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EFFECT OF PULMONARY VENOUS CONGESTION ON RESPIRATORY RATE IN DOGS

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SUMMARY

1. The effect of pulmonary venous congestion on the respiratory rate was examined in dogs anaesthetized with α-chloralose. The study was done on both spontaneously breathing and artificially ventilated animals. Pulmonary venous congestion was produced by partial obstruction of the mitral valve sufficient to raise the left atrial pressure by 5 mmHg.

2. In artificially ventilated dogs, pulmonary venous congestion increased significantly the activity in phrenic nerves. Both the number of bursts/min and the total number of impulses/min increased. However, there was no significant change in the number of impulses/burst.

3. In spontaneously breathing dogs, pulmonary venous congestion produced a significant increase in the frequency of breathing with a significant shortening of the inspiratory and expiratory durations.

4. Cooling of the cervical vagi to 8–9 °C abolished both the above responses.

5. Pulmonary venous congestion (left atrial pressure +5 mmHg) stimulated the rapidly adapting receptors of the airways. This effect was abolished by cooling the ipsilateral vagus proximally to 8–9 °C.

6. It is concluded that pulmonary venous congestion increases the respiratory rate reflexly in dogs. The afferent pathway for this reflex response resides in the vagus and the rapidly adapting receptors are likely to be the receptors involved in this response.

INTRODUCTION

Pulmonary congestion, when it occurs in a clinical setting as a sequel to acute left ventricular dysfunction, is often accompanied by an increase in the respiratory rate (McFadden & Ingram, 1984). However, in experimental animals, it has been difficult to demonstrate a clear relationship between pulmonary congestion and respiratory response. In general, these experiments have taken two forms. In the first, pulmonary congestion was produced by increasing the blood flow to a lung, isolated vascularly *in situ* (e.g. Daly, Ludany, Todd & Verney, 1937; Lloyd, 1978). In the second, pulmonary congestion was produced by obstructing the venous return from the lung (e.g. Marshall & Widdicombe, 1958). In a few studies, these two techniques were combined (Churchill & Cope, 1929; Aviado, Li, Kalow, Schmidt, Turnbull,

Peskin, Hess & Weiss, 1951; Downing, 1957). In all these investigations, the magnitude of the stimulus applied was physiologically excessive (e.g. pulmonary artery pressure > 40 mmHg, left atrial pressure of 20–40 cmH_2O). There are no studies to date in which a stimulus of physiological proportions was applied to examine the relationship between pulmonary congestion and the pattern of breathing.

Recent investigations have demonstrated that small degrees of pulmonary venous congestion produced by mitral valve obstruction, sufficient to increase the left atrial pressure by 5 mmHg, resulted in activation of the rapidly adapting receptors (RARs) in the dog lung (Kappagoda, Man & Teo, 1987*a*; Kappagoda, Ravi & Teo, 1987*b*). The investigations described in this paper were carried out in dogs to determine whether such a stimulus influenced the respiratory rate. The effect on respiratory rate was assessed by recording the activity in single functional units of the phrenic nerve and by recording the frequency of breathing. The former experiments were done on artificially ventilated dogs and the latter in dogs breathing spontaneously.

METHODS

Twenty-one dogs (body weight 20–32 kg) were anaesthetized with an intravenous infusion of α-chloralose (0·1 g/kg) after premedication with morphine sulphate. After induction of anaesthesia, the animals were ventilated artificially at the rate of 15 breaths/min. The inspired air was supplemented with oxygen (40% v/v). The details of these procedures have been described previously (Kappagoda *et al.* 1987*a*).

The chest was opened in the mid-line in some experiments and in the fourth intercostal space in others. The expiratory outlet from the ventilator was kept immersed in 2–3 cmH_2O. Catheters were introduced into the descending aorta through the femoral artery and the left atrium through the atrial appendage for recording their respective presssures. A septostomy catheter (size 5F, capacity 2·0 ml, Fogarty Dilation Catheter, Edwards Laboratories, Santa Ana, CA, USA) was introduced through the omocervical artery retrogradely and its balloon was positioned distal to the tip of the arterial catheter in the descending aorta. A second balloon-tipped catheter was introduced into the left atrium. This balloon was inflated with small volumes of saline as and when required to obstruct partially the flow of blood through the mitral valve and thus cause pulmonary venous congestion. The balloon of the septostomy catheter was inflated during this manoeuvre in order to prevent the fall in pressure in the aortic arch and its branches. A catheter placed in the femoral vein was used for intravenous infusions.

