J. Physiol. (1981), **316**, *pp.* 177–190
With 7 text-figures
Printed in Great Britain

INSPIRATORY INHIBITION OF VAGAL RESPONSES TO BARORECEPTOR AND CHEMORECEPTOR STIMULI IN THE DOG

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(*Received 4 August 1980*)

SUMMARY

1. Single and few-fibre cardiac efferent filaments were dissected from the cervical vagus nerve of dogs anaesthetized with chloralose and paralysed with pancuronium.

2. Brief selective baroreceptor or chemoreceptor stimuli, given during the expiratory phase of the central respiratory cycle and while the lungs were motionless, evoked trains of action potentials in cardiac vagal efferent fibres. These vagal responses outlasted the duration of the stimuli by 1–3 s.

3. Brief selective baroreceptor or chemoreceptor stimuli given during the inspiratory phase of the central respiratory cycle (monitored as phrenic discharge) but while the lungs were motionless, failed to evoke reflex increases in discharge. Background vagal discharge was also inhibited during central inspiratory activity.

4. Brief baroreceptor or chemoreceptor stimuli given during lung inflation but in the expiratory phase of the central respiratory cycle (phrenic silence), also failed to evoke any reflex increase in discharge, but left resting vagal tone relatively unaffected. Only when vagal tone was high was it markedly inhibited by lung inflation, in the absence of central inspiratory activity.

5. A point of contrast between the inhibitory effects of lung inflation and of central inspiratory activity is that both tonic and reflexly evoked vagal discharge are inhibited during central inspiratory activity, but lung inflation more markedly inhibits reflexly evoked vagal discharge than tonic vagal discharge.

6. A model is suggested to explain the different mechanisms of inhibition by lung inflation and by central inspiratory activity.

INTRODUCTION

Anrep, Pascual & Rossler (1936*a*, *b*) attributed sinus arrhythmia to phasic interruption of vagal outflow to the heart by both central inspiratory activity and lung inflation. It was subsequently shown that reflexes which excite cardiac vagal efferents can do so only, or more effectively, during the expiratory phase of the respiratory cycle (e.g. Koepchen, Wagner & Lux, 1961; Haymet & McCloskey, 1974, 1975; Neil & Palmer, 1975; Gandevia, McCloskey & Potter, 1978*b*; McAllen & Spyer, 1978*b*). Refractoriness of vagal pathways to excitatory inputs delivered in inspiration was shown to be imposed by both central inspiratory activity and by the activity

of intrapulmonary receptors sensitive to the rate of lung inflation (Gandevia, McCloskey & Potter, 1978*a*).

These phenomena have been thoroughly studied by Daly and his co-workers, in experiments which have demonstrated their importance for oxygen conservation and delivery (see Daly, 1972, for review). Stimulation of the arterial chemoreceptors evokes bradycardia (and arteriolar vasoconstriction) as a 'primary' reflex response which is best seen when ventilation is kept steady (Daly & Scott, 1958), or halted (McCloskey, 1979). When ventilation is allowed to increase in response to chemoreceptor stimulation, however, tachycardia (and vasodilatation) occur (MacLeod & Scott, 1964; Daly, 1972). Increased breathing, by activating the central and reflex mechanisms outlined above, blocks primary reflex bradycardia (and also, presumably, vasoconstriction: Daly & Robinson, 1968). These responses favour oxygen delivery when ventilation can increase, and oxygen conservation when it cannot (Daly, 1972; McCloskey, 1979).

The study reported here analyses in more detail the central and reflex inhibitory influences exerted by respiratory mechanisms on cardiac vagal motoneurones. The experiments to be described involved recording discharges in cardiac efferent nerve fibres dissected from the cervical vagus in anaesthetized dogs.

Part of this work has been reported briefly (Potter & McCloskey, 1980).

METHODS

Experiments were performed on fourteen adult mongrel dogs of both sexes weighing 5·5–18 kg. The animals were premedicated with morphine sulphate (1–2 mg/kg), then anaesthetized with chloralose (α-chloralose: British Drug Houses: 60–100 mg/kg I.V.), after induction with thiopentone (15 mg/kg). In each dog the trachea was cannulated low in the neck and a nylon cannula placed into a femoral vein for administration of supplements of anaesthetic. A balloon-tip cannula was inserted through the femoral artery and advanced so that the inflatable balloon lay in the upper abdominal aorta. This was used to raise central arterial pressure mechanically by obstruction of the abdominal aorta. Rectal temperature was kept between 37 and 39 °C.

In all animals nylon cannulae were inserted into the external carotid and lingual arteries on the right-hand side, so that their tips lay close together facing into the carotid sinus. One cannula was used for recordings of pressure within the carotid sinus. Through the other cannula selective baroreceptor stimuli were delivered by sudden retrograde injections of 2–5 ml air-equilibrated saline, after first clamping the common carotid artery caudal to the carotid sinus (Haymet & McCloskey, 1975). Selective chemoreceptor stimuli were given by injections (approx. 0·5 ml) of carbon-dioxide-equilibrated saline into the carotid sinus. These small volumes did not change carotid sinus pressure, and have been shown previously not to affect baroreceptor nerve endings (Haymet & McCloskey, 1975).

