ASSESSMENT OF DIFFERENTIAL BLOCK OF CONDUCTION BY DIRECT CURRENT APPLIED TO THE CERVICAL VAGUS NERVE

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Abstract. As investigation has been made of the adequacy of direct current to block conduction in the myelinated fibres of the cervical vagus nerve, leaving the nonmyelinated fibres conducting normally. Conduction was assessed from the compound electroneurograms, and from single fibre recording. Conduction of spontaneous activity and the responses to inflation and deflation in single fibres from lung irritant receptors and pulmonary stretch receptors were completely abolished when the A-B wave of the electroneurogram was absent but the C wave was intact. When the direct current was first applied to the nerve, and for periods lasting up to 30 sec, there was sometimes a continuous discharge in the single fibres being studied. These results suggest that this method of producing a differential block of conduction in a mixed nerve such as the vagus may be superior to cooling.

INTRODUCTION

There are at least three groups of pulmonary vagal afferent fibres — firstly, myelinated fibres from the slowly adapting pulmonary stretch receptors (conduction velocities 14–59 m/sec in cats) which contribute to the A wave of the compound action potential (Paintal 1953); secondly the smaller myelinated fibres from "lung irritant receptors" lying between cells of the bronchial and bronchiolar epithelium (conduction velocities 3.6–25.8 m/sec in rabbits) which contribute to the Aδ wave (Mills et al. 1969); thirdly the nonmyelinated fibres from the "J-receptors" situated between alveolar wall and pulmonary capillary endothelium (Paintal 1970), which contribute to the C wave.

One approach to the study of the role of the nonmyelinated fibres in rabbits has been to produce a differential block of conduction in the cervical vagus nerve by applying a direct current (Guz and Trenchard 1971). The compound action potential of the vagus nerve has been used to indicate the degree of block, and it was assumed that all conduction in myelinated fibres had been abolished when the A-B complex had disappeared, while the C wave was maintained. Under these circumstances it was demonstrated that conduction in the nonmyelinated fibres allowed retention of the tachypnoea of such pathological conditions of the lung as haemorrhage, oedema, infarction, patchy areas of collapse and pulmonary microembolism (Guz and Trenchard 1971). However, both irritant receptors and J-receptors respond to similar stimuli, for example pulmonary congestion, microembolism, inhalation of irritant gases, and injections of phenyl diguanide (Mills et al. 1969, Paintal 1970, Guz and Trenchard 1971). The efficacy of the vagal differential block has been tested solely by the monitored compound action potential, and there is the possibility that some of the fibres from irritant receptors could still have been conducting, although the wave to which they were contributing had apparently been abolished. This point is of importance since Casey and Blick (1969), using a direct current (d-c) block of the sural nerve in cats, showed that although the $A\delta$ wave of the compound action potential was eliminated, some of the small myelinated fibres contributing to it were still conducting.

We have therefore tested the effect of d-c block of the vagus nerve, with recording of single fibre activity. Previous studies of d-c block have been with somatic nerves (Mendell and Wall 1964, Zimmermann 1968, Casey and Blick 1969, Manfredi 1970) which have simpler fibre spectra than does the vagus and, with one exception (Casey and Blick 1969) have not been tested by single fibre recording.

METHODS

Twelve rabbits were anaesthetized by intravenous sodium pentobarbitone (Nembutal, approximately 50 mg/kg) and a tracheal cannula was inserted. Transpulmonary pressure was measured from an air-filled polyethylene cannula tied into a lower right anterior intercostal space, and from a wide bore needle inserted through the tracheal cannula, using a differential capacitance manometer (I.R.C. Development Co.) range ± 50 cm H_2O. Air flow and tidal volume were measured from a Fleisch pneumotachograph (linear range 0–110 ml/sec) connected to an inductance differential pressure recorder and integrator (Godart). Arterial blood

pressure was recorded with a strain-gauge manometer (Consolidated Electrodynamics).

