

## RAPID COMMUNICATION

### Fixed Breathing Frequency Decreases End-Tidal $P_{CO_2}$ in Humans

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#### Summary

We tested the effect of a fixed breathing frequency on the partial pressure of  $CO_2$  in the end-tidal air ( $PET_{CO_2}$ ) in resting healthy subjects. In the first experiment, three different rates of breathing were dictated: the same frequency of breathing as the subject's control one ( $1f$ ), a double frequency ( $2f$ ), and half of the control frequency ( $0.5f$ ). 10 min dictate of  $1f$  and  $2f$  induced a decrease of  $PET_{CO_2}$ . The dictate of  $0.5f$  had no significant effect on  $PET_{CO_2}$ . In the second experiment,  $1f$  was dictated for 30 min, inducing a decrease of  $PET_{CO_2}$  throughout the duration of the dictate. These results demonstrate that fixing the breathing frequency by the dictate affects the chemostatic control of ventilation.

#### Key words:

Control of breathing – Dictate of breathing frequency – Hyperventilation

#### Introduction

The primary role of breathing is lung ventilation. Breathing is also involved in behavioural acts, like phonation or sniffing, as well as in other activities which include the participation of respiratory muscles, like posture maintenance or locomotion. Demands related to these activities may possibly be competing.

Under basal conditions (general anaesthesia, slow wave sleep) breathing is regulated so as to maintain an adequate supply of oxygen and to prevent accumulation of carbon dioxide. During wakefulness, other influences contribute to the drive for breathing and the chemical control becomes less rigid (von Euler 1986).

The chemostatic control is clearly modified during voluntary hypo- or hyperventilation or during speech (Bunn and Mead 1971, Phillipson *et al.* 1978). In these situations, both tidal volume and breathing frequency are controlled by a nonhomeostatic mechanism. We wanted to find out, whether chemoregulation will maintain normal  $P_{CO_2}$  when confronted with nonhomeostatic control of the breathing frequency i.e. only one of these variables. Therefore, we studied the effect of a controlled frequency of breathing on the partial pressure of  $CO_2$  in the end-tidal air ( $PET_{CO_2}$ ).

## Methods

**Subjects:** 31 volunteers were examined in the study (mean age 34 years, range 20 to 60 years, 18 males and 13 females). All subjects reported having no respiratory impairment. Mean height in men was 183.3 cm and mean weight 77.8 kg, whereas 167.4 cm and 67.1 kg in women.

**Measurements:** the air was sampled continuously with a small tube at the nose opening through an infrared gas analyzer (Jaeger CO<sub>2</sub> Test). From the record, the breathing frequency and the PETCO<sub>2</sub> were measured.

**Dictating the breathing frequency:** Prior to the study the subject was instructed to breath in after each beep of a computer (IQ 151). The computer programme allowed to produce three different frequencies of beeps: a) identical with the control frequency of each subject measured during spontaneous breathing (*1f*), b) one half of the control frequency (*0.5f*), c) twice the control frequency (*2f*).

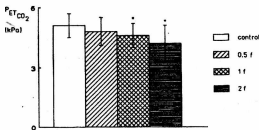
**Protocol:** the subject was seated in a comfortable chair in a quiet room. The room temperature remained constant at 22 °C. The subjects did not eat, drink or smoke for 2 h prior to the study. The sampling tube was positioned, and the subject rested for 15 min. The control measurements were taken (three measurements during 10 min) and the control frequency was calculated. In the first experiment (12 subjects) three different frequencies, namely *1f*, *0.5f* and *2f* were then dictated by regular beeps of the computer in a random order, each for 10 min. Between the runs, 15 min of spontaneous breathing were allowed. In the second experiment (25 subjects), the control measurement was followed by dictating the frequency of breathing identical with the subjects control one for 30 min. PETCO<sub>2</sub> was measured in the 1st, 5th, 10th, 20th and 30th min of the dictate and in the 1st and 5th min after stopping the dictate, when spontaneous pattern of breathing was resumed.

**Statistical evaluation:** Analysis of variance and paired t-test were used to evaluate our data.  $P < 0.05$  was considered significant.

## Results

### PETCO<sub>2</sub> during controlled frequency at different rates

The dictate of frequency of breathing identical with the control one and the dictate of twice of the control frequency were followed by a decrease of PETCO<sub>2</sub> (Fig. 1). When the frequency of one half of the control frequency was dictated, the PETCO<sub>2</sub> did not change significantly.

