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COMPARATIVE INFLUENCE OF PROPRIOCEPTORS AND CHEMORECEPTORS IN THE CONTROL OF RESPIRATORY MUSCLES

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Abstract. Previously we have demonstrated that continuous positive pressure breathing (PB) depresses diaphragm activity and excites expiratory activity in the abdominal muscle (AMR) via vagal proprioceptive impulses. During prolonged PB the AMR persists at a constant level whereas inhibition of the diaphragm wanes, possibly as a result of CO_2 retention. This study measures CO_2 retention during PB and compares the responses of the abdominal muscle and diaphragm to chemostimulation alone and to chemostimulation and PB in combination. Continuous recordings of minute ventilation, integrated EMGs of the diaphragm and abdominal muscle, and mass spectrometer analysis of airway gases were obtained during PB on air, 5.25% CO_2 and 12.4% O_2 in eight Dial-anaesthetized cats. Between 0 and 15 cm H_2O the steady-state end-tidal CO_2 rises about 0.6 mm Hg/cm H_2O, diaphragm activity decreases and AMR increases exponentially with each increment in PB. When 5.25% CO_2 is inspired, diaphragm activity is augmented at every pressure suggesting algebraic summation of proprioceptive and chemoreceptive effects at the respiratory centre. In contrast, the AMR is not significantly altered by hypercapnia. The absence of all abdominal muscle expiratory activity after bilateral vagotomy suggests that the role of active expiration is to regulate thoracic-lung volume, not blood gases.

INTRODUCTION

Previous investigations from this laboratory have elucidated some of the proprioceptive neural mechanisms by which reflex expiratory activity is initiated in the abdominal muscles of cats whenever expiration is opposed (Bishop 1963, 1964, 1967, 1968*ab*, Bishop and Bachofen 1971). The abdominal muscles are the major expiratory muscles of the body

and yet they ordinarily do not participate in quiet breathing. To study their expiratory activity in an anaesthetized animal it is necessary to compromise ventilation in order to activate them. One reliable way of evoking active expiration is to oppose expiration by elevating airway pressure (Bishop 1967). Figure 1 shows sample traces of diaphragm and abdominal muscle responses during continuous positive pressure breath-

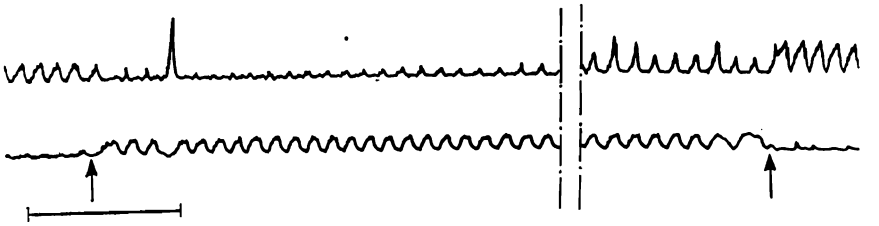

Fig. 1. Integrated electromyograms recorded from the slip of the diaphragm (upper trace) and the external oblique abdominal muscle (lower trace) before, during (between arrows) and after +10 cm H_2O continuous pressure breathing. Note that the diaphragm is initially suppressed but its activity gradually returns whereas abdominal muscle expiratory activity remains constant throughout the elevated pressure. The time mark indicates 30 sec. Two min have been removed where the record is interrupted.

ing. The integrated electromyogram of the abdominal muscle (lower trace) is silent at the outset before pressure breathing. With the onset of pressure breathing (at the arrow), the abdominal muscle becomes active on the first expiration. It discharges at essentially the same level of electrical activity during each successive expiration until pressure breathing is terminated.

In contrast, the diaphragm is initially depressed by the elevated pressure, but it gradually resumes its inspiratory discharge in spite of the maintained elevation of intrapulmonary pressure. Presumably the initial inhibition of the diaphragm at the onset of pressure breathing is due to the Hering–Breuer inflation reflex (Widdicombe 1954, Aviado and Schmidt 1955). Bilateral vagotomy abolishes both the initial inhibition of the diaphragm and the expiratory response of the abdominal muscles, suggesting the important role of the lung proprioceptors in these reflex responses (Bishop 1964).

