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FUNCTIONAL CHARACTERISTICS OF SLOWLY ADAPTING PULMONARY STRETCH RECEPTORS IN THE TURTLE (*CHRYSEMYS PICTA*)

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SUMMARY

1. Single nerve fibre discharge has been recorded from slowly adapting pulmonary stretch receptors in single-pithed turtles on artificial ventilation.

2. Receptor discharge during static and dynamic lung inflations showed that lung volume was the major stimulus of these receptors. The rate and degree of change in transpulmonary pressure were without direct effect.

3. The response of these receptors to static and dynamic lung inflation differed only quantitatively from those of bronchopulmonary stretch receptors in mammals. The lower discharge frequencies and sensitivities of the turtle receptors may arise from the low body temperature of these animals.

4. The sensitivity of turtle pulmonary receptors to CO_2 was greater than that recorded for bronchopulmonary receptors of mammals although the effects of CO_2 on receptor discharge were qualitatively similar. In several instances, receptor discharge was totally inhibited throughout the ventilatory cycle by inflation with 5–10% CO_2 in air.

INTRODUCTION

The classic study of mammalian pulmonary receptors by Adrian (1933) differentiated two discharge patterns, one elicited by lung inflation and one by deflation. In later work (Knowlton & Larrabee, 1946; Larrabee & Knowlton, 1946) responses from pulmonary endings were differentiated by their adaptation rate during maintained inflation and their threshold to stimulation as rapidly and slowly adapting. Knowlton & Larrabee (1946) found that the rapidly adapting inflation sensitive receptors also fired during lung deflation. More recently Paintal (1955) identified units which only responded to deflation. There are now considered to be three basic types of pulmonary receptors; slowly adapting pulmonary stretch receptors; irritant receptors (rapidly adapting tracheal receptors), and J receptors (deflation receptors) (Paintal, 1973). Recent examinations of the location and functional characteristic of the slowly adapting stretch receptors, however, indicate that distinct populations of tracheal and bronchial (intrapulmonary) receptors with different response characteristics may exist (Miserocchi, Mortola & Sant'Ambrogio, 1973; Bartlett & Sant'Ambrogio, 1976; Bradley & Scheumier, 1977).

These receptors are the afferent limb of a series of vagal respiratory reflexes and

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were claimed to be insensitive to both O_2 and CO_2 levels in the respiratory tract (Adrian, 1933; Larrabee & Knowlton, 1946). In the past few years the CO_2-sensitivity of pulmonary receptors has been reinvestigated and receptors, whose discharge is affected by CO_2 levels in the airways, have now been demonstrated in a variety of animals. Birds possess intrapulmonary chemoreceptors having no apparent mechanosensitivity but responding solely to changes in airway CO_2 concentrations throughout the breathing cycle (Fedde & Petersen, 1970; Osborne & Burger, 1974; Fedde, Gatz, Slama & Scheid, 1974*a*, *b*). Similar receptors have been described in the lizard (Fedde, Kuhlman & Scheid, 1977). The discharge of slowly adapting pulmonary stretch receptors in cats, dogs and rabbits is partially modified by the level of alveolar CO_2 (Mustafa & Purves, 1972; Schoener & Frankel, 1972; Bartoli, Cross, Guz, Jain, Noble & Trenchard, 1974; Sant'Ambrogio, Miserocchi & Mortola, 1974) as is the discharge of bronchial stretch receptors in the extrapulmonary airways of the dog (Bartlett & Sant'Ambrogio, 1976). The effect of CO_2 on pulmonary receptor discharge in the bird is a major, if not dominant factor in the regulation of avian respiration (Kunz & Miller, 1974*a*, *b*). Although not a major factor in control of mammalian respiration, the effect of CO_2 on the discharge of mammalian pulmonary receptors does account for a vagally mediated tachypnoeic response to inhaled CO_2 (Mustafa & Purves, 1972; Bartoli *et al.* 1974; Bradley, Noble & Trenchard, 1976).

Recently there have been preliminary observations of slowly adapting pulmonary stretch receptors in turtles (Milsom & Jones, 1976) and lizards (Fedde *et al.* 1977) which are typically mechanosensitive but which exhibit a range of variation in their sensitivity to CO_2 which encompasses the different sensitivities to CO_2 found in the avian and mammalian receptor types. As a consequence, the role of lung afferents in controlling breathing in reptiles is of interest because the stimulus modalities may change independently of one another to give potentially conflicting afferent information. However, before the role of these receptors in breathing can be studied it is necessary to carefully characterize them. The present study was undertaken to provide a detailed analysis of the static and dynamic characteristics of slowly adapting stretch receptors in the turtle and the effects of changes in airway CO_2 concentrations on receptor response.