In those animals with a lateral chest incision, the chest was closed by suturing the muscles and the skin. The animals were disconnected from the ventilator and permitted to breathe spontaneously. A catheter was inserted into the intrapleural space and the pneumothorax was reduced by suction. This catheter was subsequently used for recording intrapleural pressure. All the cannulae for recording pressures were connected to strain gauge manometers (Model P23 DB, Statham Instruments Ltd, Hato Rey, Puerto Rico), the output of which was amplified and recorded on a light-sensitive paper (Model, VR 12, Electronics for Medicine/Honeywell, Pleasantville, New York, USA). The electrocardiogram (lead II) was also recorded in the same system.

The temperature of the animals was measured using a thermistor inserted into the oesophagus and was maintained at 37 ± 1 °C. The artificially ventilated animals were paralysed by giving gallamine triethiodide (1 mg/kg, Flaxedil, R.P. Pharmaceuticals Ltd, Canada) and this was repeated every hour (0·5 mg/kg). The arterial blood gases were monitored periodically and maintained in the normal range by adjusting ventilation and by infusing sodium bicarbonate (8·4% w/v).

Recording of phrenic activity

Nerve activity was recorded in fibres dissected from the central end of the fifth cervical root of the left phrenic nerve using bipolar silver–silver chloride electrodes. The output of the electrodes was amplified and recorded on the system described above. In addition, the activity in the fibres was counted electronically using a pulse discriminator (Man, Man & Kappagoda, 1983).

Recording of action potentials from the vagus

Single-afferent-fibre activity originating from RARs of the airways was recorded from the right cervical vagus using bipolar silver electrodes. The criteria used for the identification of the RARs have been described previously (Kappagoda *et al.* 1987*a*). The neural activity was recorded continuously and counted electronically (Man *et al.* 1983).

Vagal cooling

The right and left vagi were cooled in the neck using a silver thermode (Kappagoda, Linden & Sivananthan, 1979). In those dogs in which afferent vagal activity was recorded, only the right vagus was cooled and the thermode was positioned caudal to the recording electrode. In both instances, once the vagi had been cooled, a further 5 min were permitted to elapse before additional manoeuvres were undertaken.

Definition of inspiratory duration (T_i) and expiratory duration (T_e)

T_i and T_e were measured from the intrapleural records of the spontaneously breathing dogs in the manner described by Marshall & Widdicombe (1958) and Anand & Paintal (1980). T_i was measured from the sharp downward deflection to the nadir of the intrapleural pressure record. T_e was measured from the nadir to the beginning of the next sharp downward deflection.

Experimental protocols

Protocol 1: effect of pulmonary venous congestion on phrenic nerve activity. When a recording from a phrenic nerve was obtained, the neural activity was allowed to stabilize for 10 min. At the end of this period, the phrenic activity was recorded for an initial control period of 2 min. Pulmonary venous congestion was produced by partial obstruction of the mitral valve sufficient to raise the left atrial pressure by 5 mmHg for 2 min and the neural activity was recorded continuously. Then, the congestion was relieved and the neural activity was recorded for a final control period of 2 min. (During the period of congestion, the balloon in the thoracic aorta was inflated to prevent a fall in mean pressure in the aorta.)

Following this step, the effect of cooling the vagi on the changes in phrenic activity produced by pulmonary venous congestion was examined. For this purpose, the vagi were cooled to 8–9 °C and the protocol described above was repeated. Finally, the vagi were rewarmed to 37 °C and the protocol repeated once more.

Protocol 2: effect of pulmonary venous congestion on spontaneous respiration. This protocol was carried out in spontaneously breathing dogs. After the surgery was completed, 20–30 min was permitted to elapse for stabilization of the blood pressure, respiration and blood gases. Experimental recordings were made for an initial control period of 2 min. Then, pulmonary venous congestion (left atrial pressure +5 mmHg) was produced and recordings were made for a further 2 min. Finally, the congestion was relieved and the recordings were continued for a final control period of 2 min.

As in protocol 1, the sequence of recordings was repeated after both the vagi were cooled to 8–9 °C and again after they were rewarmed to 37 °C.

Protocol 3: effect of vagal cooling on the responses of rapidly adapting receptors to pulmonary venous congestion. After a RAR was identified, the preparation was permitted to equilibrate for 10 min. At the end of this period, the neural activity was recorded for an initial control period of 5 min. Pulmonary venous congestion (left atrial pressure +5 mmHg) was produced for 3 min. Then the congestion was relieved for a final control period of 3 min. The activity in the RAR was recorded throughout this protocol. This protocol was repeated after cooling the vagus to 8–9 °C and again after rewarming it.

Statistical analysis

Group data were expressed as mean ± S.E.M. In all protocols, the data obtained during the experimental periods were compared with those during the control periods using an analysis of variance. Where the analysis was significant ($P < 0.05$), the differences between means were detected by a least-significant-difference test.

