The rate of change of mouth occlusion pressure during exercise

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(Received 26 June 1978; accepted 25 October 1978)

Summary

1. The initial rate of change of pressure at the mouth \(dP/dt\) during a brief occlusion of the airways at the beginning of inspiration has been estimated in nine healthy subjects at rest, during exercise and during the first 2 min of recovery. Exercise was carried out with progressively increasing loads to the maximum tolerated (progressive exercise) and also for a period of 6 min at a constant load of 60% of the maximum (steady-state exercise).

2. A highly significant linear relationship was found between work loads and \(dP/dt\) during progressive exercise in all our subjects.

3. A highly significant linear relationship was found between ventilation and \(dP/dt\) in both forms of exercise, but the slope of the regression line was steeper during progressive than during steady-state exercise in six out of nine subjects.

4. The pattern of breathing \((V_{TI}, f, V_{T}/T_{insp}, T_{insp}/T_{tot})\) did not account for the difference in the relationship between \(dP/dt\) and ventilation during the two forms of exercise.

5. These results are in agreement with the hypothesis that \(dP/dt\) is an index of central inspiratory drive.

Key words: central inspiratory drive, exercise, mouth occlusion pressure, recovery.

Introduction

It has been suggested that mouth pressure during a brief period of occlusion of the airway at the beginning of inspiration could be a simple and useful index of central inspiratory drive and that it could be used to estimate the sensitivity of the respiratory centres to different stimuli (Whitelaw, Derenne & Milic-Emili, 1975). This suggestion is based upon observations by Lourenço, Cherniack, Malm & Fishman (1966), who showed that phrenic nerve activity was a simple function of the force of isometric contraction of the diaphragm during obstructed inspiration in experimental animals. Similar findings have been described in human subjects by Altose, Kelsen, Stanley, Levinson, Cherniack & Fishman (1976). These workers related the electrical activity of the diaphragm to the pressure developed at the mouth in 0.1 s from the beginning of inspiration \((P_{0-1})\) during obstruction. Previously, Whitelaw et al. (1975) showed that the rate of change of mouth pressure over a period of 0.1–0.2 s of inspiratory obstruction was closely correlated with end-tidal \(CO_2\) and pulmonary ventilation. Mouth occlusion pressure has also been shown to increase during hyperventilation induced by exercise (Goldstein, Goldstein, Urbanetti & Anthonisen, 1975). However, this was not studied systematically. We have studied the initial rate of change of mouth occlusion pressure in more detail during progressive and steady-state exercise and assessed the use of this ratio as an index of inspiratory drive during exercise.

Subjects and methods

Subjects

Nine healthy young men were studied. Their physical measurements and estimates of lung function are shown in Table 1. All lived an active life, though none was in physical training. Four
TABLE 1. Some of the physical characteristics and results of tests of lung function in the nine male subjects used in the experiments.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Wt. (kg.)</th>
<th>Ht. (cm)</th>
<th>Raw (kPa l⁻¹ s)</th>
<th>Vtg (ml)</th>
<th>sGaw (kPa⁻¹ l⁻¹ s⁻¹)</th>
<th>FRC (ml)</th>
<th>FEV₁₀ (ml)</th>
<th>FVC (ml)</th>
<th>RV (ml)</th>
<th>TLC (ml)</th>
<th>IC (ml)</th>
<th>Smoking habits</th>
</tr>
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<tr>
<td>A.Y.</td>
<td>41</td>
<td>72</td>
<td>180</td>
<td>0.034</td>
<td>4625</td>
<td>6.36</td>
<td>4410</td>
<td>3550</td>
<td>4400</td>
<td>2760</td>
<td>7160</td>
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<tr>
<td>A.M.</td>
<td>27</td>
<td>64</td>
<td>176</td>
<td>0.165</td>
<td>3570</td>
<td>3.095</td>
<td>3150</td>
<td>4000</td>
<td>4750</td>
<td>1400</td>
<td>6150</td>
<td>3000</td>
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</tr>
<tr>
<td>N.S.</td>
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<td>70</td>
<td>178</td>
<td>0.048</td>
<td>3360</td>
<td>6.22</td>
<td>3050</td>
<td>4050</td>
<td>4550</td>
<td>1150</td>
<td>5700</td>
<td>2650</td>
<td></td>
</tr>
<tr>
<td>M.L.</td>
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<td>73</td>
<td>184</td>
<td>0.091</td>
<td>4300</td>
<td>2.55</td>
<td>4000</td>
<td>4350</td>
<td>4700</td>
<td>1400</td>
<td>6600</td>
<td>2600</td>
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</tr>
<tr>
<td>G.T.</td>
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<td>75</td>
<td>168</td>
<td>0.079</td>
<td>3420</td>
<td>7.01</td>
<td>3000</td>
<td>3800</td>
<td>4750</td>
<td>1000</td>
<td>5800</td>
<td>2800</td>
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<td>176</td>
<td>0.103</td>
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<td>3.82</td>
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<td>3300</td>
<td>4200</td>
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<td>5500</td>
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<tr>
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<td>3850</td>
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<td>6100</td>
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<td>Cigarettes</td>
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<tr>
<td>R.M.</td>
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</table>