METHODS

Experiments were done on thirty turtles (*Chrysemys picta*, body mass 0·5–1·5 kg), single-pithed and restrained in a ventral position at room temperature (22–23 °C). A pneumotachograph with a side arm for tracheal pressure measurement and gas sampling was attached to a tracheal cannula inserted as low in the neck as possible. The distal end of the tracheal cannula was attached to a constant volume positive pressure respiration pump for tidal ventilation. A catheter was inserted into the abdominal cavity through a hole drilled in the carapace and was sealed in place with dental acrylic cement. Intratracheal pressure (P_{it}), taken as an index of intrapulmonary pressure, and intra-abdominal pressure (P_{ia}) were measured with Statham P23V pressure transducers (Statham Instruments Inc., Oxnard, Cal., U.S.A.). Since turtles possess a pleuro-peritoneal cavity, the difference between abdominal cavity pressure and tracheal pressure, measured by a Hewlett–Packard 267 BC differential pressure transducer (Hewlett–Packard Co., Colorado Springs, Colo., U.S.A.) is the transpulmonary pressure (P_{tp}). The pressure across the pneumotachograph screen during tracheal air flow was measured with a Hewlett–Packard 268 BC differential pressure transducer and this air flow signal was fed into a Hewlett–

Packard 350–3700 A integrating preamplifier to give tidal volume. All measurements, pressures, flow and volume were continuously recorded on magnetic tape and displayed on a Sanborn 4 channel chart recorder writing on rectilinear co-ordinates. The O_2 and CO_2 composition of inspired and expired gases was determined either on samples taken through the side arm of the pneumotachograph and measured on a Fisher–Hamilton gas partitioner (Fisher Scientific, Boston, Mass., U.S.A.) or by continuous sampling with a Centronic 200MGA clinical mass spectrometer (Twentieth-Century Electronics Limited, New Addington, Croydon, England).

Either the right or left vagosympathetic nerve was cut high in the neck, dissected free of surrounding tissue and placed on a dissection platform. Small filaments were dissected from the distal cut end of the nerve and single unit action potentials from slowly adapting stretch receptors were recorded by conventional means using bipolar silver electrodes. This activity was amplified, monitored with an oscilloscope, audio-amplifier and instantaneous rate meter, and recorded on magnetic tape.

Location of pulmonary receptors

Receptor discharge was attributed to pulmonary stretch receptors if the discharge was modulated by artificial ventilation, unaffected by pulmonary artery occlusion and was slow or non-adapting during maintained lung inflation. For confirmation, the precise locations of seventeen slowly adapting stretch receptors were further determined in ten turtles. The chest of these animals was opened by removal of the carapace using a necropsy saw and the lungs were exposed by surgical removal of all obstructing viscera. While the activity of each receptor was being monitored, its longitudinal and circumferential position within the lung was determined by gentle probing with a fine bristle. For nine of these units, conduction velocities were also measured from photographic records of evoked potentials during simultaneous stimulation with two pairs of stimulating electrodes placed 0·5 cm apart on the pulmonary vagus where it emerged from the lung.

Experimental protocol

While monitoring the discharge of each receptor, the turtles were ventilated with a Harvard positive pressure respirator (Harvard Inc., Millis, Mass., U.S.A.), using mixtures of humidified air containing 0, 5 or 10% CO_2 at pump frequencies from 3 to 20/min and tidal volumes of 10–50 ml. The pump was stopped to give either maintained deflation of the lungs equilibrated to atmospheric pressure or inflation at various volumes. The rate of inflation to, or deflation from these volumes was altered by changing the pump rate along with the pump inflation–deflation phase ratio.

In five animals, the inguinal and cervico-axillary pockets were tightly packed with plasticene and bound with glass reinforced tape which, in conjunction with the shell, rendered the body of the animal inflexible. An adjustable pressure reservoir was connected to the body cavity through a hole drilled in the carapace so that intra-abdominal pressure could be varied at will. The ventilation pump was arranged to give sinusoidal pumping of a fixed volume by connecting the exhaled gas tube to the pump inlet tube. Care was taken to ensure that the first inflation always began from a constant functional residual capacity. By adjuting the volume pumped and/or the intra-abdominal cavity pressure, receptor discharge could be monitored while the peak transpulmonary pressure was varied at any given inflation volume or while the same peak transpulmonary pressure was developed for a variety of inflation volumes.

Measurements and analysis

All data stored on magnetic tape was analysed on a Digital PDP Lab 8e mini-computer using conventional software (Digital Equipment Corp., Maynard, Mass., U.S.A.). From receptor discharge the variables measured were peak inspiratory discharge, end-expiratory discharge and instantaneous discharge rate throughout each breathing cycle. In several instances both time interval histograms and post-stimulus time histograms were constructed from 5 to 10 successive pump cycles to analyse the effects of CO_2 on the relations between instantaneous discharge and inflation volume or pressure throughout the phases of the pump cycle. Lung pressures and volumes were plotted against one another (X–Y plot) on a Hewlett–Packard 1201 A storage

oscilloscope to provide pressure–volume curves for determination of dynamic lung compliance. Also receptor discharge was plotted against the appropriate pressure or volume to observe the degree of hysteresis in the pulmonary receptor discharge versus pressure and versus volume for any ventilation cycle.