RESULTS

The experiments were performed on a total of twenty-one dogs. At the commencement of the experiments, the heart rate, mean arterial blood pressure, mean left atrial pressure and peak intratracheal pressure in the open-chested animals were 155·0 ± 11·2 beats/min, 128·3 ± 10·1 mmHg, 5·5 ± 0·34 mmHg and 5·0 ± 0·52 mmHg, respectively. The pH, P_{CO_2} and P_{O_2} were 7·38 ± 0·01, 39·3 ± 0·6 mmHg and 143·8 ± 6·0 mmHg, respectively.

TABLE 1. Effect of pulmonary venous congestion, caused by partial obstruction of the mitral valve, on the activity of single functional phrenic nerve units ($n = 11$) (left atrial pressure increased by 5·2 ± 0·5 mmHg)

	Control	Pulmonary venous congestion	Control
Total impulses/min	68·6 ± 16·9	147·9 ± 31·1*	86·7 ± 26·9
No. of bursts/min	5·1 ± 1·0	10·3 ± 1·4*	6·0 ± 1·6
Impulses/burst	15·4 ± 3·2	16·8 ± 3·1	15·5 ± 3·5

* $P < 0.01$, significantly different from controls.

Protocol 1: effect of pulmonary venous congestion on phrenic activity

Eleven phrenic units were examined in eleven dogs. During the control period, these units showed spontaneous bursts of activity which were not synchronized with the ventilator. The ratio of the frequency of bursts/min to the ventilatory cycles varied from 1:8 to 1:2. When pulmonary venous congestion was produced by partial obstruction of the mitral valve, there was a significant increase both in the number of bursts/min ($P < 0.01$) and in the total number of impulses/min ($P < 0.01$). However, there was no significant increase in the number of impulses/burst. The activity returned to its control value when pulmonary venous congestion was relieved. An example obtained from a single phrenic unit is shown in Fig. 1. These findings are summarized in Table 1.

The heart rate, mean arterial blood pressure and mean left atrial pressure in the control period were 145·7 ± 7·3 beats/min, 135 ± 8·6 mmHg and 5·5 ± 0·4 mmHg, respectively. These values are the averages of the initial and final control values. During pulmonary venous congestion, the corresponding values were 156·3 ± 8·6 beats/min, 134·2 ± 9·5 mmHg and 10·7 ± 0·6 mmHg. The change in mean arterial blood pressure was not significant ($P > 0.05$). The increases in heart rate and in left atrial pressure were significant ($P < 0.05$).