Arterial pressure was measured from the lingual artery using a Statham P23 AC transducer and recorded on one channel of a Grass polygraph. A signal proportional to tracheal air flow was obtained by passing a nylon tube (2 mm internal diameter) into the trachea and measuring the pressure drop between its tip and the atmosphere, using a Statham P23 Db transducer. The same catheter and transducer were used to measure intra-tracheal pressure in paralysed animals (see below).

Each animal was prepared for recordings from cardiac vagal efferent fibres as described in the preceding paper (McCloskey & Potter, 1981). Briefly, the entire pharynx and larynx were removed and the right cervical vagus was divided into filaments. Cardiac vagal efferents were identified according to physiological criteria established by Jewett (1964) and by Iriuchijima & Kumada (1963). Neural activity in the filaments containing one or a few active fibres were recorded with preamplifiers (Neurolog NL103/106: band pass between 10 Hz and 1 kHz), a loudspeaker and storage oscilloscope. Criteria for definition of single-unit activity were those used by McCloskey & Potter (1981). Records of cardiac vagal efferent activity were obtained by direct photography from

the oscilloscope screen. Alternatively, the cardiac efferent spikes were used to trigger a spike trigger (Neurolog NL200). These trigger pulses could then be counted in steps (usually two to five spikes per step; Neurolog NL603) and every step of the counter raised the analogue output of a pulse integrator (Neurolog NL600) by one unit. The integrator could be reset to zero at required intervals. The analogue output of the integrator was then recorded on one channel of the Grass polygraph. By this method it was possible to obtain a record of spike frequency on a pen recorder.

The animals were paralysed using pancuronium bromide (Pavulon: Organon: 40–80 μg/kg). In these animals respiratory activity was recorded from the central end of the cut and desheathed right phrenic nerve through platinum electrodes. This activity was integrated using a Grass 7P3B preamplifier ('leaky' integrator: time constant 0·05 s). The paralysed animals were ventilated on pure oxygen using a Starling 'Ideal' pump, adjusted so that phrenic nerve activity was not entirely suppressed. Intra-tracheal pressure was recorded in these animals during artificial ventilation.

RESULTS

Respiratory effects on vagal tone

The separate contributions to inhibition of vagal tone from central inspiratory activity and from lung inflation were studied in paralysed dogs. Observations were made in periods during which artificial ventilation was temporarily halted: throughout these periods (usually $\leqslant$ 1 min) the animals remained well oxygenated as they had been ventilated on pure oxygen before the pump was stopped. Central inspiratory activity was reflected in phrenic neural discharge. Inflation of the lungs could be achieved independently of this activity by the experimenter simply blowing into the tracheal tube.

Lung inflation and central inspiratory activity did not inhibit cardiac vagal motoneurones equally effectively. When a moderate degree of resting vagal tone was present each burst of central inspiratory activity completely inhibited it, whereas inflation of the lungs with pressures within the physiological range (up to 15 mmHg) had little or no effect on it. Inflation to just beyond these pressures (to approx. 20 mmHg) frequently decreased tonic vagal discharge without suppressing it entirely. These effects are illustrated in Fig. 1.

When vagal tone was increased as, for example, by inflating an intra-aortic balloon so as to raise arterial pressure and stimulate arterial baroreceptors, each burst of central inspiratory activity remained associated with complete inhibition of vagal activity. At higher levels of vagal tone, however, lung inflation became a more effective inhibitory input. This was so for all levels of inflation (see Fig. 2). The effects of lung inflation were demonstrable in the absence of secondary changes in arterial pressure. They were abolished by cutting the left vagus nerve (cf. Gandevia *et al.* 1978*a*; the right had been cut before recording from it). In no animal, however, did lung inflation completely abolish cardiac vagal activity in the way that was typical of the action of the central inspiratory drive.

Respiratory effects on baroreceptor and chemoreceptor reflexes

Effects of central inspiratory drive. It is known that stimuli delivered to arterial baroreceptors or chemoreceptors during central inspiratory activity are prevented from evoking reflex vagal bradycardia (Koepchen *et al.* 1961; Davidson, Goldner & McCloskey, 1976; Gandevia *et al.* 1978*a*). Bradycardia is evoked only by stimuli given in the expiratory phase of the central respiratory cycle.