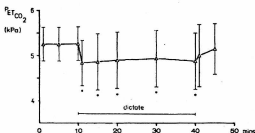


**Fig. 1**

End-tidal PCO<sub>2</sub> during control breathing (control) and different dictated breathing frequencies. *1f* = the same as control; *0.5f* = half and *2f* = twice the control rate of breathing. Means  $\pm$  S.D. are given. \*  $p < 0.05$  compared to control breathing (paired t-test).

*Dictate of breathing frequency identical with the control one.*

During the 30 min lasting dictate of frequency, identical with the control one, the  $P_{ETCO_2}$  declined (Fig. 2). When the dictate stopped and spontaneous breathing was resumed, the frequency of breathing decreased and  $P_{ETCO_2}$  started to return to its control value. Mean value of the breathing frequency during control breathing and during dictate was  $17.4 \text{ c.min}^{-1}$ , one min after resuming the spontaneous breathing it was  $14.4 \text{ c.min}^{-1}$  ( $p < 0.05$ ).



**Fig. 2**

End-tidal  $P_{CO_2}$  during the control period of breathing, during breathing with frequency dictated at the same rate as in the control period (dictate) and during recovery. Means  $\pm$  S.D. are given. \*  $p < 0.05$  compared to control breathing.

## Discussion

We attempted to test the role of the chemoreceptive feedback mechanism in the regulation of breathing during voluntary control of the breathing frequency. To evaluate efficacy of this feedback, we measured  $P_{ETCO_2}$  when the frequency of breathing was dictated. A change of  $P_{ETCO_2}$  during the dictate signalled that the chemoregulation was unable to adjust the alveolar ventilation so as to maintain constant  $P_{CO_2}$ .

In our first experiment, such adjustment could have been achieved by only small changes of ventilation. Assuming an unchanged dead space during the dictate, a decrease of tidal volume to 65 % of its control value would keep alveolar ventilation constant when the rate of frequency was doubled. Thus the decrease of  $P_{ETCO_2}$  in this case suggests that the chemical control was overruled by other influences. The hyperventilation with the dictate of a high frequency was reported earlier (Feitová and Novák 1982). We were surprised by the decrease of  $P_{ETCO_2}$  during the dictate of *If*. This hyperventilation lasted throughout the 30 min duration of the dictate without a sign of normalization of the  $P_{ETCO_2}$ .

Dictate of the *If* could affect the breathing in two ways: by its behavioural effect (sensory stimulation, increased mental activity), or by stabilizing the duration of the cycle. It is well known that during resting breathing the duration of cycle is not absolutely stable but there occur some oscillations (Gardner 1977). By dictating

the onset of inspiration we might have blocked these oscillations. However, the view that the increase of ventilation is mainly due to the behavioural effect of the dictate is supported by observations of changes in the pattern of breathing and ventilation during mental activity (Golla and Antonovich 1929), opening of eyes (Asmussen 1977) or during visual or auditory stimulation (Shea *et al.* 1987).

Shea *et al.* (1987) quantified the effect of short lasting (5 min) visual and auditory stimulation on the breathing pattern. They found that both stimuli increased ventilation by approximately 6 %. This increase was due to an increase in the rate of breathing only. Comparing their and our results one can hypothesize that the changes of mental activity increase the respiratory drive. The increased drive causes primarily an increase of breathing frequency. When the changes of frequency are blocked (dictate), other changes, possibly those of the tidal volume, occur.

In our study, the  $PET_{CO_2}$  during dictate of *If* decreased by 10 %. This means that the same relative change of alveolar ventilation took place. With the frequency unchanged, either an increase of tidal volume or a decrease of dead space could be responsible. We have no data to support either of these possibilities, but the increase of tidal volume seems more likely.

What caused the presumed increase of ventilatory drive during the dictate is unclear. From the point of view of the importance of the chemostat, two explanations are possible: 1) the chemical control was during the dictate overruled by non-chemical control; 2) the chemostatic reference point was set to a lower  $P_{CO_2}$  during mental activity (especially when it is concerned with breathing) and, therefore,  $PET_{CO_2}$  was maintained low.

The decrease of  $PET_{CO_2}$  during the fixed frequency of breathing shows that in awake human subjects the non-chemostatic control of breathing frequency can induce changes of alveolar ventilation. This means that control of the arterial  $P_{CO_2}$  is weaker than it has often been implied.

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