Measurement of mouth occlusion pressure

The rate of change of mouth occlusion pressure was measured by a method described by Matthews & Howell (1975). The apparatus is shown diagrammatically in Fig. 1. The subjects breathed through the mouthpiece into a valve (P.K. Morgan 71522), which separated inspired and expired gas to avoid rebreathing. Flexible tubing connected the valve through a Y-piece to a heated pneumotachograph (Fleisch no. 4), which allowed inspired and expired flow rates to be measured. The flow signals were integrated with respect to time to give tidal volume. The resistance to gas flow of the whole assembly was less than 0.2 kPa l⁻¹ s⁻¹ at a gas-flow of 2 litres/s. Continuous measurements of CO₂ concentrations at the mouth made by a rapid CO₂ analyser (Hartmann-Braun, URS 4) failed to reveal any evidence of rebreathing of expired gas throughout the experiments.

Mouth pressure was measured continuously by a photoelectric pressure transducer (Mercury Electronics, M 2/555).

Obstruction at the mouth was achieved by the small delay in opening of the spring-loaded valve. During this brief obstruction mouth pressure fell before the valve opened (Fig. 2). The opening pressure of the valve, measured continuously, was found to be about 0.1 kPa during quiet breathing and moderate exercise. However, moisture accumulating in the valve increased the opening pressure by the end of the exercise. This increase was found to be about 0.2-0.25 kPa in eight out of nine subjects in both forms of exercise. The ninth subject showed an opening pressure of 0.4 kPa at the last minute of the progressive exercise. The duration of the occlusion was not constant but depended upon the rate of change of pressure at the mouth, varying from about 0.040 s at high rates to about 0.200 s at low rates, measured from the flow trace (arrow in Fig. 2).

The frequency response of the system was tested by applying a square wave of pressure at the mouthpiece. The rise time of the mouth pressure signal was less than 10 ms to 95% of the total response.

Discussion of the method

The great advantage of using a valve instead of a mechanically operated shutter is that the inter-
ruption to flow is very brief, almost noiseless and undetected by the subject. It does not therefore modify the pattern of breathing and makes it possible to measure the initial slope of the pressure \(\frac{dP}{dt}\) on every breath.

One objection to the use of the valve may be that the time of occlusion is too brief to allow pressure equilibration throughout the lung. However, Mead & Whittenberger (1954) estimated the time of equilibration to be about 0.018 s in healthy subjects. In our experiments the shortest duration of occlusion was about three times this value.

Another objection may be that the opening pressure of the valve by the end of the exercise test is high enough to be an effective inspiratory resistive load (Lopata, La Fata, Evanich & Lourenço, 1977). However, the opening pressure in the last minute was less than 0.25 kPa in eight subjects. Even in one subject (no. 9) where the pressure rose to about 0.4 kPa he was not aware of any load at the mouth.

Finally, the relationship between the neural input to the inspiratory muscles and the muscle tension, measured as \(\frac{dP}{dt}\), is linear only if we assume that the drop of the pressure is produced during isometric contraction of the muscles. This drop is about 0.1 kPa (pressure required to open the valve) and it follows that the change in lung volume due to this is of the order of 0.1%. At a lung volume of 3.5 litres this is about 3.5 ml and is therefore considered small enough to justify the assumption of isometricity.