These findings were confirmed here by direct recordings from cardiac vagal

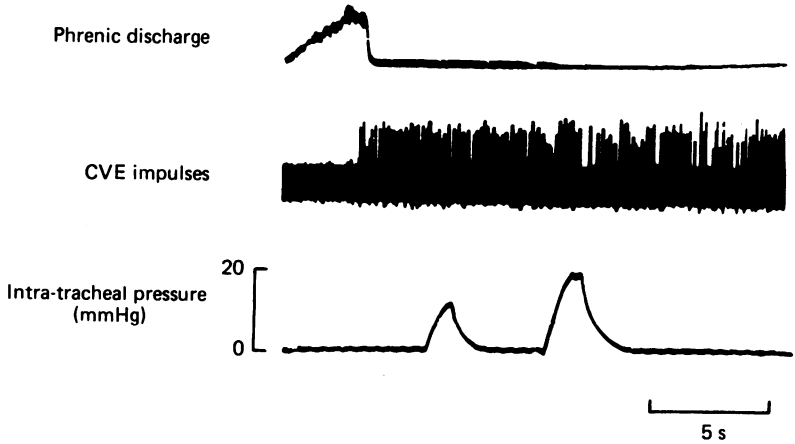

Fig. 1. Dog, anaesthetized with chloralose, paralysed with pancuronium. Records of integrated phrenic nerve activity, cardiac vagal efferent (CVE) impulses recorded from a single active fibre dissected from the cervical vagus, and intra-tracheal pressure are shown. Cardiac vagal efferent activity is completely inhibited during activity in central inspiratory centres (indicated by phrenic nerve activity) while lungs remain uninflated. Lung inflation to 10 mmHg (during the expiratory phase of central inspiratory cycling) has little effect on cardiac vagal efferent activity. Lung inflation to 20 mmHg has a slight inhibitory effect on cardiac vagal efferent activity.

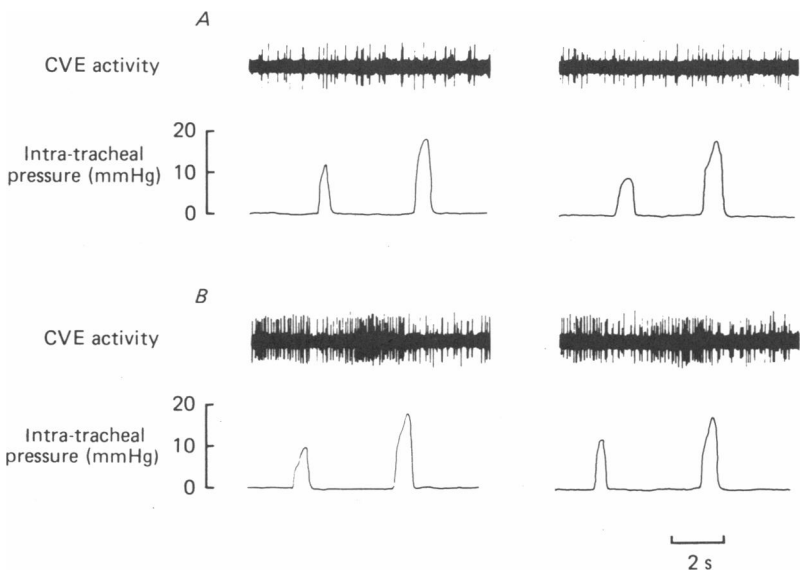

Fig. 2. Dog, anaesthetized with chloralose, paralysed with pancuronium. Records show few-fibre cardiac vagal efferent (CVE) activity in a filament dissected from the cervical vagus and intra-tracheal pressure, at two levels of vagal tone. When vagal tone is low (*A*) lung inflation of either 10 or 20 mmHg given during the expiratory phase of central respiratory cycling has little or no inhibitory effect on cardiac vagal efferent activity. When vagal tone is high (*B*) lung inflations of 10 and of 20 mmHg inhibit vagal activity: note vagal activity is not completely inhibited even when the lungs are inflated to 20 mmHg.

efferents. In paralysed animals, while artificial ventilation was temporarily halted, brief selective stimulation of arterial chemoreceptors or baroreceptors evoked bursts of vagal discharge only when delivered during periods of phrenic silence (see Figs. 3*A* and 4*A*). Similar stimuli delivered during bursts of phrenic activity had little or no effect on vagal activity (see Figs. 3*B* and 4*B*). These phenomena are analysed further below.

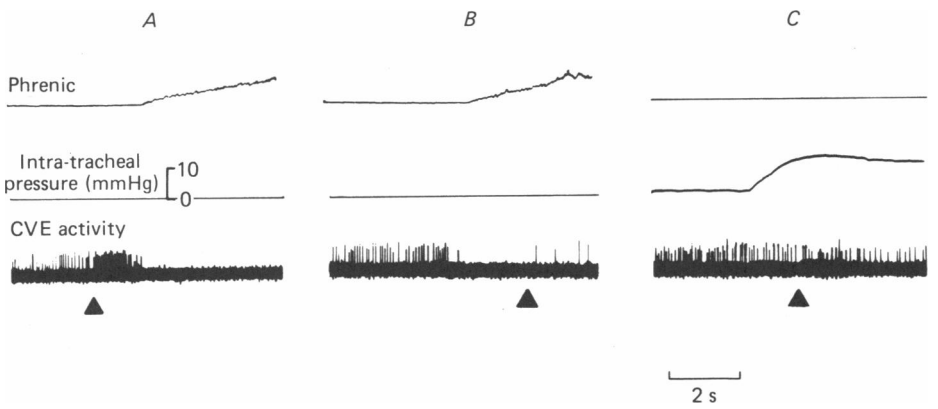

Fig. 3. Dog, anaesthetized with chloralose, paralysed with pancuronium, respiratory pump temporarily halted. Records of 'integrated' phrenic neural activity (indicating central inspiratory activity), intra-tracheal pressure, and activity in a single cardiac vagal efferent (CVE) fibre dissected from the cervical vagus are given, showing cardiac vagal responses to brief, selective chemoreceptor stimuli. *A*, the response when a stimulus is given while the phrenic nerve is silent and the lungs are motionless. Note the prolonged response evoked in the vagal fibre. *B*, a similar stimulus given during central inspiratory activity (indicated by phrenic discharge) but while the lungs remain motionless: the reflex increase in vagal discharge previously evoked by stimulation of chemoreceptors is inhibited, together with tonic vagal discharge. *C*, a similar stimulus given during lung inflation but while phrenic discharge is absent: this also fails to evoke a reflex increase in discharge, but note that tonic vagal activity is relatively unaffected.