RESULTS

(a) *Response of pulmonary stretch receptors to changes in lung volume*

The discharge pattern in sixty-two fibres studied varied from a low threshold pattern (n = 54) lasting throughout the respiratory cycle to a high threshold pattern (n = 8) in which discharge occurred only during inspiration and the early

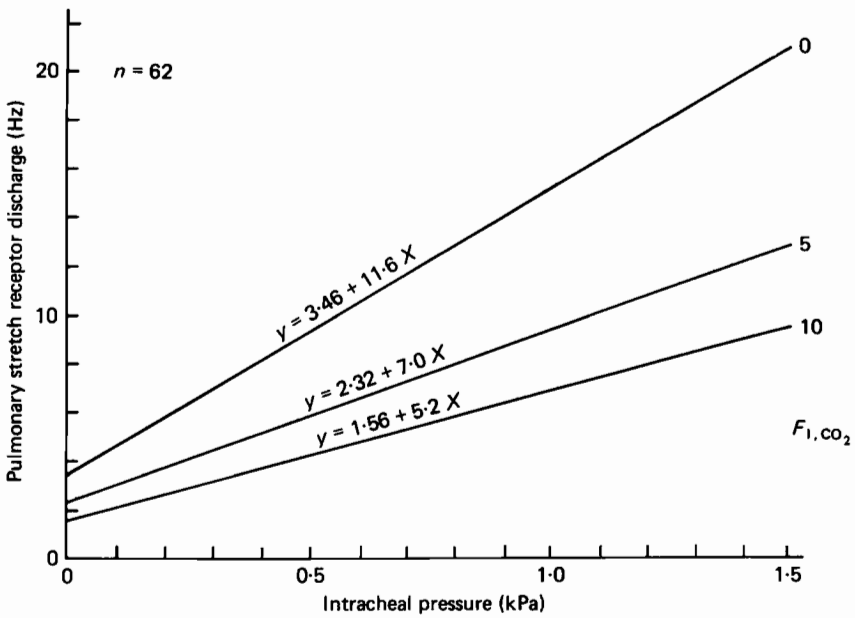


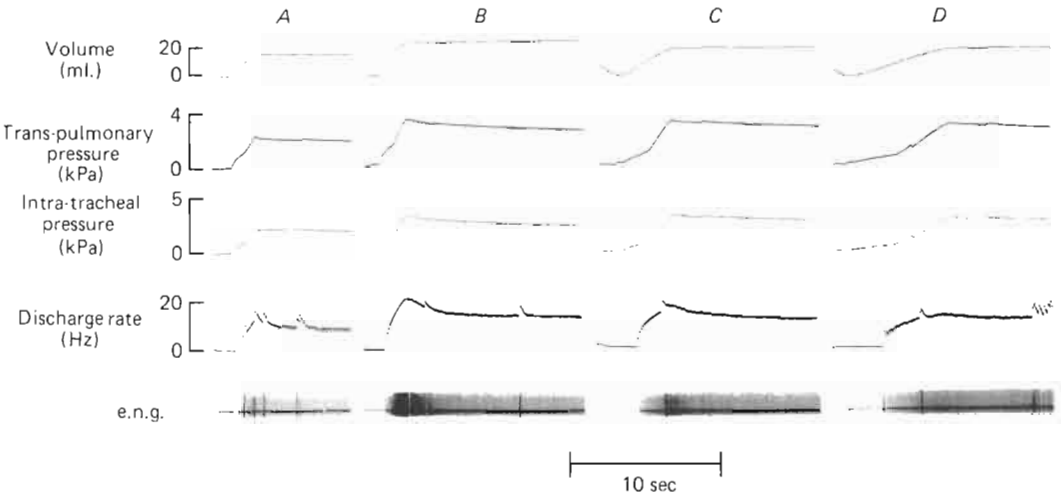
Fig. 1. The effect of changing inspired CO_2 (F_{I,CO_2}) on the relationship between discharge frequency of pulmonary stretch receptors (n = 62) and intratracheal pressure at least 30 sec after completion of inflation to various volumes. Curves and equations are from linear regression analysis of values recorded at three levels of inspired CO_2 (0%, r = 0·64; 5%, r = 0·72; and 10%, r = 0·74).

part of expiration. All fibres exhibited some adaptation to a step change in pressure over a 2 kPa range but the rate of adaptation estimated from Index 1 of Davis, Fowler & Lambert (1956) was always less than 30% (Index 1 = $[(F_1 - F_2)/F_1] \times 100$, where F_1 and F_2 = discharge frequency 1 and 2 sec, respectively, after the end of inspiratory flow during maintained inflation). The conduction velocities of nine of these fibres, at 23 °C, ranged from 3 to 16 m/sec (mean = 7·4) suggesting fibres 3–11 μm in diameter (Erlanger & Gasser, 1937). Seventeen of the receptors were localized, by punctate stimulation, to the main bronchus and internal septa which divide the lung.

The steady discharge of these fibres was measured, after adaptation, in response to maintained lung inflation to various volumes above end-expiratory volume. The

relation between discharge rate and lung volume was linear over the range studied (0–1·5 kPa tracheal pressure) (Fig. 1).

