tions was observed by various other salt stimuli after the tongue was adapted to water, Q-HCl or acetic acid. Some examples are illustrated in figure 3. Intracellular responses to 0.1 M NH_4Cl (A2), 0.1 M KCl (B2) and 0.1 M $MgCl_2$ (C2) following water and to 0.1 M NaCl (D2) following 0.001 M acetic acid are shown. In these and other taste cells studied, the initial phasic depolarization was scarcely observed by application of various salt stimuli under the Ringer adaptation (A1-D1).

2 theories have been presented as to taste receptor stimulation: One, proposed by Beidler[9], suggests that taste response is related to the number of occupancies of receptor sites by a stimulus. The other suggests that taste response is related to the rate of occupancy of receptor sites[10]. Since the initial phasic depolarization of taste cells was sensitive to the rate of stimulus onset, this would appear to support the rate theory concerning taste stimulation. However, the generation of phasic depolarization can probably be explained even by the Beidler's 'occupation' theory, if the amount or rate of conformational change of receptor sites occupied by a taste stimulus is presumed to be larger at the rising phase of the stimulus onset than at the static phase of the stimulus.

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Carbon dioxide sensitivity of pulmonary receptors in the frog[1]

W. K. Milsom and D. R. Jones

Department of Zoology, University of British Columbia, Vancouver, British Columbia V6T 1W5 (Canada), 8 March 1977

Summary. Pulmonary mechano-receptors have been found in the frog lung that are sensitive to CO_2 concentrations in the lungs and airways comparable to the physiological levels recorded in frogs. These results support the suggestion that a pulmonary receptor with distinct mechano- and chemosensitive properties may represent the functional precursor of the more specialized pulmonary receptor types which have evolved in birds and mammals.

The rate and degree of inflation of the lungs during breathing are monitored by receptors within the lungs and airways in all animals which have been studied[2]. There are at least 2 sets of stimuli which vary with the rate and extent of lung inflation; mechanical factors such as lung volume or transpulmonary pressure and chemical factors such as the concentration of gases in the airways. The pulmonary receptors of mammals respond primarily to the transpulmonary pressure developed during each breathing cycle but their discharge is partially modified by high levels of alveolar CO_2[3–10]. Avian pulmonary receptors have little or no mechanosensitivity responding primarily to changes in airway CO_2 concentration throughout the breathing cycle[11–16]. Reptilian pulmonary receptors are typically mechanosensitive but 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[17]. Consequently it appears that the divergent receptor types found in birds and mammals may have arisen from a less specialized receptor type such as that found in the more phylogenetically ancient reptiles. Amphibia, however, have evolved from the evolutionary stem line at an even earlier date, possess structurally simple lungs and represent some of the earliest forms of semi-terrestrial lunged vertebrates. This study was undertaken to determine whether there are receptors present in the lungs of these early forms which are sensitive to CO_2.

Frogs (Rana pipiens), weighing between 120 and 160 g, were used in these experiments. The frogs were double pithed and unidirectionally ventilated with a continuous gas flow under slight positive pressure, air entering the lung through a tracheal cannula and leaving the lung by a cannula sewn into the caudal tip of the lung. The lung could be inflated during ventilation at any desired volume by altering the resistance of the outflow cannula from the lung. Single and multi fibre nerve activity were recorded from pulmonary afferent fibres in vagal slips using bipolar silver electrodes. The intratracheal pressure was recorded with a pressure transducer and with neural activity were amplified, visually displayed on an oscilloscope and stored on magnetic tape for later analysis on a PDP Lab 8e mini-computer using conventional software.

On the basis of changes in discharge frequency following lung inflation, frog pulmonary receptors have been classified into 3 groups; rate receptors, proportional receptors and rate plus proportional receptors[18]. The discharge frequency of rate receptors is modulated solely by the rate of increase in lung volume. 6 of 25 fibres we recorded from were of this type. Although these fibres were continuously active, their static rate of discharge was unaffected by the volume of the lung; discharge increased only during the period of lung inflation and then returned