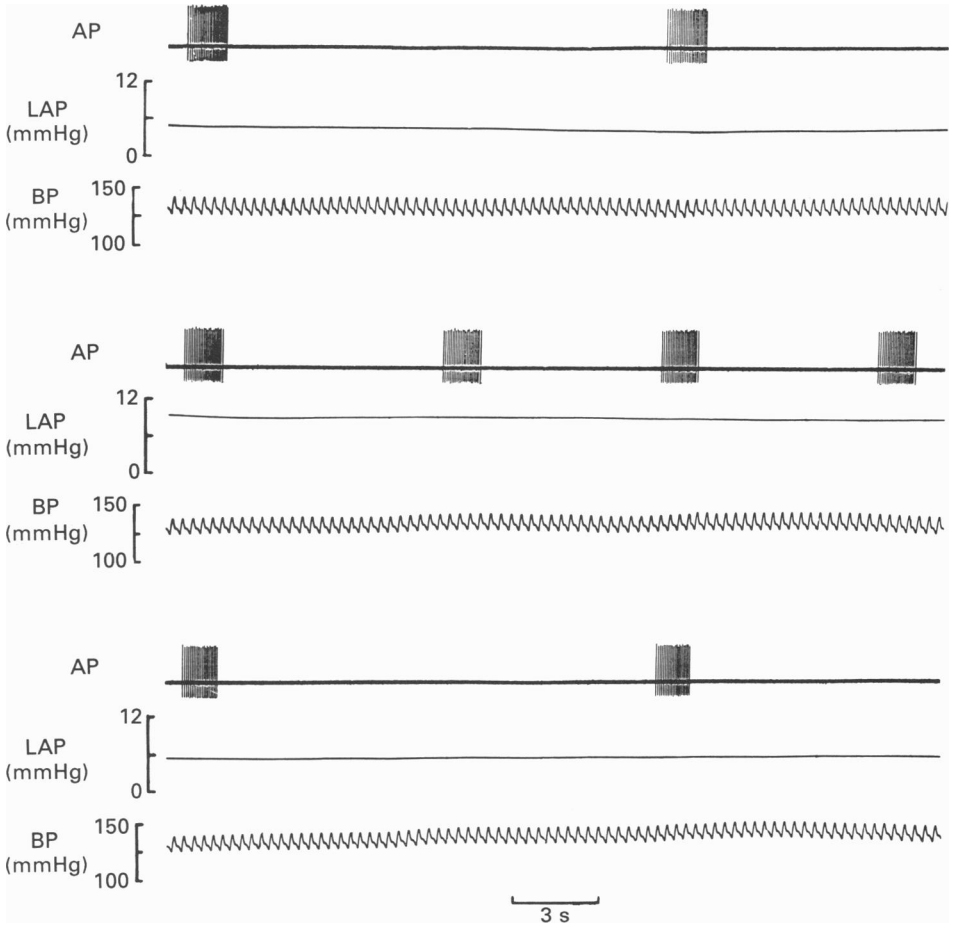

Fig. 1. Effect of pulmonary venous congestion on the activity of single functional units of the phrenic nerve. The neural activity during the initial control period, pulmonary venous congestion and final control period are shown in the upper, middle and lower panels, respectively. In each panel, the upper trace shows the action potentials (AP) recorded from the phrenic nerve, the middle trace shows the mean left atrial pressure (LAP) and the lower trace, the arterial blood pressure (BP). Note the increase in the number of phrenic bursts/min during congestion which occurred without a significant change in the number of phrenic impulses/burst (shown in the middle panel).

Effect of vagal cooling

The effect of vagal cooling was examined in six units. When the vagi were cooled, the number of phrenic bursts/min increased from $3{\cdot}4 \pm 0{\cdot}7$ to $5{\cdot}8 \pm 0{\cdot}5$. This increase was found to be statistically significant ($P < 0{\cdot}05$). There was a corresponding increase in the number of impulses/min ($P < 0{\cdot}05$, Table 2). However, the number of impulses/burst was not significantly altered ($P > 0{\cdot}05$, Table 2).

After the vagi were cooled, pulmonary venous congestion resulted in a reduction in the number of bursts/min from $5{\cdot}8 \pm 0{\cdot}5$ to $4{\cdot}1 \pm 0{\cdot}2$. This reduction was significant

($P < 0.01$). However, when congestion was relieved, the activity remained unchanged at 3.8 ± 0.3 bursts/min. Thus, in contrast to the circumstances when the vagi were warm, pulmonary venous congestion failed to increase the activity in the phrenic units. The response was restored after rewarming the vagi. These effects are summarized in Table 2.

TABLE 2. The effect of cooling the cervical vagi to 8–9 °C on the responses in single functional phrenic nerve units during pulmonary venous congestion produced by partial obstruction of the mitral valve ($n = 6$)

	Control	Pulmonary venous congestion	Control
(i) Before cooling			
Total impulses/min	53·5 ± 27·7	149·0 ± 58·2*	77·2 ± 50·1
No. of bursts/min	3·4 ± 0·7	10·0 ± 2·0**	4·2 ± 1·4
Impulses/burst	16·0 ± 5·2	17·6 ± 5·5	16·6 ± 6·1
(ii) Vagi at 8–9 °C			
Total impuses/min	83·7 ± 23·2	59·0 ± 25·5†	56·7 ± 23·6†
No. of bursts/min	5·8 ± 0·5	4·1 ± 0·2††	3·8 ± 0·3††
Impulses/burst	16·3 ± 5·7	15·2 ± 6·9	14·4 ± 6·4
(iii) After rewarming			
Total impulses/min	50·5 ± 24·4	109·3 ± 54·4*	47·7 ± 27·2
No. of bursts/min	3·3 ± 1·0	6·0 ± 1·1**	4·3 ± 1·1
Impulses/burst	14·3 ± 4·6	17·6 ± 4·9	10·7 ± 3·7

* $P < 0.05$ and ** $P < 0.01$, significantly different from both controls. † $P < 0.05$ and †† $P < 0.01$, significantly different from initial control only.

Protocol 2: effect of pulmonary venous congestion on spontaneous respiration

This protocol was completed in five dogs. In the control state, respiratory rate was 14.4 ± 2.2 breaths/min. During pulmonary venous congestion (left atrial pressure $+5.4 \pm 0.2$ mmHg), there was a significant increase in the frequency of breathing ($P < 0.05$). This increase occurred with a significant decrease in both T_i ($P < 0.01$) and T_e ($P < 0.05$). An example obtained from one dog is shown in Fig. 2. These results are summarized in Table 3.