The right cervical vagus nerve was cleared from surrounding tissue and cut high in the neck. Platinum stimulating electrodes (8 mm apart) were placed on the nerve as low in the neck as possible, and adjacent to them were placed the saline wick electrodes (10 mm apart, with the anode central) through which was passed the d-c. The d-c was supplied from a 20 v dry battery with variable resistors in the circuit to adjust the strength of the current, which was measured by a micro-ammeter. The nerve was grounded to surrounded tissues between the blocking and recording electrodes. The remainder of the cut end of the nerve was placed in a trough containing liquid paraffin. The sheath was removed and a small strand was teased out from which to obtain a "single fibre" preparation from a pulmonary stretch or lung irritant receptor. This preparation was placed on a pair of platinum electrodes, and the bulk of the
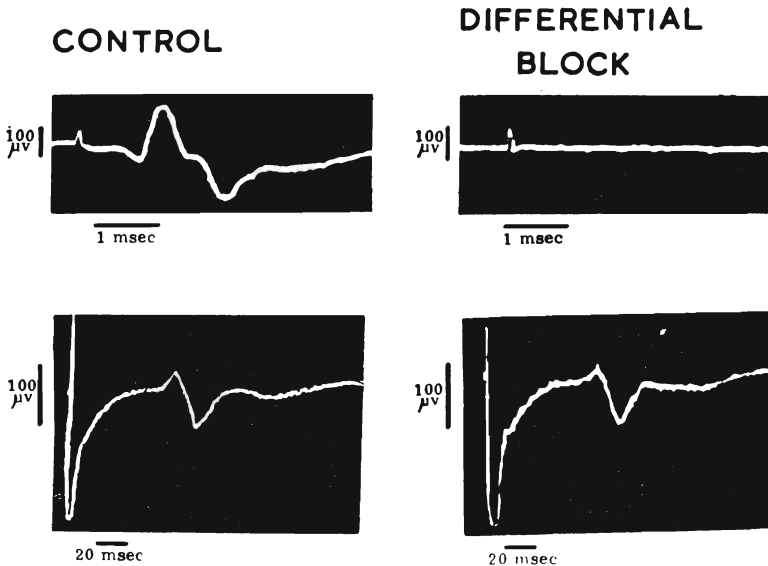

Fig. 1. Cervical vagal electroneurograms showing differential block of conduction. Upper records: biphasic A wave resulting from stimulation of myelinated fibres. The control wave (left) is preceded by a small stimulus artefact. After the differential block has been established (right) only the stimulus artefact remains, indicating that no conduction is present in fibres contributing to that wave. Lower records: biphasic C wave resulting from stimulation of nonmyelinated fibres. The larger stimulus artefact, due to the increased voltage of stimulation, shows a sharp upward deflection, followed by a slowly declining downward deflection. There is no change in the form of the C wave after the differential block has been established.

nerve was placed on another pair of platinum electrodes for recording the compound action potential. After amplification (Tektronix, type 122) both the potentials from single fibres and the compound action potentials were displayed on oscilloscopes (Tektronix, types 502 and 564B).

The compound action potentials were induced at a frequency of 1/sec. Two stimulators (Devices, Mk. IV) were used, both triggered by a Digitimer (Devices). One stimulator elicited the A-B complex (myelinated fibres) wave of the compound action potential with shocks of 0.5–1.8 v and 50 μsec duration; the second stimulator, which was triggered 6 msec after the first, elicited the C-wave (nonmyelinated fibres) with shocks of 8–15 v and 0.5–1 msec duration. The two waves were continuously monitored on separate oscilloscopes which permitted the desired level of block to be achieved easily. The d-c was applied to the nerve and gradually increased. The A-B waves gradually became temporally dispersed and reduced until they were invisible, even though the gain of the amplifier was increased tenfold. The C-wave was unchanged in size at this time (Fig. 1). The strength of current used to produce this level of block was in the range 20–100 μa.

Transpulmonary pressure, airflow, blood pressure and action potentials were recorded on a 7-channel FM tape recorder (Ampex, SP300) and later photographed for analysis (Cambridge Scientific Instruments).