At low inflation volumes there was no difference in the maximum discharge frequency attained whether the lungs were inflated slowly or rapidly. For larger inflation



	Rate of volume increase (ml./sec)	Rate of pressure increase l.t.p. (kPa/sec)	Rate of pressure increase T.p.p. (kPa/sec)	Rate of discharge increase (/sec)	Discharge/unit volume mid-inflation (Hz/ml.)	Discharge/unit pressure mid-inflation (Hz/kPa)
A	11·3	1·2	1·2	10·3	0·76	9·2
B	12·5	1·5	1·5	14·1	0·81	10·5
C	6·3	0·9	0·9	8·0	0·96	11·0
D	3·3	0·4	0·4	4·2	0·83	10·3

Fig. 2. The effect of changing the rate of lung inflation on inflation volume, transpulmonary pressure, intratracheal pressure and the discharge rate and electroneurogram of a single pulmonary stretch receptor. *A* and *B* represent inflations of the same approximate rate but to different maximum lung volumes. *B*, *C*, and *D* are the responses to lung inflations of equal volume at varying rates. The rates of change in volume, pressure and discharge are tabulated beneath with the relative sensitivity (discharge per unit volume or per unit pressure at mid-inflation) of the fibre.

volumes, however, maximum discharge rate was a function of both the rate and volume of inflation (Fig. 2). Despite this, discharge in any given fibre fell to the same level within 5 sec of maintained inflation regardless of inflation rate (Fig. 2*B–D*). Discharge per unit volume or per unit pressure at mid-inflation showed very little rate dependency implying that the graded overshoot in maximal discharge rate seen at different inflation rates was a function of rate dependent changes in lung mechanics. Deflation rate had no effect on end-expiratory discharge rate. The range of inflation and deflation rates used in these tests corresponded to the range found in spontaneously breathing turtles (5–10 ml./sec.kg).

(b) Effect of changing inspired CO_2 concentration on pulmonary stretch receptor discharge

The discharge rate of all fibres during maintained lung inflation to various volumes decreased as the level of inspired CO_2 increased (Fig. 1). The relation between rate of discharge and tracheal pressure remained linear, the greatest changes in receptor discharge occurring over the lower range of airway CO_2 concentrations.

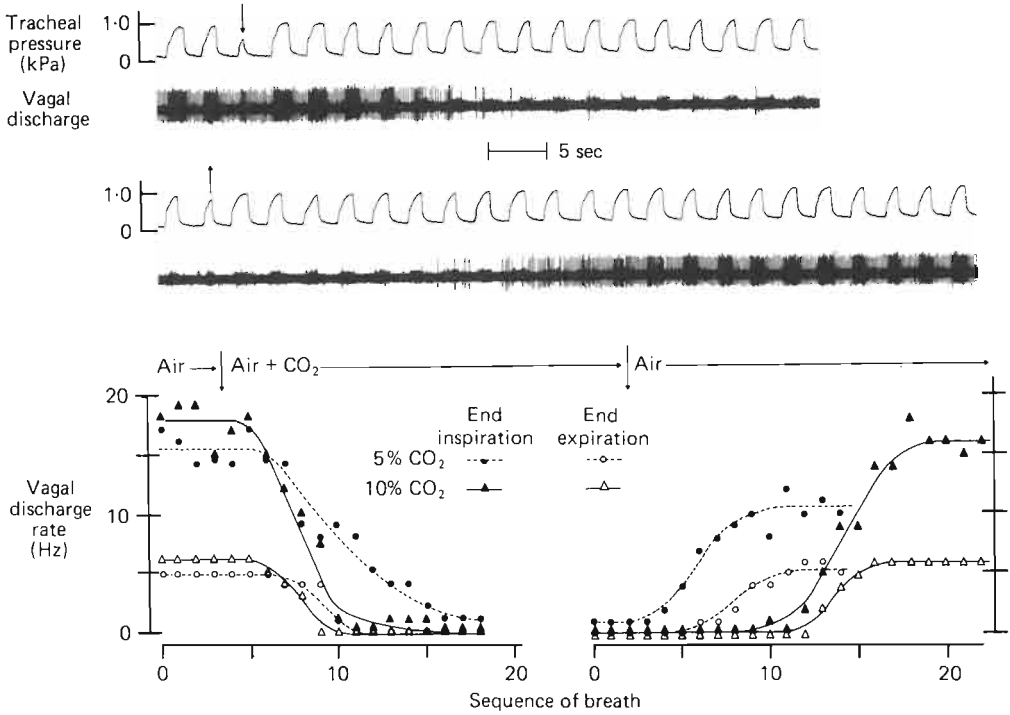


Fig. 3. The time relationship between changes in the level of inspired CO_2 and pulmonary receptor discharge. The upper pair of traces illustrate the effects of introducing 10% CO_2 to the inspired gas and the second pair of traces illustrates the return to ventilation with air. In both pairs of recordings, the top trace is the intratracheal pressure and the lower trace the discharge of a single pulmonary receptor during pump ventilation. The time relationships portrayed below these traces represent the breath by breath end-inspiratory (filled symbols) and end-expiratory discharge (open symbols) of the same receptor following the introduction (arrow, left) and removal (arrow, right) of 5% (dashed lines) and 10% CO_2 (continuous lines) to the ventilatory gas.