In Fig. 2 the diaphragm discharge at the onset of positive pressure breathing is compared with that after several minutes of pressure breathing when a new steady state has been established. The length of the arrows indicates the extent of the increase in the electrical activity of the diaphragm during three levels of sustained pressure breathing. It is not known whether this increase in diaphragm activity during prolonged

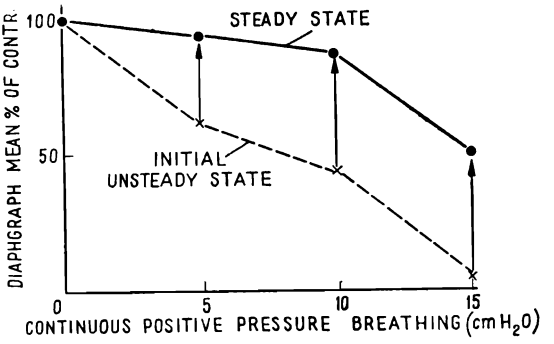

Fig. 2. Initial and steady-state amplitudes of the integrated EMGs of the diaphragm (ordinate) expressed as mean percentage of the amplitude during quiet air breathing just prior to onset of pressure breathing (abscissa).

pressure breathing is due to chemostimulation or adaptation of the pulmonary stretch receptors. Whichever the explanation, the abdominal muscles appear to escape the influence.

Figure 3 shows that the abdominal muscle activity during steady-state conditions of pressure breathing is not different from that during the initial period of pressure breathing. This constancy of the abdominal

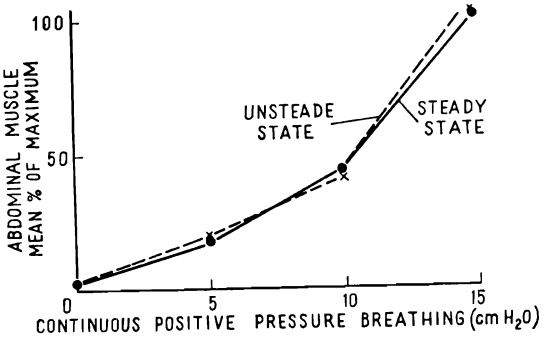

Fig. 3. Initial and steady-state amplitudes of the integrated EMGs of the abdominal muscle expiratory activity expressed as mean percentage of the maximal response to pressure breathing.

muscle activity for the whole period of pressure breathing suggests that the expiratory neurons in the brain stem which drive the expiratory activity of the abdominal muscles must receive different sensory inputs than the inspiratory neurons driving the phrenic motoneurons (Woldring 1965, Fenley et al. 1971).

One purpose of the present study was to determine whether or not continuous positive pressure breathing causes CO_2 retention. Another

purpose was to compare the responses of the diaphragm and abdominal muscle to chemostimulation alone and to chemostimulation and pressure breathing in combination.

METHODS

To obtain the data eight adult cats were anaesthetized with an i.p. injection of Dial (Ciba; 0.6 cc/kg of body weight) and their tracheas were cannulated. The methods have been described in detail previously (Bishop and Bachofen 1971). Bipolar needle electrodes, inserted into the diaphragm at its attachment to the xyphoid process and into the exposed external oblique abdominal muscle, detected the muscle action potentials which were recorded as the integrated electromyograms after amplification and averaging by a Grass EMG differential amplifier (Model 5P3). Airway gas was continuously sampled from the tracheal cannula for instantaneous mass spectrometer analysis (Model MS4, Associated Electrical Industries, Ltd., Manchester, England).