All rabbits were breathing spontaneously. The lungs were inflated and deflated by sucking and blowing air by the mouth of the experimenter through the tracheal cannula. The spontaneous activity in the fibres from pulmonary stretch and lung irritant receptors and the responses to inflation and deflation were first determined, and then redetermined during stimulation of the compound action potentials to ensure that this electrical stimulation did not interfere with these responses. The d-c was then applied to produce differential block of conduction, and inflations and deflations were repeated. When the d-c was later removed, control responses to inflations and deflations were again determined.

RESULTS

The activity in ten fibres from lung irritant receptors and in eight fibres from slowly adapting pulmonary stretch receptors was investigated. The criteria for identification of the lung irritant receptors have been described previously (Mills et al. 1969, 1970); seven of these ten fibres showed spontaneous activity unrelated to respiratory rhythm, and all gave rapidly adapting irregular responses to inflations and deflations (Fig. 2 and 3, upper records). The pulmonary stretch receptors gave regular and slowly
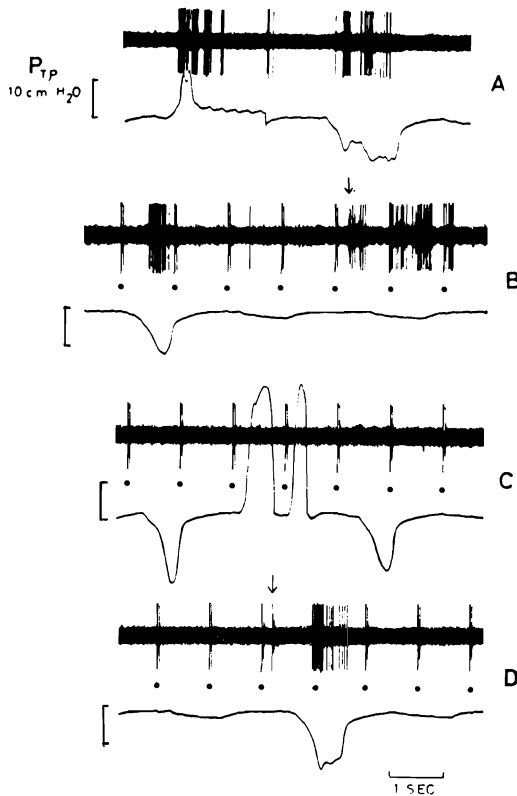
Fig. 2. Effect of differential block of conduction on both spontaneous activity and evoked responses in a single fibre from a lung irritant receptor. In each record the upper trace is the activity in the fibre and the lower trace is the transpulmonary pressure (P_{TP}). *A* shows the evoked responses to a deflation followed by an inflation. *B* shows firstly the response to an inflation in the presence of the electrical stimulation (indicated by dots) necessary to elicit the waves of the vagal electroneurogram; the response is unchanged. At the arrow direct current was applied to the nerve, and this is immediately followed by a burst of activity lasting approximately 2 sec. *C* indicates the lack of any discharge in the fibre in response to an inflation and deflation when the differential block has been established, *D* shows the prompt return of the response to an inflation when the direct current is removed (at arrow).

adapting discharges in response to lung inflation (Fig. 3, upper records) and all had spontaneous respiratory activity in "eupnoea".

When the desired level of differential block had been obtained, as judged from the monitored electroneurograms (Fig. 1) no fibres showed spontaneous discharge or responded to inflations and deflations (Fig. 2C and Fig. 3, middle record). In 6 of the 10 fibres from irritant receptors and 6 of the 8 fibres from pulmonary stretch receptors there was a burst of

activity when the d-c was first applied, which disappeared within a few seconds in 2 of the fibres from irritant receptors (Fig. 2 and 3, at first arrows). In the remaining four fibres from irritant receptors and two from pulmonary stretch receptors the discharge was continuous (frequency approximately 100/sec) while the strength of the current was being raised, but had ceased by the time the A-B wave had been abolished and the differential block established.