When animals were given CO_2 during pump ventilation, a reduction in the rates of peak-inspiratory and end-expiratory discharge were noticeable after two to four ventilation cycles (Fig. 3). As alveolar CO_2 levels rose to a new steady level, there was a progressive reduction in the levels of peak inspiratory and end-expiratory discharge (reduced sensitivity) and in the onset of discharge during inspiration (increased threshold). The rates of decrease in peak-inspiratory and end-expiratory discharge were similar and dependent on the degree of change in inspired CO_2 levels (Fig. 3).

There was a marked depression of activity throughout the entire respiratory cycle in fifty-nine of sixty-two stretch receptors studied. Fig. 4 illustrates the typical effects of CO_2 on one fibre. The time interval histograms represent the discharge profiles of each of eight successive breaths during pump ventilation and the post-stimulus time histograms represent the cumulative average of the discharge

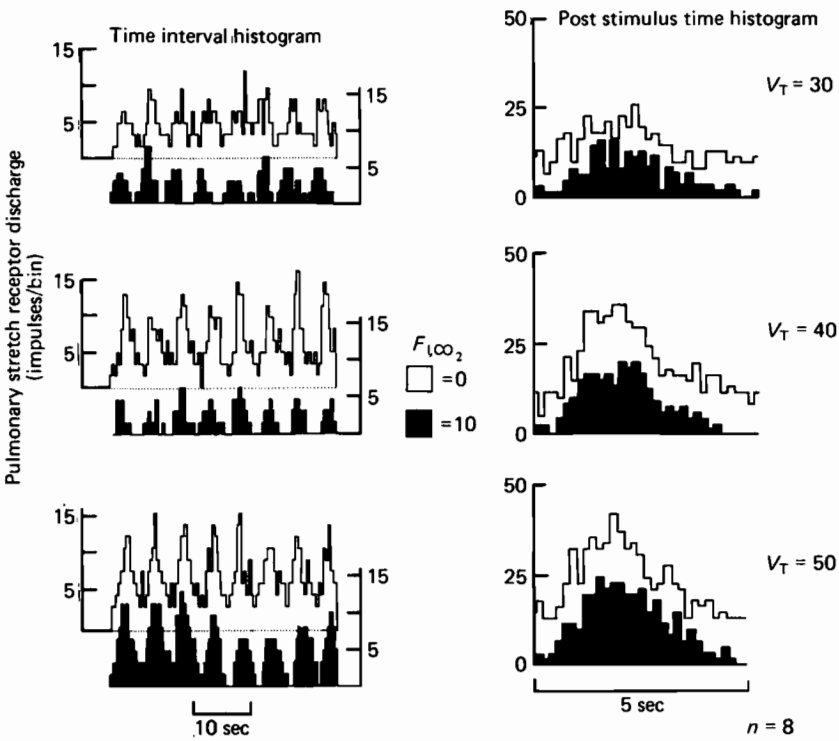


Fig. 4. Effect of changing inspired CO_2 on pulmonary stretch receptor discharge throughout the ventilation cycle. The time interval histograms and post-stimulus time histograms of eight successive breaths are shown at two levels of inspired CO_2 and three levels of inflation volume (V_T). The bin lengths for the time interval histogram were 500 msec, and 150 msec for the post-stimulus time histogram.

during these same eight ventilation cycles portrayed over the time course of a single cycle. It can be seen that CO_2 reduces discharge almost equally throughout all phases of the ventilation cycle regardless of ventilation volume. Fig. 5 shows the relative effect of increasing the inspired CO_2 concentration on the peak-inspiratory and end-expiratory discharge of all fibres studied. There is a large range of variation in response between fibres. As under steady state conditions, the response was most sensitive over the lower range of airway CO_2 concentrations.

Recovery to previous discharge levels on return to breathing room air was much slower than the inhibition of discharge during CO_2 administration (Fig. 3). Recovery rates were inversely related to the CO_2 levels employed and peak-inspiratory discharge rate usually recovered quicker than end-expiratory discharge rate (Fig. 3).

(c) *Effect of changing the inspired CO_2 concentration on lung mechanics*

There was little or no effect of low levels of CO_2 on lung compliance in these studies. At higher levels of CO_2, in eight animals examined, there was usually a slight decrease in dynamic compliance; average values falling from $0{\cdot}96 \pm 0{\cdot}09$ (S.E. of mean) to $0{\cdot}82 \pm 0{\cdot}10$ ml./kPa.kg in animals breathing air and 10% CO_2 in air respectively.