The heart rate, mean arterial blood pressure and the mean left atrial pressure during the control period were 160.6 ± 8.2 beats/min, 122.6 ± 9.8 mmHg and 4.6 ± 0.2 mmHg, respectively. These values are the average of the initial and final control values. During pulmonary venous congestion, the corresponding values were 172.4 ± 6.0 beats/min, 119.8 ± 8.8 mmHg and 9.4 ± 0.5 mmHg. The increase in left atrial pressure was significant ($P < 0.001$).

When the vagi were cooled to 8–9 °C, the increase in frequency of breathing caused by pulmonary venous congestion was abolished (Fig. 3, Table 3). On rewarming the vagi, this response was restored.

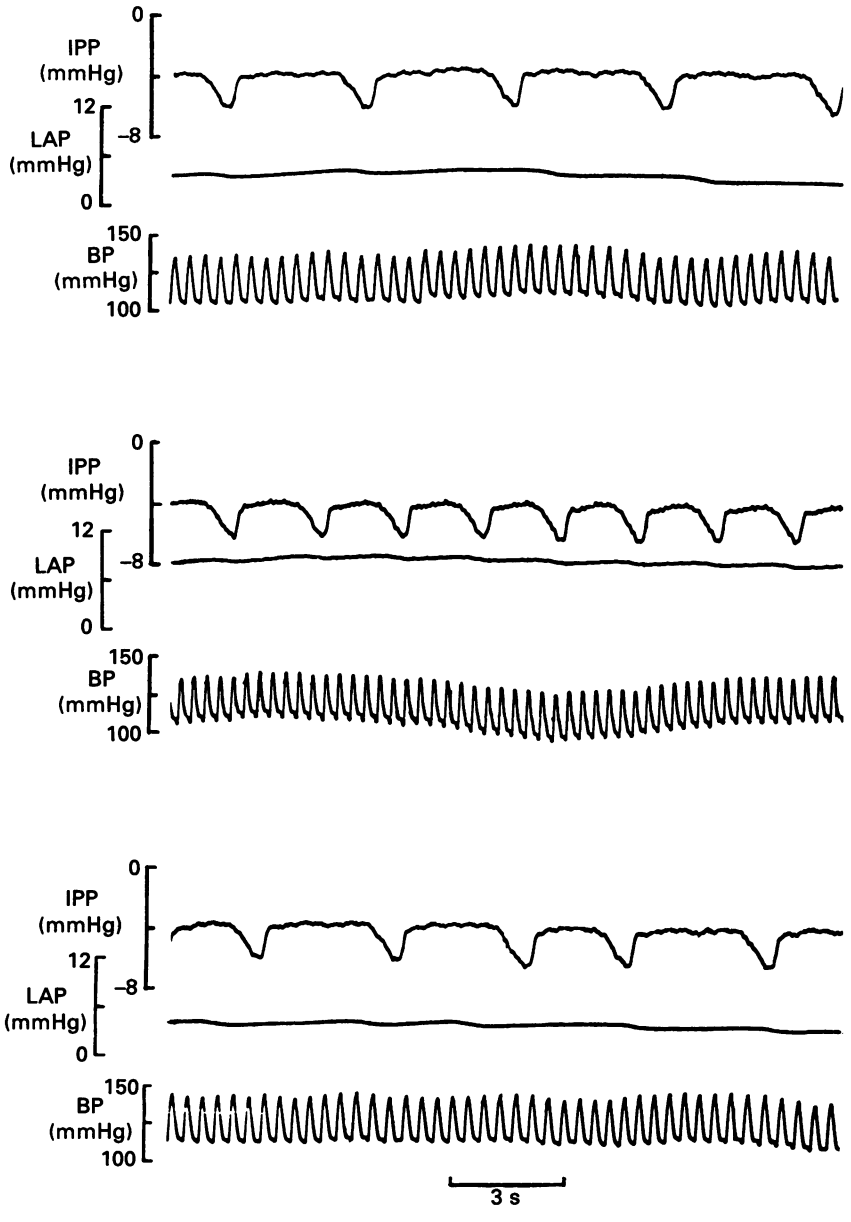

Fig. 2. Changes in respiration during pulmonary venous congestion in a spontaneously breathing dog. Experimental records during the initial control period, pulmonary congestion and final control period are shown in the upper, middle and the lower panels respectively. In each panel, the upper trace is a record of the intrapleural pressure (IPP), the middle trace, mean left atrial pressure (LAP) and the lower trace, arterial blood pressure (BP). Note the increase in respiratory rate during congestion occurring with a shortening of T_i and T_e (shown in the middle panel).

