Voluntary isocapnic hyperventilation and breathlessness during exercise in normal subjects

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SUMMARY

1. Nine normal subjects performed 6 min, constant-workload, exercise tests on a bicycle ergometer at either a ‘high workload’ or at a ‘low workload’. During the first ‘high workload’ test their spontaneous breathing pattern was recorded on to magnetic tape. During one subsequent ‘high workload’ test and one ‘low workload’ test they voluntarily copied their recorded breathing pattern. During a second ‘low workload’ test they breathed spontaneously. Isocapnia was maintained by the operator throughout both the copying tests. During the exercise tests ventilation was recorded and subjects indicated the level of their sensation of breathlessness every 30 s.

2. Subjects felt markedly less breathless when a proportion of their ventilation was produced by voluntary effort than when the same total level of ventilation was produced entirely by the stimulus of exercise. Furthermore, voluntary isocapnic hyperventilation during exercise did not increase breathlessness above that normally associated with that level of exercise.

3. These results suggest that it is reflexly driven ventilation, and not simply the level of ventilation itself, which relates to the level of breathlessness during exercise.

Key words: breathlessness, exercise, hyperventilation, sensory scaling, ventilatory stimulation.

Abbreviations: LSD, least significant difference; VAS, visual analogue scale.

INTRODUCTION

Several recent studies have demonstrated that the severity of the sensation of breathlessness for a given subject does not depend only on the level of ventilation [1–3]. This is true for both normal subjects and patients with respiratory disease. In a previous study [1], we have shown that subjects indicated more breathlessness when their breathing was stimulated by added CO₂ than when they voluntarily reproduced this increased ventilation while isocapnia was maintained. When CO₂ was added unbeknown to the subjects, at similar concentrations but during the voluntary hyperventilation, this again increased the indicated breathlessness. We concluded that it was the reflexly stimulated component of ventilation, rather than simply the overall level of ventilation itself, that was associated with the sensation of breathlessness.

It could be argued that exogenous CO₂ is an artificial stimulus to ventilation and may not be analogous to natural stimuli to ventilation, such as occur during exercise. In the present study, normal subjects had their ventilation increased by combinations of exercise at different workloads and voluntarily overbreathing. Our aim was to determine whether ventilation produced voluntarily was associated with a different amount of breathlessness than ventilation driven naturally by the exercise stimulus.

METHODS

Subjects

We studied nine normal subjects (four female) aged 21–34 years. All had forced spirometry indices (forced vital capacity and forced expiratory volume in 1 s) within their normal range; three were regular smokers.

All subjects had been familiarized with the use of the visual analogue scale (VAS) for breathlessness [4] during preliminary tests but they were unaware of the design or purpose of this study. They were told that they were to perform a number of exercise tests lasting some of which they would be asked to breathe to a specific pattern.

Exercise tests

Each subject undertook four different exercise test protocols during either one or two sessions. Exercise was performed on an electrically braked bicycle ergometer (Lode instruments) with a facility to allow the operator to control the workload outside the subjects’ field of view. Tests consisted of a 3 min ‘build up’ period in which
workload increased each minute in equal increments to a level which was then maintained steady for 6 min. Tests differed in the level of work for this 6 min period.

Test A: ‘high workload’. The steady workload was 150 W (males) or 100 W (females). During this test the tidal volume ($V_T$) signal was recorded on an FM tape recorder.

Test B: ‘low workload with copy’. The steady workload was less, at 100 W (males) or 65 W (females). During this test the $V_T$ signal recorded during Test A was replayed against time on to one channel of an oscilloscope screen mounted in front of the subject. The subjects were requested to ‘copy’ this breathing pattern by following the replayed $V_T$ trace with their current $V_T$ trace exhibited on a second channel of the oscilloscope at the same volume calibration. Subjects were not told that the $V_T$ trace they were copying was that of the previous test, or that the workload was different. The operator maintained end-tidal $PCO_2 (P_{ETCO_2})$ at the resting level by titrating CO$_2$ into the inspirate as necessary.

Test C: ‘low workload only’. This was a repeat of test B but with the subject free to breathe spontaneously.

Test D: ‘high workload’. This was a repeat of test A.

Test E: ‘high workload with copy’. This was a repeat of test A (or D) but with the subject copying the breathing pattern recorded during test A (or D). The operator again maintained $P_{ETCO_2}$ if the subject overbreathed while copying.

Four subjects completed the study in a single session performing only tests A, B, C, and E (as described above), with a recovery period of not less than 30 min between tests. Test D was not performed in this group of subjects. Five further subjects completed the study over two sessions within the space of 1 week, being unable to give sufficient time to complete all the tests within a single session. During the first session these subjects completed tests A, B and C, and during the second session they completed tests D and E. It was necessary to perform test D (a repeat of test A) since we only made comparisons between tests performed within a single session.