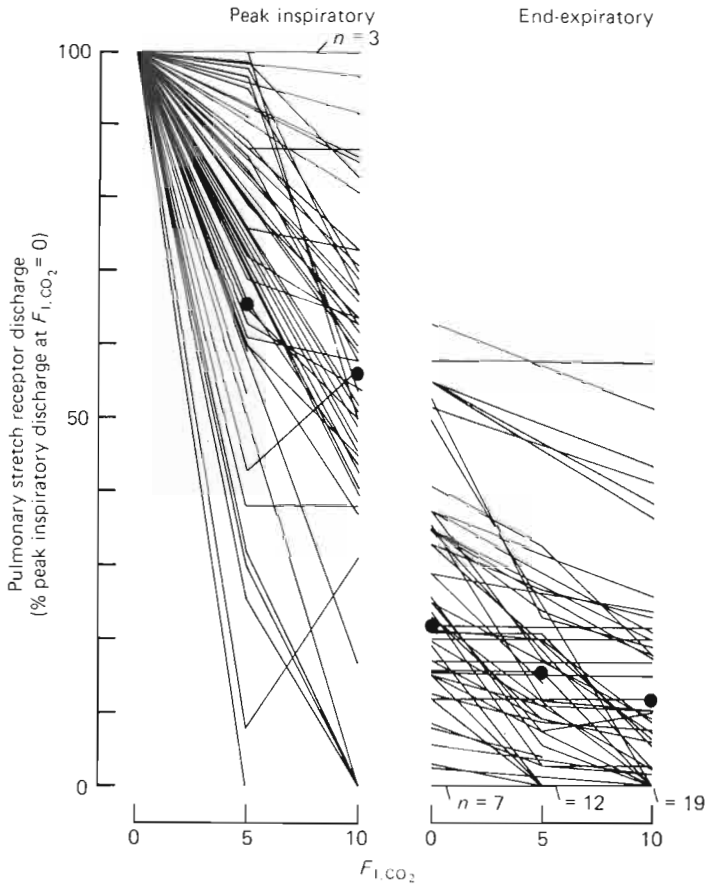


Fig. 5. The effect of changing airway CO_2 concentrations on pulmonary receptor discharge during pump ventilation. Peak inspiratory and end-expiratory discharge frequency in sixty-two pulmonary stretch receptors at inspired CO_2 concentrations of 0, 5 and 10% are shown. The mean values for all fibres at each gas concentration are shown by the filled symbols. The *n* values are the number of receptors represented by the line.

(d) *Effect of changes in transpulmonary pressure and lung volume on pulmonary stretch receptor discharge*

The independent effects of transpulmonary pressure and lung volume on pulmonary stretch receptor discharge were analysed on six fibres in five animals. Large scale changes in transpulmonary pressure achieved by altering intra-abdominal pressure during constant volume ventilation, had very little effect on pulmonary receptor discharge (Fig. 6*A*). Only when transpulmonary pressure was reduced to very low values was there any response in receptor discharge rate. Changes in ventilation

volume during inflation to constant peak transpulmonary pressure, on the other hand, were always successful in altering receptor discharge rate (Fig. 6*B*). Further, during pump ventilation, for any given lung volume, transpulmonary pressure is always greater during inflation. This gives rise to a clockwise rotating hysteresis