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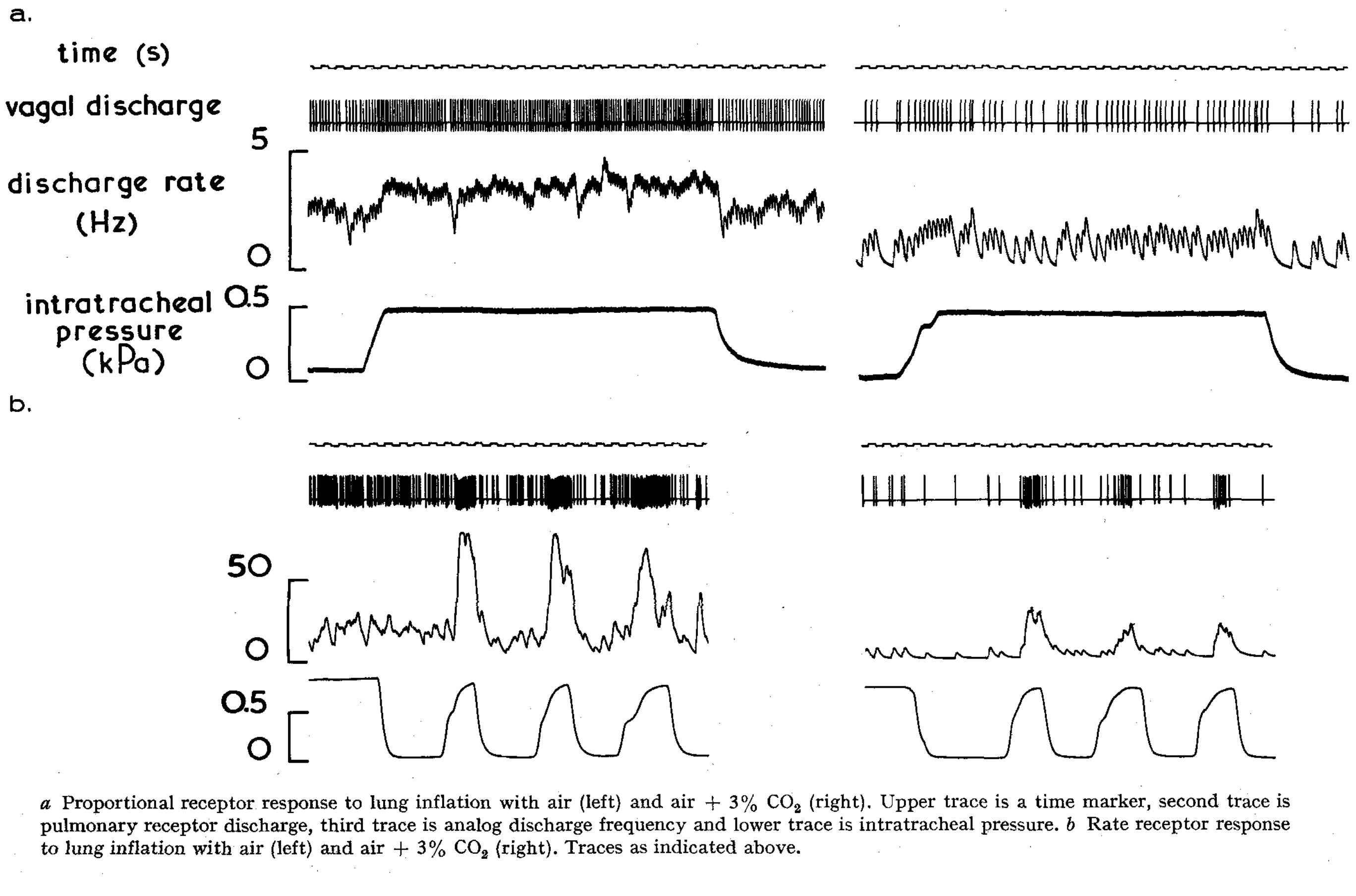
immediately to the previous level of discharge (figure, b). Addition of 10% CO_2 to the ventilating gas caused a decrease in the static discharge rate of these receptors of 56% (10.6 ± 6.0 Hz falling to 4.7 ± 1.0 Hz) (each value is the mean ± SEM) and the modulation in discharge occurring during lung inflation was reduced by 50% (41.3 ± 7.8 Hz falling to 20.6 ± 2.7 Hz) at an inflation rate of 1.0 ml sec^{-1}. One unit was particularly sensitive to CO_2 showing a 75% reduction in static discharge rate and a 74% reduction in the discharge associated with lung inflation with 3% CO_2 present in the ventilating gas (figure, b) and 67% and 64% reductions in discharge rate during ventilation with 1% CO_2 in air. The discharge rate of proportional receptors increases with increasing lung volume and for any given lung volume discharge is maintained with only slight diminution as long as the lung volume is constant (figure, a). 3 of the receptors we have recorded from fit this category. All units were active during lung deflation when intratracheal pressure approached atmospheric. The addition of 10% CO_2 to the ventilating gas caused a reduction in this discharge rate of 56%. There was a reduction of 45% in the discharge rate associated with lung inflation to an intratracheal pressure of 0.5 kPa. One unit was very sensitive to CO_2 and was 75% reduced during deflation and 61% reduced during inflation to 0.5 kPa intratracheal pressure with the addition of 3% CO_2 (figure, a) (65% and 43% reduced respectively by 1% CO_2). The remaining 16 fibres recorded were from rate and proportional sensitive receptors which exhibited a peak discharge frequency during inflation as well as an increase in static discharge frequency with increasing lung volumes. 15 units were active during lung deflation at an average discharge frequency of 6.9 ± 1.3 Hz which increased to an average discharge frequency of 19.2 ± 3.0 Hz on lung inflation to 0.5 kPa intratracheal pressure. The peak discharge frequency associated with a 1 ml sec^{-1} rate of inflation was 51.6 ± 7.0 Hz. With 10% CO_2 present in the ventilating gas these discharge frequencies fell to average values of 5.3 ± 1.0 Hz, 15.4 ± 3.2 Hz and 35.8 ± 5.9 Hz respectively representing 23, 20 and 31% reductions in the discharge frequencies. One fibre increased its discharge frequency in the presence of 10% CO_2. In all cases the changes in activity began during the first few seconds following a step change in the CO_2 content of the ventilating gas. All units were isolated to locations within the lung by punctate stimulation. No fibres could be found which were sensitive to step changes in CO_2 content in the ventilating gas but insensitive to mechanical stimuli.

This study has shown that the pulmonary mechanoreceptors in the frog lung are sensitive to CO_2 concentrations in the lungs and airways; in some instances extremely sensitive to very low levels of CO_2 comparable to the physiological levels recorded in frogs[19]. These results are similar to those recorded from the turtle[17] and support the suggestion that a pulmonary receptor with distinct mechano- and chemosensitive properties may represent the functional precursor of the more specialized pulmonary receptor types which have evolved in birds and mammals.



a Proportional receptor response to lung inflation with air (left) and air + 3% CO_2 (right). Upper trace is a time marker, second trace is pulmonary receptor discharge, third trace is analog discharge frequency and lower trace is intratracheal pressure. *b* Rate receptor response to lung inflation with air (left) and air + 3% CO_2 (right). Traces as indicated above.

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