Effects of lung inflation. Gandevia *et al.* (1978*a*) showed that rapid inflation of the lungs with pressures of 5–10 mmHg, in the absence of central inspiratory activity, could prevent reflex bradycardia occurring in response to stimuli delivered at the same time to arterial baroreceptors or chemoreceptors. They showed that the potency of this inhibition was related to the rate of lung inflation and that it gradually declined with time when the lungs were held inflated. These effects were attributable to activity in rate-sensitive inflation receptors in the lungs, probably pulmonary stretch receptors, and were abolished by surgical denervation of the lungs.

These findings were also confirmed here by recording cardiac vagal activity directly. In paralysed animals, during periods of cessation of artificial ventilation, brief selective stimuli were delivered to carotid baroreceptors or chemoreceptors. During the expiratory phase of the central respiratory cycle, while the lungs remained at the relaxation volume, these stimuli reliably evoked bursts of cardiac vagal discharge (see above, and Figs. 3*A* and 4*A*). However, when the stimuli were

delivered in the expiratory phase of the central cycle but during, or soon after, inflation of the lungs with pressures of approximately 10 mmHg, the usual bursts of vagal discharge were not evoked. This is shown in the records of Figs. 3*C* and 4*C*. While lung inflation effectively blocked the vagal responses to baroreceptor or chemoreceptor stimuli, its effect on tonic vagal discharge was as outlined above. That

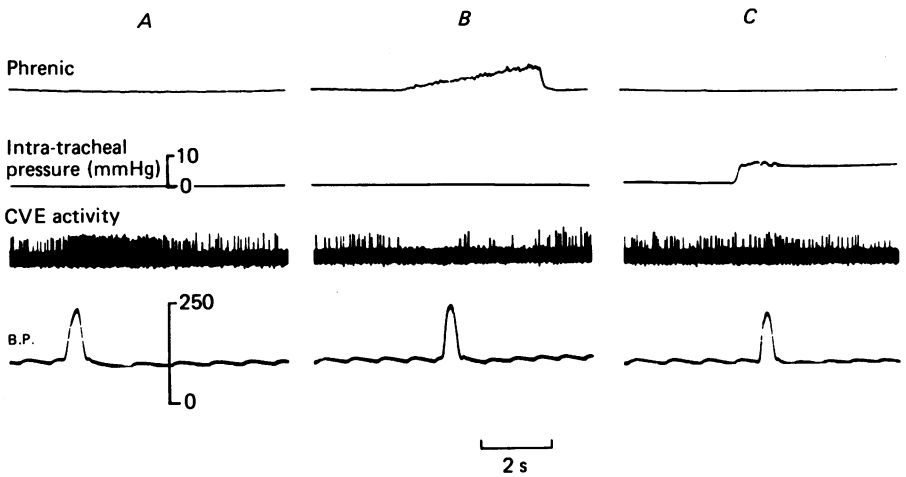

Fig. 4. Dog, anaesthetized with chloralose, paralysed with pancuronium, respiratory pump temporarily halted. Records of 'integrated' phrenic neural activity (indicating central inspiratory activity), intra-tracheal pressure, activity in a single cardiac vagal efferent (CVE) fibre dissected from the cervical vagus, and blood pressure (B.P.) measured in the carotid sinus are given, showing cardiac vagal responses to brief, selective baroreceptor stimuli. *A*, the response when a stimulus is given while the phrenic nerve is silent and the lungs are motionless. Note the prolonged response evoked in the vagal fibre. *B*, a similar stimulus given during central inspiratory activity (indicated by phrenic discharge) but while the lungs remain motionless: the reflex increase in vagal discharge previously evoked by stimulation of baroreceptors is inhibited, together with tonic vagal discharge. *C*, a similar stimulus given during lung inflation but while phrenic discharge is absent: this also fails to evoke a reflex increase in discharge, but note that tonic vagal activity is relatively unaffected.

is, inflation did not completely inhibit tonic discharge (as central inspiratory activity did: see Figs. 3 and 4) although it frequently clearly reduced it, especially in cases where resting vagal tone was high. These findings are analysed further in the following section.

Properties of the vagal excitatory pathway

Pulses of pressure of 50–200 ms duration delivered into the carotid sinus selectively stimulate afferent baroreceptor fibres in the carotid sinus nerve for the duration of the pressure pulse (Haymet & McCloskey, 1975). The cardiac vagal responses to such stimuli are bursts of activity which outlast the stimulus pulses (Fig. 5). This phenomenon was seen in all animals in the present study and formed the basis of the further experiments described below.