The animal breathed through a two-way valve connected to the tracheal cannula. The inspiratory side of the valve was connected to a Fleisch-type pneumotachograph (Fleisch 1956). The differential pressure signals from the flowmeter were amplified and integrated with an operational amplifier (Model UPA2, Philbrick Research Inc., Boston, Mass.) and recorded directly to provide respiratory minute volume. The pneumograph was, in turn, connected via a three-way stopcock to a 20 litre balloon slung in a rigid 20 litre bottle. The expiratory side of the breathing valve was connected to a 200 litre pressure reservoir via a three-way stopcock. The pressure reservoir and rigid bottle were in open connection so that it functioned as a simple bag-in-box system. Pressure in the system was maintained at any desired level by a Fischer valve (type R 230; Fischer Governor, Marshalltown, Iowa). The flaccid balloon could be filled with any desired inspired gas.

RESULTS AND DISCUSSION

All levels of continuous positive pressure breathing always depressed ventilation. In Fig. 4 the abscissa indicates the reservoir pressure during continuous pressure breathing and the ordinate indicates the mean steady-state ventilation expressed as the percentage of the control ventilation on air just prior to pressure breathing. When air was the inspired gas (filled circles) the ventilation was depressed in direct proportion to the elevation of the pressure. Most of this ventilatory depression was due to a reduction in tidal volume (Bishop 1967, Bishop and Bachofen 1971).

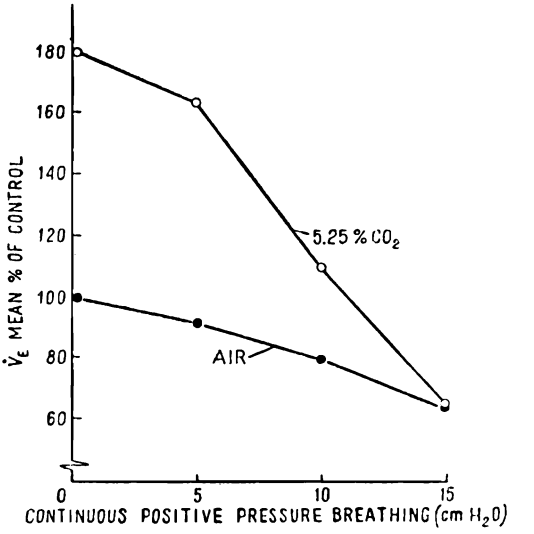

Fig. 4. Minute ventilation, expressed as mean percentage of ventilation while breathing air just prior to onset of pressure breathing, at three levels of pressure breathing. Inspired gas was either air (filled circles) or 5.25% CO_2 in air (open circles).

Rate of breathing may or may not be slowed by continuous pressure breathing.

The consequence of the depressed ventilation is, of course, a rise in end-tidal CO_2. The filled circles of Fig. 5 show the mean steady-state, end-tidal CO_2 during three levels of pressure. The slope of this curve is about 0.6 mm Hg/cm H_2O.

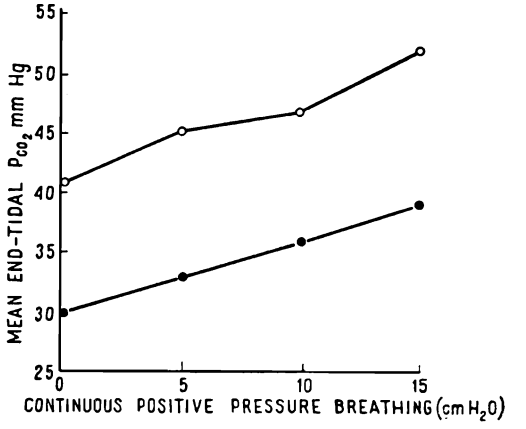

Fig. 5. Rise in mean end-tidal CO_2 tension in mm Hg at ambient pressure (0 cm H_2O) and at 3 levels of pressure breathing on air (filled circles) and on CO_2 (open circles).

