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THE EFFECTS OF CHANGES OF EXTRAMURAL, 'INTRATHORACIC', PRESSURE ON AORTIC ARCH BARORECEPTORS

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SUMMARY

1. The isolated aortic arch was perfused by a method enabling the mean pressure, pulse pressure and pulse frequency to be varied independently. The preparation was also subjected to phasic and non-phasic changes of extramural pressure.

2. The aortic arch baroreceptor impulse activity in single or few-fibre preparations was increased by raising the intra-aortic pressure and by applying a negative extramural pressure at constant intra-aortic pressure.

3. Curves relating impulse frequency and negative extramural pressure were similar to those relating impulse frequency to intra-aortic pressure. The effective stimulus to the aortic arch baroreceptors is the transmural pressure resulting from the algebraic difference of the intra-aortic and extramural pressures.

4. Rhythmical alterations in extramural pressure caused phasic changes in baroreceptor impulse activity. As the pressure became more negative, the impulse frequency increased and other baroreceptors were recruited.

5. During pulsatile perfusion of the aortic arch the maximum impulse activity occurred when the negative phase of extramural pressure coincided with the systolic phase of the perfusion pressure.

6. These findings are discussed in relation to the effects of changes of intrathoracic pressure on aortic baroreceptor activity *in vivo*

INTRODUCTION

Due to its anatomical position in the thorax the aortic arch is subjected to rhythmical changes of extramural pressure during normal breathing and to larger changes of pressure during for instance, coughing, sneezing, and a Valsalva manoeuvre. Hitherto no systematic studies have been made of the effect of these intra-thoracic pressure changes on the aortic arch baroreceptors.

In this paper the results of experiments are described in which the isolated aortic arch was perfused under controlled conditions and subjected to non-phasic and phasic changes of negative extramural pressure to mimic the changes in intrathoracic pressure occurring with respiration. The effects on the aortic arch and right subclavian baroreceptors were studied in single- or few-fibre preparations of the left and right aortic nerves. Some of the results have been described briefly elsewhere (Angell James, 1968).

METHODS

New Zealand white rabbits weighing 1·8–2·9 kg were anaesthetized with urethane (25 g/100 ml. deionized water) in a dose of 1·6–2·5 g/kg.

A tracheostomy was performed and the animals were ventilated with a respirator pump (C. F. Palmer Ltd.). The aortic arch was approached through a mid line thorocotomy.

Isolation and perfusion of the aortic arch

The aortic arch was isolated by ligating the left and right subclavian arteries, the internal mammary arteries, the left common carotid artery and any anomalous branches arising from the aortic arch and its main branches (Angell James, 1969). The descending thoracic was ligated at the level of the left pulmonary artery. The preparation was perfused with Krebs–Henseleit solution through a brass cannula which was passed through the wall of the left ventricle so that its tip lay in the ascending aorta, and the effluent drained out through a nylon cannula ('Portex' o.d. 1·65 mm) tied into the right common carotid artery. The temperature of the perfusate ranged from 37·5 to 38·5° C (mean 38·2° C). The mean pressure, pulse pressure and pulse frequency were controlled independently using the method described by Daly (1955). Full details of the techniques are described elsewhere (Angell James, 1968, 1969, 1971*a*, *b*).

The whole preparation including the heart, lungs and prevertebral tissues was excised, whilst perfusion was continued, and it was then placed in an artificial thorax.

Artificial 'thorax'

This consisted of an air-tight Perspex box, details of which are shown in Fig. 1. Its dimensions were: length 21·6 cm, width 14 cm, depth 7·6 cm, wall thickness 0·6 cm except for the lid which was 1·3 cm. The lid was sealed with Silicone grease and held in position by springs (F) at the four sides. Positive or negative pressures were applied to the inside of the box via a tube sealed into one of its sides. The apparatus was capable of withstanding internal pressure in excess of -100 to $+200$ mm Hg.

The box was provided with adjustable fixtures for immobilizing the trachea (B), the carotid cannula (A) and aortic perfusion cannula (E), and the arrangement was such that the whole preparation, which lay on a black Perspex platform (D) 10·1 cm × 8·9 cm, was elevated at one end at an angle of 20° to the horizontal. This platform had a dual purpose of supporting the preparation and acting as a dark background against which the nerve fibres could be dissected.

Provision was also made for (1) supporting the carotid cannula by an adjustable clamp attached to the tracheal cannula, (2) supporting the two adjustable electrode holders (J), (3) conveying though the wall of the box the wires making connexion with the electrodes (K), thermocouple and earth lead (G) a 6-pin D.I.N. adaptor (L), and the two pressure manometer catheters (H, I), and (4) withdrawing excess fluid from the box.

The box was filled with warm Krebs–Henseleit solution up to the level of the aortic arch. The temperature of the solution was maintained constant by a coil of polyethylene tubing (C) through which water was pumped at a temperature of 40° C from a thermostatically controlled water-bath. The temperature of the perfusate ranged from 37·5 to 38·5° C (mean 38·2° C) and was measured with a copper-constantan thermocouple situated in the tip of the aortic cannula (E), using a Cambridge galvanometer and a control thermocouple in a flask of water at room temperature.