Interactions with central inspiratory activity. In paralysed dogs, during intervals when artificial ventilation was temporarily halted, intracarotid pressure pulses were delivered in varying temporal relationship to central inspiratory activity, monitored as phrenic neural discharge. The essential features of the vagal responses seen in all animals are shown in Fig. 6.

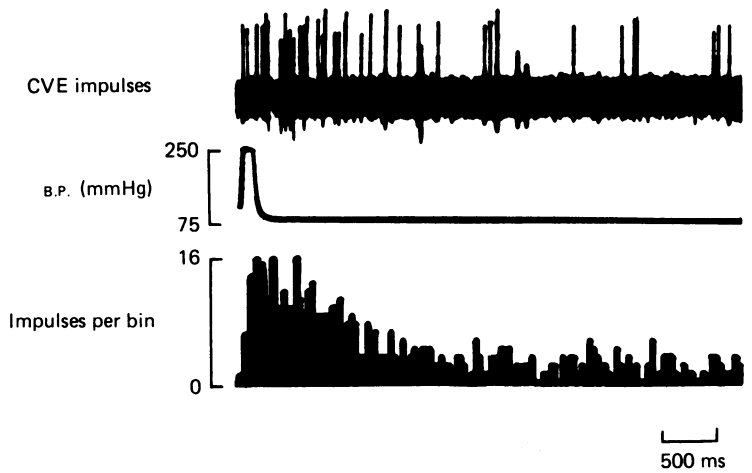

Fig. 5. Dog, anaesthetized with chloralose. Records show activity of a single cardiac vagal efferent (CVE) fibre, arterial blood pressure in the carotid sinus (B.P.) and a histogram of the activity of the vagal fibre. The records were obtained by triggering the oscilloscope trace and commencing a histogram sweep when a pulse of pressure was applied within the carotid sinus. The top trace shows the vagal responses recorded in response to such a stimulus in a single sweep of the oscilloscope. The middle trace shows thirty-two superimposed records of pressure pulses within the carotid sinus. The bottom trace shows a histogram of unitary vagal responses following these repeated pulses: that is, the histogram (bin width 19·5 ms) is accumulated from thirty-two sweeps of which the upper trace is an example. The vagal excitation evoked by a brief intracarotid pressure pulse outlasts the duration of that pulse. No vagal inhibition is seen following the excitatory response.

When baroreceptor stimuli were delivered during periods of phrenic silence, typical bursts of vagal discharge were evoked and decayed to control levels within a period, which varied from fibre to fibre, between 1 and 3 s. However, if phrenic discharge commenced soon after a vagal response had begun all vagal activity was inhibited for the duration of that phrenic discharge (Fig. 6*B*). That is, if the baroreceptor stimulus was given just *before* the phrenic discharge began, the vagal responses started, but then the typical decaying burst of vagal activity, together with tonic vagal activity, were inhibited throughout the period of phrenic discharge. If the baroreceptor stimulus was given instead *during* a period of phrenic discharge, little or no immediate vagal response was evoked. Nevertheless, whenever a stimulus was given late enough in the course of phrenic discharge for the usual duration of decaying vagal after-discharge to overlap into the period beyond the end of phrenic discharge, that increment of vagal response appeared as soon as phrenic discharge stopped (Fig. 6*C*). In every circumstance, therefore, the typical vagal response with its decaying

after-discharge appeared in full, except for that portion of it which coincided with central inspiratory activity. It was as if the stimuli always set in train similar central processes which were excitatory to cardiac vagal motoneurones, but that central inspiratory activity inhibited the ultimate vagal responses to these processes.