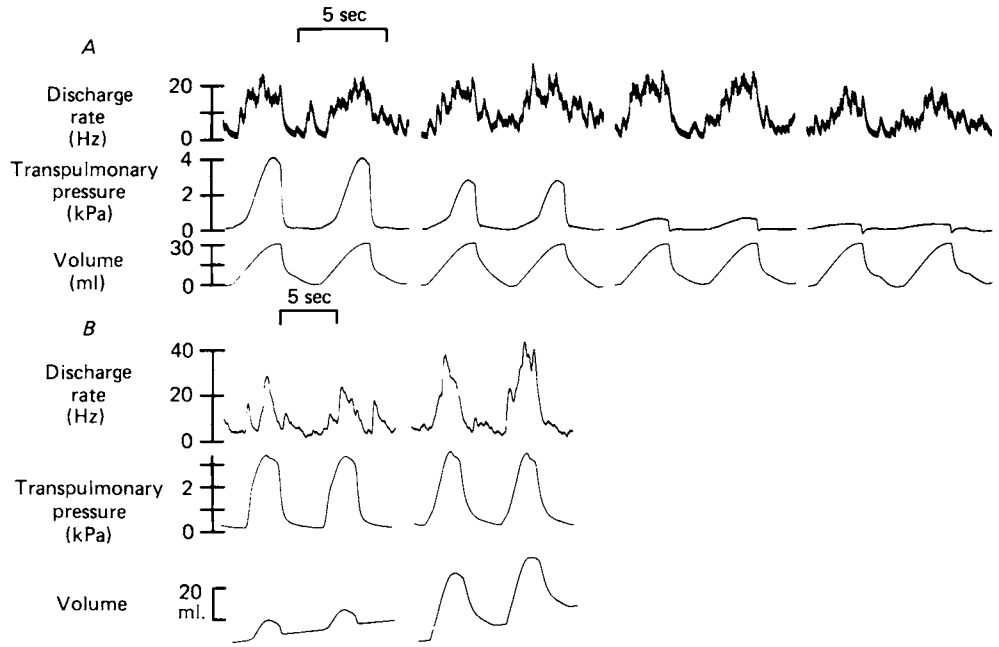


Fig. 6. *A*, the effect of changes in transpulmonary pressure at constant inflation volume on pulmonary receptor discharge. The upper trace shows the instantaneous discharge frequency of a single pulmonary receptor, the second trace shows transpulmonary pressure and the third trace shows inflation volume during two ventilation cycles to each of four peak transpulmonary pressures. *B*, the effect of changes in inflation volume with inflation to constant peak transpulmonary pressure on pulmonary receptor discharge. The upper trace is the instantaneous discharge frequency of a single pulmonary stretch receptor, the middle trace is the transpulmonary pressure and the lower trace is the inflation volume of two ventilation cycles each with two inflation volumes.

loop when transpulmonary pressure is plotted against volume through a complete pump cycle (Fig. 7). When the discharge rate of a pulmonary receptor is plotted against the associated transpulmonary pressure during a single ventilation cycle, a counter clockwise hysteresis loop results. At any given level of transpulmonary pressure, discharge is always less during inflation. When the same receptor discharge is plotted against the associated lung volume for a given pump cycle, there is no hysteresis; discharge is always the same at any given lung volume regardless of whether the lungs are inflating or deflating.

DISCUSSION

The functional characteristics of slowly adapting pulmonary stretch receptors in turtles are very similar to those of mammals. Most receptors exhibited tonic activity at resting lung volume (zero transmural pressure) as do most intra- and extra-

pulmonary stretch receptors in mammals (Mustafa & Purves, 1972; Paintal, 1973; Miserocchi & Sant'Ambrogio, 1974; Bartlett, Sant'Ambrogio & Wise, 1976). The receptors exhibited a linear response to increasing lung volume over the range studied. At low inflation volumes peak discharge was unaffected by the inflation rate, however, as the inflation volume increased, peak discharge increased with both the rate

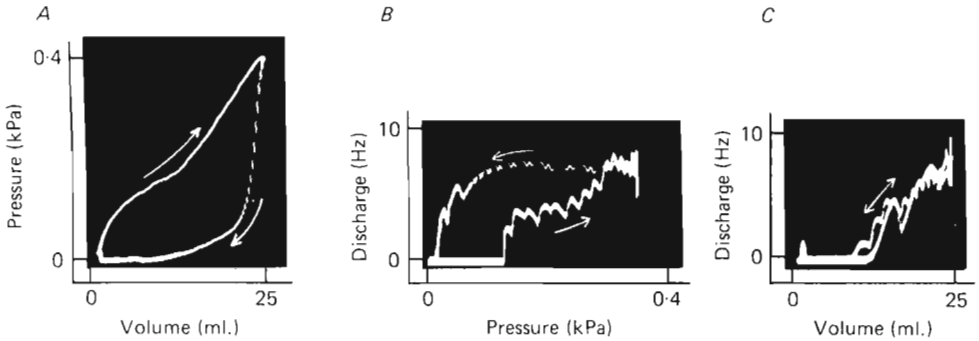


Fig. 7. The relationships between changes in transpulmonary pressure, inflation volume and pulmonary stretch receptor discharge during a single breath. *A*, plot of transpulmonary pressure versus inflation volume during a single breath. *B*, plot of discharge frequency of a single pulmonary stretch receptor versus transpulmonary pressure during the same breath. *C* plot of the same changes in discharge frequency versus inflation volume during the same breath. The time relation of each plot is indicated by the arrows.

and degree of inflation Regardless of the inflation rate, discharge always fell to a tonic level dependent only on lung volume. Similar results are well documented in the cat and dog (Adrian, 1933; Davis *et al.* 1956). The axons arising from pulmonary receptors are of similar diameter in turtles and mammals (Paintal, 1973) yet the conduction velocities in turtles ($\bar{x}$ = 7·4 m/sec) are much slower than those of mammals (36–39 m/sec) (Paintal, 1973). Also, the discharge frequencies of the receptors in turtles were much lower and the sensitivity of the receptors (defined as the change in discharge rate for a given change in pulmonary pressure during inflation) was also less; 15·1 Hz/kPa in the turtle compared to 30 Hz/kPa in the dog (Miserocchi & Sant'Ambrogio, 1974; Bradley *et al.* 1976). These differences, however, are probably attributable to the much lower body temperature of the turtles (22–23 °C).