Many factors contribute to this CO_2 retention of pressure breathing. Several investigators have shown that the elastic work of breathing is increased during pressure breathing (Fenn 1951, Marshall 1962, Widdicombe and Nadel 1963). Increased work, of course, causes an increased CO_2 production. The efficiency of breathing is reduced due to the hyper-

inflation of the chest and lungs. In addition, the elevated intrapulmonary pressure serves as a cardiac tamponade impeding venous return (Maulsby and Hoff 1962) and reducing stroke volume (Cain and Mahoney 1953, Bishop 1968*b*). The distribution of pressures between the thoracic and abdominal cavities are altered by the elevated intrapulmonary pressure (Bjurstedt and Hesser 1953, Bishop 1963). The effects of these mechanical disturbances are marked alternations in the distribution of ventilation and perfusion (Barer and Nüser 1957, Bergman 1963). In fact, Folkow and Pappenheimer (1955) demonstrated that both the series and parallel components of dead space were increased during pressure breathing in cats.

Thus, it becomes apparent that the reflex responses of the respiratory muscles (Fig. 1) in responses to continuous positive pressure breathing do not fully compensate for the imposed stress.

When the inspired gas was changed from air to 5.25% CO_2 in air and was breathed at ambient pressure, every animal increased its ventilation by increasing rate and depth of breathing, showing that the anaesthetic had not interfered with the chemoreflexes. The major increase in depth of breathing was achieved primarily by augmented activity of the diaphragm with little or no active expiration. Only two of the eight cats tested showed any expiratory activity in the abdominal muscle while breathing the 5.25% CO_2 and this activity was only about 10–15% of the maximal response to pressure breathing.

The open circles of Fig. 4 and 5 show mean percentage ventilation and mean end-tidal CO_2 while breathing 5.25% CO_2 at ambient pressure (0 cm H_2O) and at three levels of continuous positive pressure breathing. Although mean ventilation was augmented 80% (range of increase 30 to 110%) by the addition of 5.25% CO_2 to the inspired mixture, this facilitation of ventilation by the CO_2 is lost during 15 cm H_2O pressure breathing. It is as if the physiological stress imposed by the elevated intrapulmonary pressure completely overrides the chemo-stimulation of ventilation caused by the hypercapnic inspired mixture. Even though minute ventilation is the same at 15 cm H_2O pressure regardless of the inspired mixture, it is important to note that this ventilation is achieved by different patterns of activity in the diaphragm and the abdominal muscle as shown by Fig. 6. All levels of pressure breathing on air (filled circles) depress the steady-state activity of the diaphragm (upper graph) as indicated by the hatched area. All levels of pressure breathing on 5.25% CO_2 (open circles) augment diaphragm activity. It is as if the CO_2 chemostimulation of the inspiratory neurons overrides the inhibitory Hering-Breuer influences at every pressure. In contrast, the activity of the abdominal muscle (lower graph of Fig. 6) in response to positive pressure is the same whether the inspired gas is air or 5.25% CO_2. This independ-

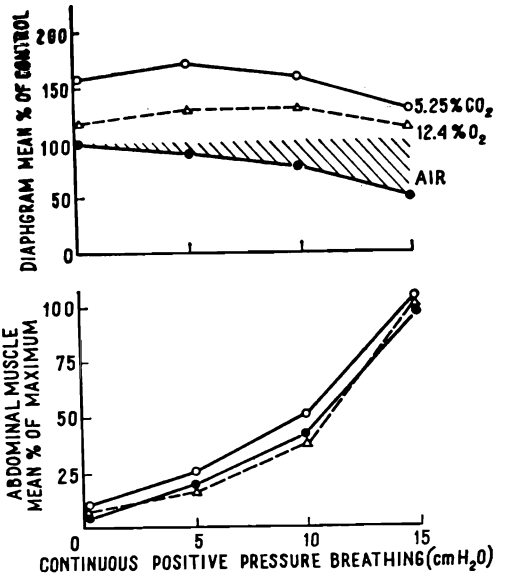

Fig. 6. Comparison of steady-state diaphragm (upper graph) and abdominal muscle (lower graph) responses to continuous positive pressure while breathing air (filled circles), 5.25% CO_2 (open circles) or 12.4% O_2 (open triangles).

ence of the abdominal muscle response from the composition of the inspired gas suggests that the expiratory neurons are spared information concerning the CO_2 tension of the blood.