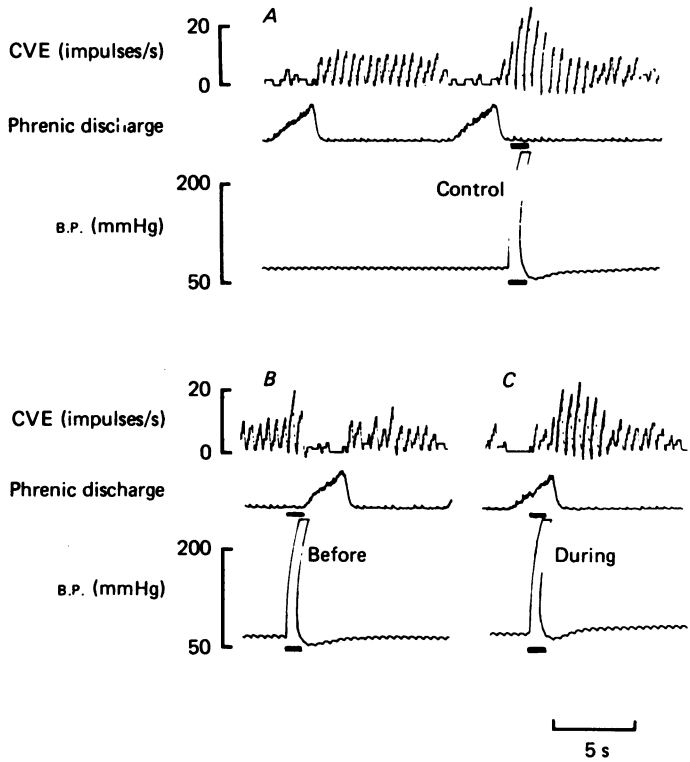

Fig. 6. Dog, anaesthetized with chloralose, paralysed with pancuronium. Records of cardiac vagal efferent (CVE) activity (counter reset every 500 ms), 'integrated' phrenic nerve activity, and arterial blood pressure measured in the carotid sinus (B.P.) are shown. *A*, a pulse of pressure delivered into the carotid sinus (baroreceptor stimulus) during phrenic silence and while the lungs are motionless: it evokes a reflex increase in vagal discharge which returns to resting level in ~ 3 s. *B*, a similar baroreceptor stimulus given just *before* central inspiratory activity begins and while the lungs remain uninflated: it evokes a reflex increase in vagal discharge but the 'tail' of this response is inhibited from the moment phrenic discharge starts. *C*, a baroreceptor stimulus given *during* central inspiratory centre activity while the lungs remain uninflated: it fails to evoke the immediate reflex increase in discharge seen in control conditions (*A*), but as soon as central inspiratory activity ceases, the 'tail' of reflex response is seen as an increase in vagal activity.

Interactions with effects from lung inflation. In the same paralysed dogs, during intervals when artificial ventilation was temporarily halted, intracarotid pressure pulses were delivered in varying temporal relationship to lung inflations with pressures of 5–15 mmHg. These lung inflations were achieved by the experimenter simply blowing into a tube connected to the trachea. All intracarotid pulses and lung