**Procedure**

Each subject performed a controlled progressive exercise test on a bicycle ergometer. During the test he breathed through the mouthpiece of the apparatus and wore a nose-clip. The test started with a recording or resting ventilation (flow, tidal volume and mouth pressure) for at least 2 min. Exercise was begun at a level of 60 W and a cycling speed of 60 rev./min. This load was maintained for 1 min and then was increased successively by 20 W increments at the end of each minute to the maximum load which could be tolerated short of complete exhaustion. At this point the subject stopped pedalling but continued breathing through the mouthpiece for 2 min. Recordings were made for the last 15 s of each minute during exercise and at intervals of 15 s during recovery. On the following day the subject performed a steady-state exercise lasting 6 min at a load of 60% of the final load of the progressive test. Recordings were made at rest, every 15 s during the first minute of exercise and at the end of every minute thereafter, and again every 15 s during the first 2 min of recovery.
Progressive Recovery

Steady-state Recovery

Calculation of results

Fig. 2 is a sample trace of a single breath at rest and during exercise. To measure the rate of change of the mouth occlusion pressure (dP/dt) a tangent was drawn coinciding with the initial part of the pressure trace, where it was approximately linear. The value of dP/dt was estimated from the slope of this line (tangent of a: Fig. 2). Mean dP/dt was calculated from five successive breaths at rest and at each level of exercise.

The tidal volume (Vₚ) of the same breaths, together with the time of inspiration (T_insp.) and the total time of the complete breathing cycle (T_tot.) were measured and averaged over the five breaths. The ventilation was measured as the product of tidal volume and respiratory frequency over the same five breaths. Since the pneumotachograph was heated, no temperature correction was needed.

Statistical methods

Standard methods have been used to calculate values for the correlation and regression coefficients. The significances of the differences between the slopes of the regression lines were calculated by estimating the variances of each value of the regression coefficient and from these the standard error of the differences between them. The actual techniques for these calculations are fully described by Smart (1963).

Results

At rest the value of dP/dt varied between individuals from 0.704 kPa/s to 1.408 kPa/s. The mean value was 1.0357 (sd 0.184) kPa/s in the nine subjects. In only one subject was there a significant difference between the values obtained on the 2 days of experiment. These values agree reasonably well with other published data from use of a similar method (Matthews & Howell, 1975). dP/dt increased immediately after the beginning of exercise and dropped abruptly at the termination of exercise. This drop was more apparent at the end of progressive exercise (Fig. 3a). Thereafter, for the 2 min of recovery, dP/dt decreased progressively (Fig. 3a, b).

During progressive exercise dP/dt continued to increase progressively up to the end of exercise. During steady-state exercise after the initial increase, dP/dt continued to rise progressively until the second or third minute, thereafter remaining almost constant (Fig. 3b).

Response of dP/dt to the work load

During progressive exercise there was a very close correlation between the work load and dP/dt. The correlation coefficient (r) was between 0.8734 and 0.9909, highly significant in all subjects (P < 0.001). The coefficients of linear regression varied
between the subjects from 0.0208 to 0.0916 kPa s\(^{-1}\) W\(^{-1}\). Fig. 4 shows the calculated regression lines for all subjects.

**dP/dt and ventilation**

During exercise, whether with progressively increasing work loads or with a single load, there was a very close correlation between dP/dt and ventilation.

The range of correlation coefficients (r) for all subjects under both conditions of exercise was 0.8015-0.9798, all highly significant (P < 0.01). The coefficients of linear regression varied between subjects from 4.932 to 15.354 kPa/l in the progressive exercise test and from 4.381 to 11.370 kPa/l in the steady-state test. There was a difference between the regression coefficients in the same subject during the two types of exercise, which was highly significant in six out of nine subjects. In those six individuals the regression line for progressive exercise was steeper than that for steady-state exercise. A typical example is shown in Fig. 5.

The values of dP/dt during recovery from both forms of exercise were closely related to ventilation (r = 0.671-0.986). The number of observations available for estimating r in each case was only five, so that in only 12 of 17 experiments were the values statistically significant (P < 0.05).

The slope of the linear relationship of dP/dt to \(\dot{V}_E\) during recovery was not significantly different from the slope obtained for the preceding exercise. Furthermore, the slope during recovery from progressive exercise was not significantly different from the slope during recovery from steady-state exercise in the same individual.