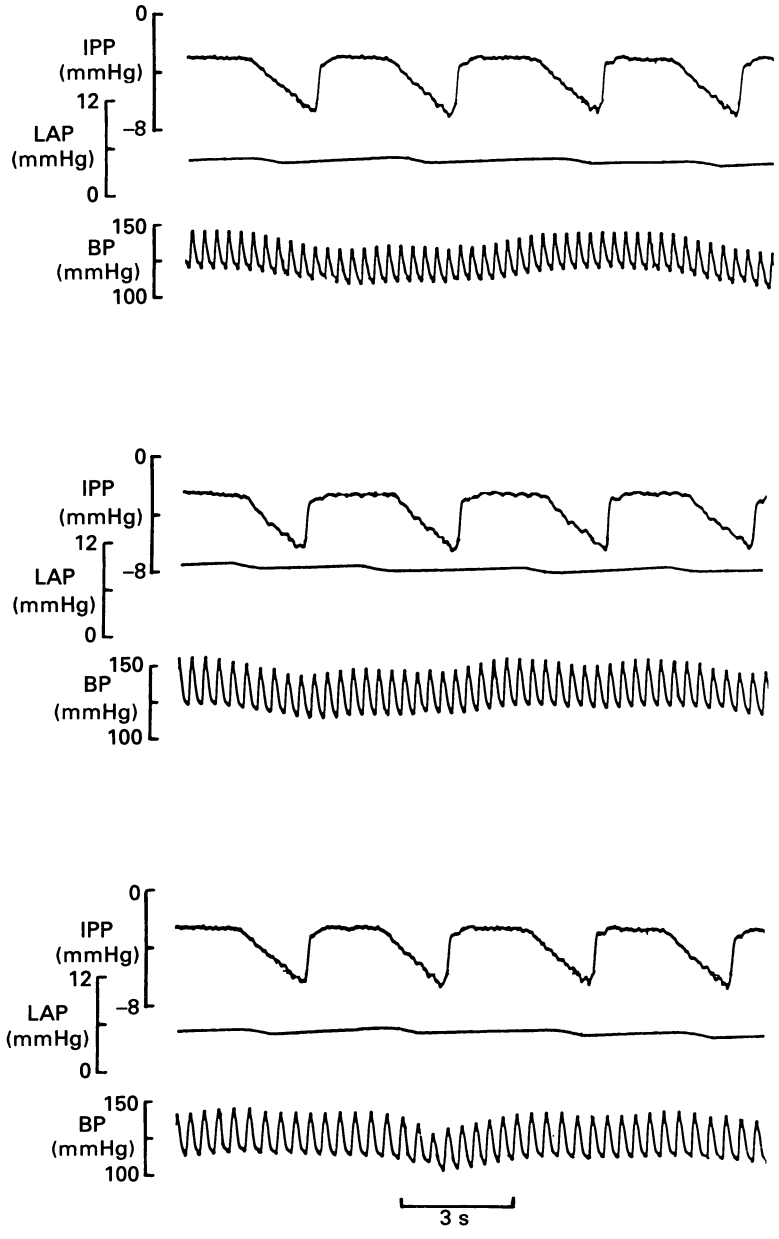

Fig. 3. Changes in respiration during pulmonary venous congestion after cooling the vagi to 8 °C. The control responses before cooling the vagi are shown in Fig. 2. The abbreviations in this figure are the same as in Fig. 2. After cooling, pulmonary venous congestion did not produce any significant change in respiratory rate (shown in the middle panel).

TABLE 3. Effect of pulmonary venous congestion produced by partial obstruction of the mitral valve on breathing before, during and after cooling the cervical vagi to 8–9 °C ($n = 5$)

	Control	Pulmonary venous congestion	Control
(i) Before cooling			
Respiratory rate (cycles/min)	14·4 ± 2·2	22·0 ± 3·8*	16·6 ± 2·2
T_i (s)	0·9 ± 0·1	0·7 ± 0·1**	0·9 ± 0·1
T_e (s)	4·0 ± 1·3	2·1 ± 0·3*	3·1 ± 0·7
(ii) Vagi at 8–9 °C			
Respiratory rate (cycles/min)	13·5 ± 1·2	13·3 ± 1·5	12·5 ± 0·9
T_i (s)	1·3 ± 0·2	1·3 ± 0·2	1·4 ± 0·2
T_e (s)	3·3 ± 0·5	3·5 ± 0·6	3·5 ± 0·5
(iii) After rewarming			
Respiratory rate (cycles/min)	15·3 ± 1·8	21·3 ± 1·8*	15·8 ± 1·6
T_i (s)	0·8 ± 0·1	0·8 ± 0·1	0·8 ± 0·1
T_e (s)	3·3 ± 0·7	2·1 ± 0·3*	3·2 ± 0·5

* $P < 0·05$ and ** $P < 0·01$, significantly different from controls.