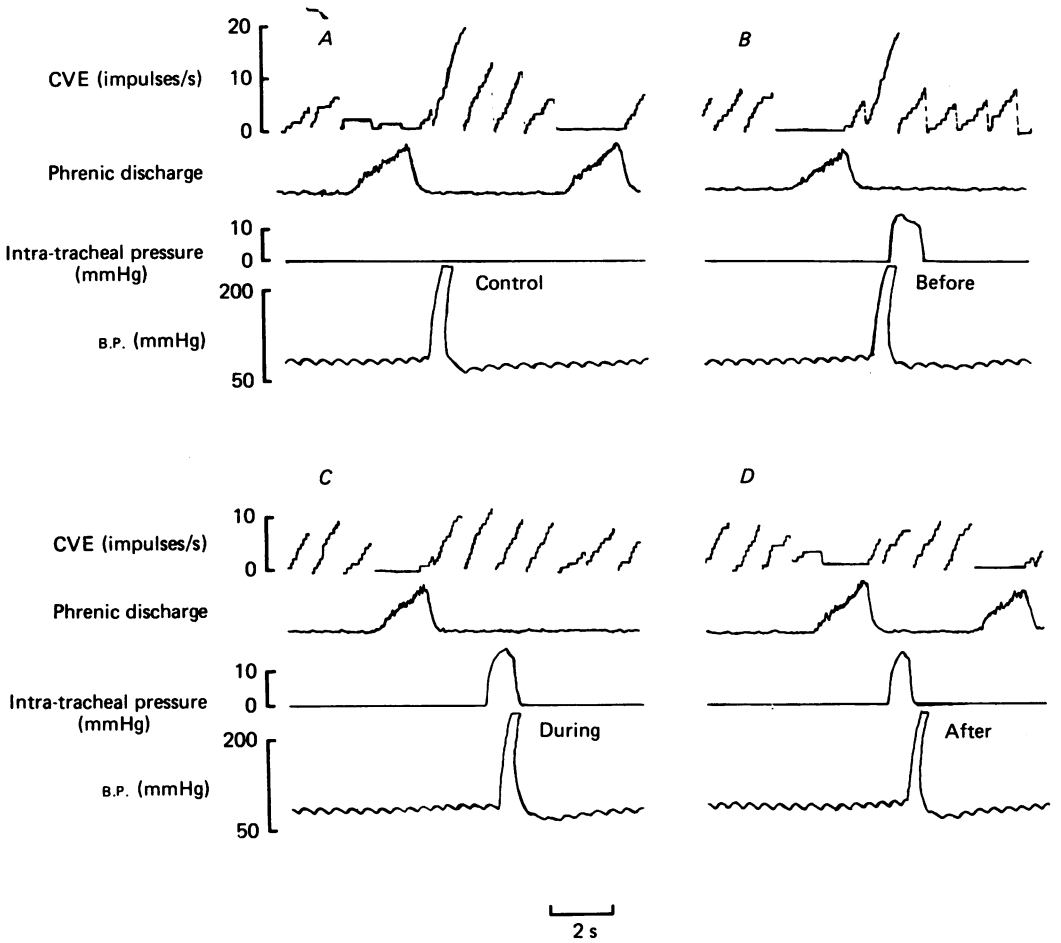

Fig. 7. Dog, anaesthetized with chloralose, paralysed with pancuronium, respiratory pump temporarily halted. Records of cardiac vagal efferent (CVE) activity (counter reset every 1 s), 'integrated' phrenic nerve activity (indicating activity in central inspiratory centres), intra-trachael pressure, and arterial blood pressure measured in the carotid sinus (B.P.), are shown. *A*, the reflex increase in discharge evoked by a pulse of pressure to the carotid sinus (baroreceptor stimulus) given during phrenic silence and while the lungs are motionless: note the typically prolonged discharge. *B*, the effect of a similar stimulus given during phrenic silence and just before lung inflation. The reflex increase in discharge is evoked, but the 'tail' of after-discharge is then inhibited, although resting vagal tone remains relatively unaffected. *C*, the response to a similar stimulus given during lung inflation while the phrenic nerve is silent. No reflex increase in vagal discharge is evoked and resting vagal discharge is relatively unaffected by lung inflation. A stimulus given just after the lungs are deflated (*D*) also fails to evoke a reflex increase in vagal discharge.

inflations in this part of the study were given during periods of phrenic silence. The essential features of the responses seen in all animals are shown in Fig. 7.

The same prolonged bursts of cardiac vagal activity were observed as above. When baroreceptor stimuli were delivered immediately *before* (0·5–1 s) commencement of lung inflations vagal responses started, but the typical decaying activity which

usually followed was cut short at the moment the lungs inflated (Fig. 7*B*). Only the increment of discharge expected in response to the baroreceptor stimulus was inhibited – the pre-existing level of tonic discharge was little affected. This contrasts with the effects of central inspiratory activity which, when similarly related in time to a baroreceptor stimulus, inhibited both the expected vagal response and the pre-existing tonic discharge (Fig. 6*B*).

If a baroreceptor stimulus was given instead *during* a brief lung inflation, little or no vagal response was evoked either immediately, or after the end of the period of inflation (Fig. 7*C*; see also Figs. 3*C* and 4*C*). Tonic vagal activity was little affected through these manoeuvres. Again the effects of lung inflation were in contrast to those of central inspiratory activity. As described above, central inspiratory activity inhibited both vagal tone and the increment in vagal firing expected in response to a stimulus, but both tone and the residual response emerged unaffected at the end of the central activity (Fig. 6*C*).

When baroreceptor stimuli were given soon *after* the end ($\leqslant 1$ s) of brief periods of lung inflation, vagal responses were again not evoked, although vagal tone was little affected (Fig. 7*D*). The responses were similar, therefore, to those seen when stimuli were applied *during* a brief period of inflation (Fig. 7*C*).

DISCUSSION

It is known that in the inspiratory phase of breathing tonic activity in cardiac vagal efferent nerves is inhibited (Anrep *et al.* 1936*a*, *b*; Rijlant, 1936; Jewett, 1964; Davidson *et al.* 1976; McCloskey & Potter, 1981). Stimuli which can evoke cardiac vagal activity usually fail to do so when delivered in the inspiratory phase of breathing (Koepchen *et al.* 1961; Haymet & McCloskey, 1975; Neil & Palmer, 1975; Lopes & Palmer, 1976; Gandevia *et al.* 1978*a*, *b*). These stimuli include inputs from arterial baroreceptors and chemoreceptors, which were documented further here, as well as the more complex inputs associated with the oculocardiac reflex, the diving reflex, and reflex responses to nasopharyngeal stimulation (Gandevia *et al.* 1978*b*). The association between inspiration and inhibition of vagal excitation seems, therefore, to be to a quite general phenomenon. The inhibition has two components (Gandevia *et al.* 1978*a*), as the present study has confirmed: one associated with central inspiratory activity and another associated with the activation of intrapulmonary receptors by lung inflation.

Seller & Illert (1969) recorded potentials evoked in neurones of the nucleus of the tractus solitarius by carotid sinus nerve stimulation, and found no differences in amplitudes or latencies of responses evoked when stimuli were delivered in different respiratory phases. This fitted well with the later observation by Jordan & Spyer (1979) that, at least for arterial chemoreceptor or baroreceptor inputs, the inhibition caused by central inspiratory activity is not exerted presynaptically on the terminals of afferents from the carotid sinus nerve. In experiments on cats McAllen & Spyer (1978*b*: see also Spyer, 1979; Spyer & McAllen, 1980) showed that pulse-synchronous activity evoked through arterial baroreceptor inputs could be recorded extracellularly from the cell bodies of cardiac vagal motoneurones throughout the respiratory cycle. Such activity was usually demonstrable during the central inspiratory phase only

after direct ionophoretic application of excitant amino acids to the vagal cell bodies. Spyer & McAllen (1980) argued that because they were able to 'demonstrate qualitatively identical inputs from the carotid sinus baroreceptors and the sinus nerve during both inspiration and expiration... that this observation excludes a respiratory "gating" of reflex inputs at an earlier stage in the reflex pathway'. Certainly their analysis does show that there is no *complete* block of access of baroreceptor inputs to vagal motoneurones during inspiration, and permits McAllen & Spyer's suggestion that central inspiratory activity exerts its vagal inhibitory action at the vagal motoneurones themselves. However, additional incomplete, but possibly quite powerful, inhibition at earlier stages of the reflex pathway is not at all excluded. Spyer & McAllen's (1980) 'qualitatively identical inputs' to the vagal motoneurones evoked responses which, during inspiration, were greatly reduced in amplitude, and also were delayed in latency to peak firing by approximately 15 ms (see their fig. 6; see also McCloskey & Potter, 1981). Inhibitory influences earlier in the reflex pathway could well have been responsible for these effects. It is argued below that inhibitory effects from intrapulmonary receptors are exerted at such earlier stages in the reflex pathway from baroreceptors to vagal motoneurones. In any case, McAllen & Spyer's (1978*a*) experiments were unsuited to demonstrating effects from intrapulmonary receptors: their observations were made in open-chested animals in which one lobe of the lung had been removed, and which were receiving a shallow artificial ventilation.