Measurements

Air flow at the mouth was measured with a pneumotachograph (Fleisch no. 3, deadspace = 185 ml, resistance = 0.148 cmH$_2$O l$^{-1}$ s$^{-1}$) and ventilation ($V_e$) was obtained from the integrated flow signal every 30 s. $PCO_2$ was measured continuously by a mass spectrometer (Cen- tronics MGA 200) with the probe at the mouth. Breathlessness was recorded every 30 s using a 10 cm VAS, the extremes of which were defined as ‘not at all breathless’ and ‘extremely breathless’. Subjects indicated their level of breathlessness on this continuum by moving the 10 cm slider of a linear potentiometer, mounted on the handlebar of the bike, which moved a point of light to a corresponding position on the 10 cm scale mounted in front of them. It was stressed that this scale was to be used only to indicate breathlessness and after exercise subjects were questioned about their own concept of the validity of their use of the scale.

Analysis

For each individual subject mean levels of $V_e$ and VAS score for breathlessness were calculated from the levels of each, for every half-minute over the final 3 min of each test. The statistical significance of differences was tested using a paired t-test and Wilcoxon’s matched-paired signed rank test; the results of the paired t-test are given alone when the Wilcoxon test gave a similar level of significance. Additionally, group mean levels of $V_e$, VAS

![Fig. 1](image.png)  
**Fig. 1.** Example from one normal subject: expired ventilation ($V_e$), and visual analogue scale score for breathlessness (VAS) and end-tidal $PCO_2 (P_{ETCO_2})$ during four exercise tests. Test A, ‘high workload’ ( ); test B, ‘low workload’ with copy of ventilation of test A ( ); test C, ‘low workload only’ ( ); test E, ‘high workload’ with copy of ventilation of test A ( ). See the Methods section for explanation of exercise protocols.
breathlessness score and $P_{ET\text{-}CO_2}$ were compared between tests for the full 6 min of steady workload exercise using a two-way analysis of variance \cite{5} as follows: (i) test number (five levels) and (ii) time (12 levels). Statistical significance was tested for by using Fisher’s least significant difference (LSD) \cite{6} for comparison of any two mean levels between runs. In all cases $P<0.05$ was taken as indicating that conventional statistical significance had been attained.

**RESULTS**

All nine subjects were able to complete the study protocol satisfactorily. They all reported that they considered that they had used the VAS appropriately to reflect their degree of breathlessness during the tests. None of them became aware of the protocol details, but most of them were able to tell the difference between ‘low’ and ‘high’ workloads and commented on this. They were aware that they were breathing ‘more than they needed to’ during test B.

Fig. 1 is an example of the results obtained in one subject. It shows that the subject achieved a good match of the high workload ventilation (test A) when copying (tests C and E) and that the low workload ventilation (test B) was substantially lower. The breathlessness indicated on the low workload tests (B and C) was substantially lower than for the high workload tests, whether or not the subject was copying a higher ventilation.

The results for the calculation of the individual mean levels of $V_e$ and VAS score for breathlessness for all nine subjects are shown in Table 1. Group mean levels of these variables and additionally for $P_{ET\text{-}CO_2}$, for each of the five tests, are shown in Fig. 2.

The experimenter was able to maintain $P_{ET\text{-}CO_2}$ during both copying tests (B and E) with no significant differences between these and the original tests (A or D); there was a maximum mean difference between any two tests of 4.6 mmHg (Fig. 2). There was a trend for $P_{ET\text{-}CO_2}$ to gradually fall during the original tests (A and D); the experimenter reproduced this pattern when maintaining CO$_2$ during the copying tests (B and E).

The subjects achieved a good voluntary copy of the high workload ventilation (test A) when exercising at the low workload (test B); there were no significant differences in $V_e$ between tests A and B either for individual mean levels (Table 1) ($P>0.2$ by paired t-test) or for the group as a whole (Fig. 2). When exercising at the low workload without any copying of ventilation (test C) mean $V_e$ was 67% of the mean $V_e$ of the high workload (test A) and this difference is significant at the 0.1% level for individual results and at the 5% level, for 2 min onwards, for the group as a whole (LSD = 15.4 litres/min). Copying of the high workload ventilation (test D) while performing the same high workload (test E) produced a good match of $V_e$ but with a tendency for the ‘copy’ ventilation (test E) to be consistently slightly higher throughout ($P=0.05$ by paired t-test of individual results), but failing to reach statistical significance at any point for the group as a whole.

