, our data show that the increase in pulmonary ventilation at the onset of exercise is a true hyperventilation, not just a hyperpnea associated with elevated metabolic rate. The heart rate increase is consistent, with an increase in sympathetic discharge and an increase in venous return to the heart from movement of the muscles during PLM. HR increases may also be associated with increased

metabolic work during PLM. Thus, it appears that the PLM phase of the experiment was not entirely passive. Nonetheless, the increases in $\dot{V}E/\dot{V}O_2$ and R suggest that pulmonary ventilation, above that required by metabolic demands, occurred. These data also suggest that the neurogenic command for ventilation diminished or was overridden by chemoreceptors as PLM was maintained over the five-minute period. Thus, these data suggest that cortical radiation is not necessary for increased pulmonary ventilation at the onset of movement. Further research will need to be conducted to delineate the relative importance of joint versus cardiodynamic stimulation.

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