Protocol 3: effect of vagal cooling on the responses of rapidly adapting receptors to pulmonary venous congestion

Five RARs were examined in this protocol. Their activity during the control period was 1·8 ± 0·5 impulses/s. During pulmonary venous congestion (left atrial pressure +5 mmHg), the activity increased to 3·0 ± 0·6 impulses/s ($P < 0·05$). During the final control period, the activity was 1·7 ± 0·5 impulses/s.

When the vagus was cooled to 8–9 °C, the control activity was abolished in four units. At this temperature, pulmonary venous congestion did not cause an increase in the activity of these units. In the fifth unit, the activity during the control period was 2·5 impulses/s and it was not altered by pulmonary venous congestion. On rewarming the vagus, the responses to pulmonary venous congestion were restored. The activity increased from 1·7 ± 0·4 to 2·9 ± 0·4 impulses/s during pulmonary congestion and returned to 1·6 ± 0·4 impulses/s during the final control period.

DISCUSSION

This investigation has demonstrated that pulmonary venous congestion, produced by partial obstruction of the mitral valve sufficient to increase the left atrial pressure by 5 mmHg, caused a consistent reflex increase in the respiratory rate. This effect was evident when the respiration was monitored both in terms of the activity in phrenic units (in ventilated animals) and in the overall rate of respiration (in spontaneously breathing animals). The reflex nature of these responses was established by abolishing both effects by cooling the cervical vagi to 8–9 °C.

There are two aspects of the present study which are novel. The first is that the responses were elicited by a relatively small degree of pulmonary venous congestion.

The second is that the response was a consistent increase in respiratory activity with no preceding period of apnoea. It is of interest to compare the present findings with those reported in the literature in which comparable experimental techniques were employed. Of particular interest is that reported by Marshall & Widdicombe (1958) who examined this phenomenon in cats. In experiments where the left atrial pressure was increased to 20–40 cmH_2O by inflating the balloon in the left atrium for periods less than 2 min but usually for 30 s, there was an increase in the frequency of breathing (see Fig. 5*A*, Marshall & Widdicombe, 1958). After cooling the vagi to 8 °C, pulmonary congestion produced long and powerful inspiratory efforts (see Fig. 5*B*, Marshall & Widdicombe, 1958). The latter observation differs from the findings reported here (see Fig. 3). While species variation cannot be discounted, it is likely that activation of other reflex pathways (e.g. baroreceptors) could have contributed to their findings. In the present study, the obstruction to pulmonary venous drainage was small (left atrial pressure +5 mmHg) and the systemic arterial blood pressure was controlled.

Effects on respiration

The present study has been confined to examining the effect of pulmonary venous congestion on the respiratory rate. In the first part, the activity in single phrenic units was used as the index of the central respiratory drive (Tenney, 1963; Severinghaus, 1966). It was found that the bursts of activity in the phrenic nerves did not coincide with the cycling of the rate of the ventilator. This asynchrony, which has been described previously (Man *et al.* 1983), continued during pulmonary venous congestion also, even though there was an increase in the phrenic activity in terms of the number of bursts/min. It is known that a poor correlation exists between the number of phrenic impulses/breath and tidal volume (Eldridge, 1971). It was found that a significant number of phrenic impulses occur during the early phase of expiration. When individual phrenic units were considered, there appeared to be a selective pattern of recruitment into the phrenic discharge (Eldridge, 1971). Further, there is evidence to suggest that the effects of agents such as carbon dioxide on single phrenic units can be variable (Nail, Sterling & Widdicombe, 1969). The selective nature of the behaviour of the individual phrenic units could provide an explanation for the observations in the present study where the number of action potentials/burst remained unchanged, even though the number of bursts/min (Tables 1 and 2) and the number of breaths/min (Table 3) increased during pulmonary venous congestion. Even after cooling the vagi to 8–9 °C, when the respiration became deeper, the number of phrenic impulses/breath did not change significantly. Thus, the changes in the number of bursts/min in the phrenic units only reflected the changes in the frequency of breathing.

In the experiments in which the intrapleural pressure was recorded, the pressure tracing was found to be attenuated during pulmonary venous congestion (Fig. 2) suggesting a possible reduction in tidal volume. However, in the absence of direct measurements, no further conclusions can be drawn regarding minute ventilation.

Nature of the stimulus

The magnitude of the stimulus is important for two reasons. First, Guyton & Lindsey (1959) have demonstrated that elevation of left atrial pressure by 25 mmHg is sufficient to cause pulmonary oedema. Thus, when pressures of such magnitude are used to obstruct the venous return from the lung, it is difficult to differentiate the effects of congestion *per se* from those due to pulmonary oedema. The latter is a particularly important consideration in view of the observation that oedema activates non-myelinated afferents originating from the airways and lungs (Paintal, 1973; Roberts, Bhattacharya, Schultz, Coleridge & Coleridge, 1986). The second is that changes in systemic pressure are likely to cause concurrent changes in respiration through a change in the input from the arterial baroreceptors (Heymans & Neil, 1958; Brunner, Sussman, Greene, Kallman & Shoukas, 1982).