A different pattern emerged in the mean VAS breathlessness scores. Subjects were less breathless when exercising at the low workload and copying the ventilation of the high workload. This difference was significant at the 1% level by paired t-tests for individual results and also at the 1% level (LSD = 13.8 mm) for the tests overall; the difference failed to reach statistical significance for the

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<th>Table 1. Mean levels of ventilation and VAS breathlessness score during the last 3 min of the exercise tests in the nine subjects</th>
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Mean $V_e$ (l/min)

Mean VAS score (mm)
Fig. 2. Group mean levels from all nine subjects: expired ventilation \( \bar{\nu}_E \), visual analogue scale for breathlessness (VAS) and end-tidal \( P_{\text{CO}_2} \) \( \bar{P}_{\text{ET-CO}_2} \) during five exercise tests. Test A, 'high workload' (●); test B, 'low workload' with copy of ventilation of test A (△); test C, 'low workload' only (▲); test D, 'high workload' repeat of test A (■); test E 'high workload' with copy of ventilation of test D (□). See the text for explanation of exercise protocols. Error bars show levels of statistical significance at the \( P=0.05 \) level in terms of Fisher's LSD statistic derived from an analysis of variance; these permit comparison of mean levels both within and between experimental runs.

The level of breathlessness during the high workload exercise with ventilatory copying (test E) was not significantly different from that during the original high workload alone (test D) either for individual results \( (P>0.1 \) by paired \( t \)-test), or for group results.

DISCUSSION

In this study, our normal subjects felt substantially less breathless when a proportion of their ventilation was produced by voluntary effort (copying a ventilatory pattern) than when the same total ventilation was produced in response to the stimulus of exercise. Indeed, extra ventilation produced voluntarily did not add to the breathlessness experienced at a given level of exercise stimulated ventilation. These results are compatible with our previous findings for ventilation produced voluntarily and by \( CO_2 \) stimulation [1]. They suggest that it is driven automatic ventilation, rather than simply the level of ventilation itself, that is important in relation to the sensation of breathlessness.

It could be argued that the act of copying a pattern of ventilation reduces the sensation of breathlessness, perhaps by distracting the subjects' attention. The present study provides evidence against this, since when subjects performed exercise at a high workload, copying the ventilation of a previous exercise at a high workload, they did not indicate less breathlessness than during the initial exercise. Although most of the subjects reported that they found the ventilatory copying difficult, they were nonetheless satisfied that they had recorded their breathlessness appropriately on the scale. It is possible that the voluntary copying of a higher ventilation than necessary (test B) may have felt qualitatively different from the voluntary copying of an appropriate level of ventilation (test E). Some subjects commented that the copying in test E felt 'easier', but none of them became aware why this was so.

Confusion sometimes arises in the literature because of the different respiratory sensations considered as breathlessness, or related to breathlessness. Most subjects, and certainly respiratory patients, know quite well what is meant by the term 'breathlessness' and need no further explanation. If further description is required, the subject is reminded of the 'common feeling of being short of breath, such as you may get with exercise, say running for a bus' [7]. Previous work suggests that subjects can be aware of respiratory loading but distinguish this from breathlessness [8]. In this study, when the subjects were exercising at the low workload and copying the high workload ventilation they were aware of their ventilation being 'too high' for their requirements. They said they felt they were 'breathing more than I needed to'. However, this awareness of 'higher than necessary' ventilation was quite distinct from the sensation of breathlessness. Some subjects expressed surprise and puzzlement because they had been breathing at a level that they usually associated with quite marked breathlessness, yet had felt very little breathlessness. Presumably, afferent information from the respiratory muscles (or efferent traffic to these muscles) is a whole at any single time point. This was because of the large inter-subject variability in VAS scores (see Table 1) which resulted in a very large LSD. There was no significant difference between the amount of breathlessness recorded during the low workload with a copy of the higher ventilation (test B) and that recorded during low workload alone (test C) for either individual.
compared with the stimulus to breathe from exercise (albeit poorly understood) is involved in this feeling of the 'appropriateness' of the level of ventilation to requirements. But this is apparently quite separate from the sensation of breathlessness.

Previous work has suggested that it is the resulting ventilation, rather than the level of the stimulus (of hypercapnia or hypoxia) itself, that is more closely linked to the sensation of breathlessness [1]. If it is assumed that these previous results apply to ventilation stimulated by exercise, we are left with the conclusion that breathlessness may be related to the motor output to the respiratory muscles resulting from reflex stimulation of the medullary respiratory centres rather than to the respiratory motor output resulting from volitional cortical activity.

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REFERENCES