In another series of experiments the effects of an inspired mixture of 12.4% O_2 in N_2 were determined. Although the hypoxia produced by this mixture was insufficient to alter significantly the minute ventilation, it did cause an increase in diaphragm activity at all levels of pressure breathing as shown by the open triangles in the upper graph of Fig. 5. This augmentation of diaphragm activity by the hypoxic mixture is probably a reflex response initiated by the peripheral chemoreceptors, the only receptors known to respond to low arterial oxygen tensions (Torrance 1968). The open triangles in the lower graph of Fig. 6 show that the expiratory activity of the abdominal muscle at any level of pressure was not modified by the hypoxic mixture. From these observations we have concluded that the peripheral chemoreceptors must project far more effectively to inspiratory than to expiratory neurons. Additional evidence to support this conclusion was the abolition of the expiratory reflex of the abdominal muscles by bilateral vagotomy. In the absence of the facilitation from vagal proprioceptive impulses, chemostimulation, alone, never excited active expiration.

Following vagotomy pressure breathing, of course, no longer inhibited diaphragm activity. In the absence of the Hering–Breuer inflation reflex diaphragm activity was increasingly augmented, rather than suppressed, with each increment in intrapulmonary pressure. Ordinarily chemostimu-

lation of the inspiratory neurons is held in check by the proprioceptive inhibition from pulmonary stretch receptors.

By way of summary this study has shown that pressure breathing in the anaesthetized animal depressed minute ventilation causing a rise in CO_2. The gradual rise of diaphragm activity during a prolonged period of pressure breathing (Fig. 1 and 2) mirrored the rise in end-tidal CO_2 suggesting a chemo-facilitation of central inspiratory neurons. In addition, during pressure breathing on the hypercapnic or hypoxic mixture the diaphragm activity was always augmented at any pressure as compared to its activity during comparable pressure breathing on air (Fig. 5). Following vagotomy pressure breathing always augmented diaphragm activity indicating that central inspiratory neurons had been released from inhibitory restraints imposed by the pulmonary proprioceptors.

In contrast, the expiratory activity of the abdominal muscles was activated on the first expiration of pressure breathing and continued at a near constant level for the entire period of pressure breathing (Fig. 1 and 3). Furthermore, the expiratory activity of the abdominal muscle during pressure breathing was similar whether the inspired mixture was air, 5.25% CO_2 or 12.4% O_2. Vagotomy abolished expiratory activity in the abdominal muscles suggesting that without the proprioceptive facilitation from vagal afferents the central expiratory neurons are inexcitable by chemostimulation alone.

The observations of these experiments indicate that there are two independent but parallel control circuits regulating respiration. One regulates ventilation in such a way as to maintain the pH and pressures of CO_2 and O_2 of arterial blood nearly constant despite variations imposed by metabolism or environment. It is obvious from the present study that the chemoreceptors and the inspiratory neurons controlling the diaphragm comprise one of the major loops of this control circuit. In contrast, the expiratory neurons driving the abdominal muscles, seem to play a minor role, if any, in the regulation of the blood gases since their excitability is essentially independent of chemostimulation.

The second control circuit regulates ventilation in such a way as to maintain optimal efficiency of the respiratory muscles. The proprioceptive feedback carried by the vagal nerves activates expiratory activity in the abdominal muscles and depresses the diaphragm. These responses during pressure breathing serve to counteract the imposed lung inflation. The results of this study suggest that the pulmonary proprioceptors and their target expiratory neurons which drive the abdominal muscle expiratory activity comprise one of the major loops in this second control circuit for regulating thoracic-lung volume.

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