In mammals, the discharge of pulmonary stretch receptors associated with any given volume during lung inflation appears to consist of a component associated with the actual volume and a component associated with air flow (Davis *et al.* 1956). Since this same relation also exists between transmural pressure and volume and flow, many investigators have successfully correlated receptor discharge with the level and rate of change (dP/dt) of transpulmonary pressure, both *in vivo* (Davies *et al.* 1956; Sant'Ambrogio *et al.* 1974; Bartlett *et al.* 1976) and *in vitro* (Bradley & Scheurmier, 1977). Two separate lines of evidence presented in this study, however, show that in the turtle, pulmonary stretch receptor discharge is associated only with lung volume. Wide scale alterations in the transpulmonary pressure developed during lung ventilation failed to have much noticeable effect on peak receptor dis-

charge frequency as long as the inflation volume was held constant. When, on the other hand, a constant level of transpulmonary pressure was developed with varying inflation volumes, peak receptor discharge rate always reflected the changes in inflation volume. Further, in the absence of such manipulations, but during normal pump ventilation, pulmonary stretch receptor discharge frequency always followed the changes in lung volume excatly while both discharge and volume lagged behind the changes in transmural pressure.

There is no question that the response of a receptor to transpulmonary pressure changes requires that a net force be developed across the septa or wall containing the receptor. The extent to which this occurs decreases with each generation of airway division (Fung, 1975). In turtles, the primary bronchi (first generation) do not divide but pass the length of the lung and end. Each bronchus remains patent but is perforated along its length providing access to the eight to ten major chambers of the lung (Gans & Hughes, 1967). Each chamber is further subdivided by numerous septa and it is on these septa that the receptors are located. In view of the fact these septa must be exposed to the same pressure and flow changes on each side during inflation, it is not surprising that the receptors were insensitive to changes in transpulmonary pressure. In light of this, however, the mechanism behind the response to rate of inflation recorded at high inflation volumes remains unclear. It is possible that the response arises from transient changes in the longitudinal tension of the septa which only appear during air flow once the lungs are distended beyond a certain point. For the moment, this must remain speculative.

The average response of pulmonary receptors in the turtle to CO_2 was also similar to that reported for mammals. The sensitivity of receptors to static volume inflations was reduced to 9·2 and 6·8 Hz/kPa when animals were ventilated with 5 and 10% CO_2 respectively. These values represent 39 and 55% reductions, slightly greater than the 20–40% reductions reported in rabbits, cats and dogs ventilated with 7–9% CO_2 in O_2 (Mustafa & Purves, 1972; Kunz *et al.* 1976; Bradley *et al.* 1976). As reported for the dog (Bradley *et al.* 1976) the effects were not linear but were greater over the lower range of CO_2 concentrations both during static lung inflations and during pump ventilation. Over a range of CO_2 concentrations from 0 to 5%, during pump ventilation, there was an average reduction of 10% of control in peak discharge rate per 10 mmHg increase in P_{CO_2} and 7% of control in end-expiratory discharge per 10 mmHg increase in P_{CO_2}. These values tend to be slightly greater than those reported for mammals (Mustafa & Purves, 1972; Bradley *et al.* 1976).

The time course of the increase in mechanical threshold and decrease in sensitivity of receptors when CO_2 was administered during pump ventilation in turtles is similar to mammals (Mustafa & Purves, 1972; Schoener & Frankel, 1972; Bradley *et al.* 1976) as is the time course of recovery when CO_2 is removed (Adrian, 1933; Mustafa & Purves, 1972; Bradley *et al.* 1976; Bartlett & Sant'Ambrogio, 1976). Interestingly, however, although the time course of the reduction in peak inspiratory and end-expiratory discharge was similar when CO_2 was administered, peak inspiratory discharge rate usually recovered more quickly than the end-expiratory discharge rate when CO_2 was removed. Hypercapnia has been found to inhibit stretch receptor discharge less during the inspiratory phase of artificial ventilation than during the expiratory phase in mammals (Mustafa & Purves, 1972; Sant'Ambrogio *et al.* 1974;

Bradley *et al.* 1976; Bartlett & Sant'Ambrogio, 1976) but this only occurs during the recovery from exposure to CO_2 in the turtle.

It seems evident that CO_2 acts directly on the pulmonary receptors rather than on lung volume or transpulmonary pressure. If CO_2 induced a decrease in lung resistance in turtles there would be a corresponding decrease in transpulmonary pressure during constant volume ventilation and it has been shown that changes in transpulmonary pressure have very little effect on receptor discharge. Further, high levels of CO_2 decrease dynamic lung compliance in the turtle so, even if the receptors were sensitive to transpulmonary pressure, this effect would tend to mask not enhance the effects of the CO_2.

Finally, it is interesting that the quantification of the dP/dt sensitivity of stretch receptors in mammals has been focused primarily upon tracheal (Bartlett *et al.* 1976) receptors in the extrapulmonary airways and that these receptors are insensitive to CO_2. The pulmonary receptors which are sensitive to CO_2 appear to be the bronchial (Bartlett & Sant'Ambrogio, 1976) or type II receptors (Miserocchi *et al.* 1973) which are the exclusive receptor type in their primary location, the small bronchi ($>$ 1 mm diameter). This is a position where lung stretch (circumferential and longitudinal) and not transpulmonary pressure will be the primary stimulus. On the basis of functional characteristics, location and sensitivity to CO_2, it would appear that the turtle pulmonary stretch receptors differ only quantitatively from mammalian intrapulmonary (bronchial) stretch receptors.

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