When the current was removed, usually after it had been applied for 30–60 sec, spontaneous activity if present previously returned promptly in both types of fibre. The responses to inflations and deflations were also invariably restored when tested immediately after the d-c had been removed (Fig. 2 and 3, lowest records).
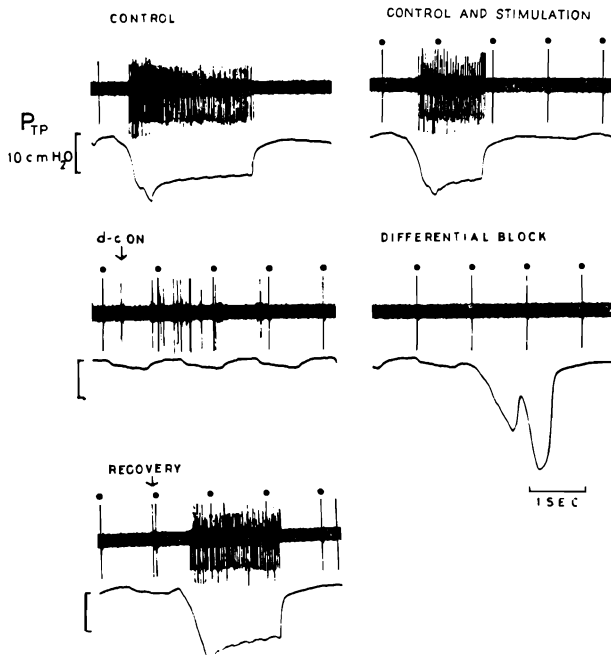

Fig. 3. Effect of differential block of conduction on the evoked responses in fibres from an irritant receptor and a slowly adapting pulmonary stretch receptor contained in the same multi-fibre strand. The uppermost records indicate the responses with and without the stimulation necessary to elicit the vagal electroneurograms (indicated by dots). The middle records show firstly the random discharge accompanying the application of the direct current (at arrow) and secondly the absence of a response in either fibre to an inflation. In the lowest record the removal of the direct current (at arrow) is immediately followed by activity in both fibres evoked by an inflation.

DISCUSSION

Previous work using differential block of conduction in the cervical vagus nerve has shown the importance of the nonmyelinated fibres in a variety of pathological conditions of the lungs (Guz and Trenchard 1971). The conclusions were based on the assumption that conduction in all the myelinated fibres, including those from irritant receptors, had been abolished when only the C wave of the cervical vagal electroneurogram remained. The present results support this assumption.

The continuous discharge which appeared in many of the fibres when the d-c was first applied and continued while its strength was being raised, was of interest since there is usually an inhibition of breathing at this time (Trenchard 1970). This expiratory apnoea lasts up to 30 sec and suggests stimulation of pulmonary stretch receptors, but occasionally other changes such as large breaths occur. The probable explanation of this disturbance is that the fibres are electrically stimulated at the cathode and the impulses can be transmitted centrally past the anode until the strength of the d-c produces sufficient anodal hyperpolarization to prevent any further passage (*see* Manfredi 1970).

The duration of application of the d-c in the present studies was 30–60 sec, and the activity in the fibres returned promptly after the current was removed. In previous studies without single-fibre recording it was found that when the d-c was applied to the vagus nerve for a longer time, for example up to 10 min, then the return of the A-B wave of the electroneurogram and the respiratory reflexes was delayed for an equivalent period of time (Guz and Trenchard 1971, Trenchard 1970).

The rapid return of activity in the fibres after removal of the d-c, and the clear differentiation between the A-B and the C waves of the electroneurogram, suggest that anodal block may be superior to cooling for producing differential block of conduction (Paintal 1965). In addition, the block due to cold depends on the frequency of discharge, at least for myelinated fibres (Franz and Iggo 1960, Paintal 1965). Our results do not indicate this is an important problem with d-c block, although we have not tested the possibility directly.

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