Striking differences between the central and intrapulmonary afferent sources of inhibition have been documented here. Tonic vagal discharge is inhibited most powerfully and consistently by central inspiratory activity. Lung inflation has relatively little effect, except when vagal tone is high. This may explain why Jewett (1964) and McAllen & Spyer (1978*a*) found little alteration in vagal discharge in response to lung inflation while others, studying vagal tone through its effects on heart rate, attributed quite powerful effects to lung inflation (e.g. Anrep *et al.* 1936*b*; Aserinsky & DeBias, 1963; Daly, 1972; Gandevia *et al.* 1978*a*, *b*). In general, those studying heart rate seem to have been working with a background of strong vagal tone, and with larger inflations.

An important analytical device in the present study was the use of the typically prolonged vagal responses to brief stimuli. These prolongations of response are mainly due to the properties of the central relays between baroreceptor inputs and vagal motoneurones, and cannot be ascribed solely to temporal dispersion of afferent volleys along the carotid sinus nerve (McCloskey & Potter, 1981). Intracarotid pressure pulses were chosen as it is known that these selectively activate arterial baroreceptors for the duration of the rise in pressure (Haymet & McCloskey, 1975). Selective, briefly acting stimuli for arterial chemoreceptors have also been described (e.g. Black & Torrance, 1971; Haymet & McCloskey, 1975), but these were less suitable for the present experiments because, while they have a rapid onset, the precise duration of an individual stimulus cannot be determined. The fast onset of vagal firing accompanying a rise in intracarotid pressure but slow decline after a fall was noted previously by Katona, Poitras, Barnett & Terry (1970). Humphrey (1967), Biscoe & Sampson (1970) and Trzebski, Lipski, Majcherczyk, Szulczyk & Chruscielewski (1975) made intramedullary recordings of responses to carotid sinus nerve stimulation and to pulses of intracarotid pressure, and described cells which

discharged promptly and maintained their activity beyond the duration of the stimuli. Such cells may be involved in the effects described here.

In attempting to account for the differences between the inhibitory effects of central inspiratory activity and of lung inflation the following findings must be explained. Central inspiratory activity inhibits both tonic and specifically evoked vagal discharge, but leaves unaffected the residua of 'expected' responses to stimuli delivered while it is in progress. Lung inflations more effectively inhibit vagal responses to brief stimuli than tonic discharge, and this inhibition extends to involve also the residua of 'expected' responses to stimuli given during a period of inflation.

All vagal activity is inhibited for the duration of a central inspiratory burst, although the prolonged central excitatory state induced by a brief stimulus seems unaffected except in its ability to evoke a vagal response. It is as if the central inspiratory drive inhibits only the outflow of vagal impulses from the C.N.S., without interfering with the processes which normally evoke those impulses. Such an action would be consistent with the central inspiratory drive acting towards the end of the baroreceptor–vagal pathway and, indeed, there is no reason from the present study to suppose that it is not acting on the vagal motoneurones themselves, as suggested by McAllen & Spyer (1978*b*). Additional effects at other points in the baroreceptor–vagal pathway cannot be entirely excluded.

The inhibitory effects of receptors excited by lung inflation are more complicated. Lung inflation seems to have its main actions on phasic inputs, leaving responses to sustained inputs relatively unaffected. Also, it appears to have its inhibitory effect earlier in the vagal excitatory pathway (although not directly on the baroreceptor afferent terminals: Jordan & Spyer, 1979) and perhaps at more than one site. A simple model would be that lung inflation inhibits the access of brief baroreceptor stimuli to those parts of the central pathways which are responsible for 'prolonging' a brief input (while central inspiratory activity inhibits vagal motoneurones directly). This could explain why vagal responses to brief stimuli are blocked by simultaneous lung inflation while vagal tone remains relatively unaffected.

However, a lung inflation which occurs soon *after* a brief stimulus has established a brisk vagal response, inhibits the 'tail' of vagal after-discharge usually evoked by such a stimulus (Fig. 7*C*). In these circumstances, there can be no doubt that the stimulus has gained access to the central, 'prolonging' processes which usually excite vagal responses: nevertheless, the outflow from those processes through the vagus is inhibited. Clearly in this respect the situation is more complex than the simple model above would suggest.

This work was supported by grants from the National Heart Foundation of Australia and the National Health and Medical Research Council of Australia. I thank Drs D. I. McCloskey and B. S. Nail for their comments on the work throughout its progress. Diane Madden provided expert technical assistance.

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