Both these influences could be discounted in the present study because of the modest degree of mitral valve obstruction applied. It is unlikely that oedema occurred at these levels of left atrial pressure. Further, by controlling the arterial pressure, it was possible to minimize any potential change in the baroreceptor inputs. Therefore, it is likely that the stimulus would have activated receptors either in the lung or in the left atrium. Ledsome & Hainsworth (1970) have established that stimulation of left atrial receptors which discharge into myelinated vagal fibres has no effect on respiration. In addition, these small changes in left atrial pressure are unlikely to activate the non-myelinated afferents which originate from the atria (Thoren, 1976). Thus, it is suggested that the receptors responsible for the reflex responses observed in the present study are located in the lungs.

Type of receptor

The abolition of the response by cooling the cervical vagi to 8–9 °C indicates that it was mediated by myelinated fibres in the cervical vagi. At these temperatures, transmission in the non-myelinated fibres from the heart and lungs will be intact (Paintal, 1973). There are two groups of pulmonary receptors with myelinated fibres in the vagi. These are the slowly adapting stretch receptors (SARs) and RARs. It is recognized that stimulation of SARs alters respiration by reducing the inspiratory phase and prolonging the expiratory one (Clark & von Euler, 1972; Bartoli, Bystrzycka, Guz, Jain, Noble & Trenchard, 1973). Pulmonary venous congestion resulting from larger increases in left atrial pressures activates the SARs to a small degree (Marshall & Widdicombe, 1958; Kappagoda *et al.* 1987*a*). Thus, a part of the reflex response observed, *viz.* a reduction in the T_I during congestion, could be due to stimulation of SARs. However, it is unlikely to be the main afferent mechanism mediating this response since the SARs are not activated to a significant extent by the stimulus employed (Kappagoda *et al.* 1987*a*). In contrast, the RARs are clearly activated by it (Kappagoda *et al.* 1987*a*, *b*; present results). Further evidence in support of a role for the RARs in this reflex is provided by the observation that the increase in activity in RARs during pulmonary venous congestion is abolished by cooling the ipsilateral vagus to 8–9 °C.

In anaesthetized dogs, it is recognized that stimulations of pulmonary C-fibre receptors by capsaicin (Schertel, Adams, Schneider, Smith & Green, 1986; Ravi,

1988) and bronchial C-fibre receptors by bradykinin (Kaufman, Coleridge, Coleridge & Baker, 1980; Coleridge, Coleridge & Roberts, 1983) result in rapid shallow breathing. Both these groups of afferent C fibres are stimulated by pulmonary oedema (Roberts *et al.* 1986). In an earlier investigation, it was observed that pulmonary venous congestion of a moderate nature (insufficient to cause pulmonary oedema) stimulated the bronchial C-fibre receptors but was without effect on the pulmonary C-fibre receptors (Kappagoda *et al.* 1987*a*). Hence it may be argued that the pulmonary C-fibre receptors may not have a role to play in the observations of the present study. It is possible that the changes in respiratory rate seen during pulmonary venous congestion could have contributions from bronchial C-fibre receptors. However, the abolition of the reflex responses by cooling the cervical vagi to 8–9 °C argues against this possibility. It seems reasonable therefore to ascribe the observations of the present study mainly to stimulation of RARs.

The RARs are located principally in the carina and the larger intrapulmonary bronchi (for references, see Widdicombe, 1974). A significant proportion of the venous drainage from these regions is to the pulmonary circulation (Pietra & Fishman, 1978). Thus, it is conceivable that the location of these receptors is congested when the venous drainage from the lung is compromised. Such considerations provide a physiological basis for the observations of Aviado *et al.* (1951). In experiments in which lungs were isolated vascularly and perfused, they observed that increasing the perfusion pressure alone was without effect on respiration. However, when the stimulus was combined with obstruction to the venous drainage from the lung, the respiratory rate increased. Further, retrograde perfusion of the lung produced an increase in respiration. On the basis of these studies, the authors concluded that the receptors involved in this reflex were likely to be in the vicinity of the pulmonary veins. One could speculate that the observations were due to activation of RARs by pulmonary venous congestion.

It is concluded that the findings presented in this paper support the contention that pulmonary venous congestion of a degree which is likely to occur physiologically, results in an increase in the respiratory rate and this increase is likely to be mediated by the RARs.

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