**dP/dt and \(V_T/T_{insp.}\)**

Following a suggestion by Whitelaw, Derenne & Milic-Emili (1975) that the ratio \(V_T/T_{insp.}\) could also be regarded as an index of inspiratory drive we have compared this ratio with dP/dt in each of our subjects. We found a highly significant correlation both for progressive exercise and steady-state exercise (r between 0.7573 and 0.9759). The coefficient of linear regression in the two forms of exercise was statistically significantly different in six out of nine subjects, and again the slope of the regression line during progressive exercise was steeper than that during steady-state exercise in the same subject. A typical example is shown in Fig. 6.

**Pattern of breathing during progressive and steady-state exercise**

Minute ventilation may be expressed either as

\[ \dot{V}_E = V_T \times f \]

or

\[ \dot{V}_E = \frac{V_T}{T_{insp.}} \times \frac{T_{insp.}}{T_{tot.}} \]

We plotted \(V_T f, V_T/T_{insp.}\) and \(T_{insp.}/T_{tot.}\) against ventilation during progressive and steady-state exercise to investigate the pattern of breathing. These plots failed to reveal any difference in the pattern of breathing between the two types of exercise in all subjects. An example of these plots in the same subject is shown in Fig. 7. In addition, tidal volume \(V_T\) was plotted against the time of inspiration \(T_{insp.}\) (Clark & von Euler, 1972) in the two forms of exercise. This plot showed no
Discussion

Published data have evaluated the use of mouth occlusion pressure as an index of the neural output from the respiratory centres during hyperventilation stimulated by hypercapnia or hypoxia. In our experiments we used exercise to increase ventilation and the results presented here are in agreement with the hypothesis that \( \frac{dP}{dt} \) represents an index of the central inspiratory drive. We found a linear relationship between progressively increasing work loads and \( \frac{dP}{dt} \) with a highly significant correlation coefficient in all our subjects. If the work load at each level of progressive exercise represents an index of the level of stimulation of the respiratory system, this correlation indicates that input and output of the respiratory centres are in agreement.

At the beginning and end of exercise changes in the value of \( \frac{dP}{dt} \) occurred within 5–10 s. This indicates that \( \frac{dP}{dt} \) follows closely a sudden change in ventilatory stimulus, i.e. the start or termination of exercise.

\( \frac{dP}{dt} \) was also found to correlate well with ventilation in both forms of exercise and during recovery. It is most interesting to find that the slopes of the \( \frac{dP}{dt} \) to \( V_t \) were significantly steeper during progressive than during steady-state exercise in six out of nine subjects. This suggested that less 'drive' is needed to produce the same amount of ventilation during steady-state than progressive exercise.

We do not think that this difference was an artifact due to the increase in the opening pressure of the valve as it became wet, because the opening pres-
Occlusion pressures in exercise

Pressure was similar in the two forms of exercise. The difference was still apparent in subsequent tests performed by two individuals and could not therefore be due to familiarity with the apparatus. It may have been due to factors affecting either the pattern of breathing or the mechanical efficiency of the respiratory system.

Different patterns of breathing (e.g. slow, deep or rapid, shallow breathing) may produce the same minute ventilation but \( \frac{dP}{dt} \) for each pattern would be different. We studied the pattern of breathing and found no difference between steady-state and progressive exercise for the same level of ventilation. It therefore seems probable that a change in the physical properties of the respiratory system affected its mechanical efficiency and resulted in this difference. During steady-state exercise the respiratory system had time to adopt an optimal way of producing the required ventilation, whereas during progressive exercise there may not be enough time for this adaptation before the demand for higher ventilation occurred.

Finally, we have found a similar relationship between \( \frac{dP}{dt} \) and the ratio \( \frac{V_e}{T_{insp}} \), and that between \( \frac{dP}{dt} \) and ventilation. Since both \( \frac{V_e}{T_{insp}} \) and ventilation are affected by the mechanical properties of the system (resistance and compliance) we believe that the rate of change of mouth occlusion pressure, which is presumably independent of these properties, must be a better index of central inspiratory drive.

Acknowledgments
We are grateful to Mr Richard Madgwick for essential technical assistance, to our long-suffering subjects and to our (even longer-suffering) secretary Mrs J. MacGuigan. One of us (A.M.) was supported by a grant from Boehringer Ingelheim (U.K.), to whom we are greatly indebted. N.S. was the Papanikolaou Fellow of the Dionissios Chest Institute, Athens, Greece.

References