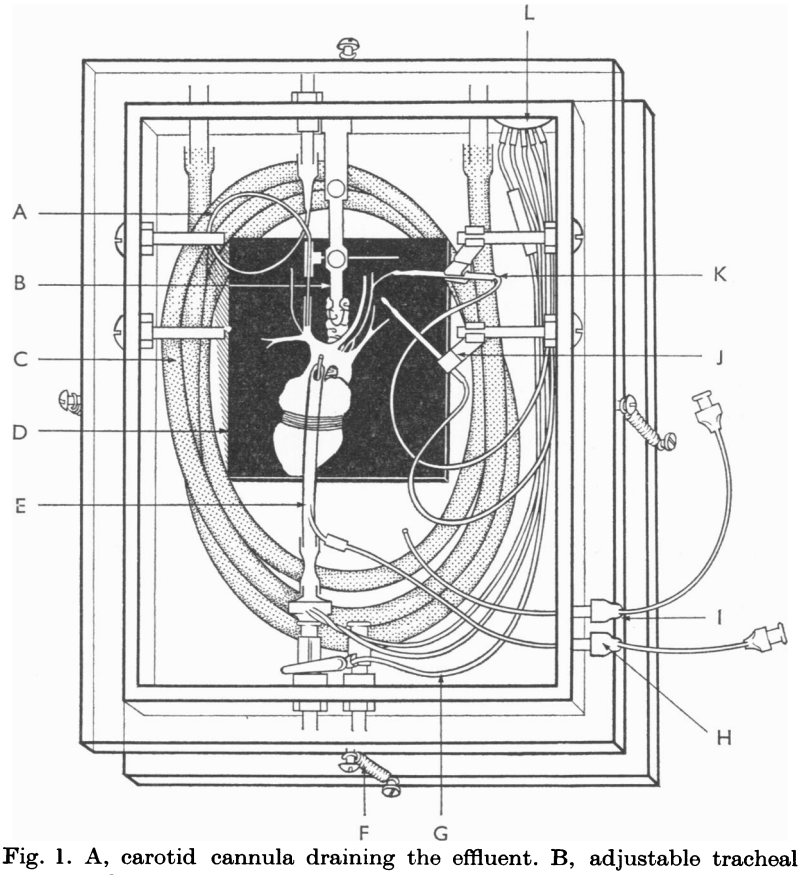

Fig. 1. A, carotid cannula draining the effluent. B, adjustable tracheal support. C, warming coil. D, black Perspex angled platform. E, aortic cannula (with the thermocouple) through which the preparation is perfused. F, springs to fix the lid down. G, earth wire. H, adaptor for electromanometer recording intra-aortic pressure. I, adaptor for electromanometer recording extramural pressure. J, adjustable electrode holder. K, saline wick, silver–silver chloride electrode.

Non-phasic changes in extramural pressure were produced by withdrawing air with a pump, the pressure being controlled by an air-leak bypass. Phasic negative pressure changes in extramural pressure were brought about by connecting the box to a bellows respiration pump (C. F. Palmer, Ltd.) the reverse way. The size of the pressure change was controlled by an adjustable air-leak bypass.

Recording methods. In experiments in which non-phasic pressures were applied to the preparation, mean intra-aortic and extramural pressures were measured with mercury manometers and recorded on a smoked paper kymograph. In experiments in which pulsatile pressures were used, the pressures were measured with Bell & Howell transducers (Type 4-326-L212) excited at 10 V d.c. The pressures were transmitted to the transducers with Sterivac polyethylene cannulae (length, 30 cm; bore 1·5 mm). The undamped natural frequency response of the intra-aortic catheter manometer system was 70 c/s (degree of damping 0·35), giving an estimated amplitude distortion of less than 5 % up to 25 c/s; the corresponding values for the catheter-manometer system measuring extramural pressure were 50 c/s, degree of damping 0·3 c/s, and 15 c/s respectively.

The output from each electromanometer was amplified by a system containing two differential operational amplifiers (Fenlow AD 2000) and was recorded on ultra-violet light-sensitive paper (Kodak Linograph Type 1843) with an ultra-violet light recording oscillograph (Type SE 2005, S.E. Laboratories Ltd) using a B450 galvanometer (S.E. Laboratories Ltd).

Action potentials from single or few-fibre preparations of the aortic nerves were recorded with saline wick electrodes with silver–silver chloride wires. They were amplified with a Tektronic 122 preamplifier and amplified and displayed on a cathode ray oscilloscope where they were photographed with a camera using Ilford paper. Alternatively they were displayed on the ultra-violet paper after amplification with a system containing differential operational amplifiers by means of A3300 galvanometer (S.E. Laboratories, Ltd). Records were also displayed on a large screen oscilloscope (Airmec type 279 with time base 370) and were also led to a loadspeaker via an A.F. amplifier (Newmarket PC5) for audible monitoring.

RESULTS

Comparison of the effects of raising the intra-aortic pressure with reducing the extramural pressure

In seven experiments a study was made of the relative effects on baroreceptor discharge of raising the intra-aortic pressure on the one hand and of reducing the extramural pressure on the other during non-pulsatile perfusion of the aortic arch.

In Fig. 2 the typical records are shown of the impulse activity in a single baroreceptor fibre from the left aortic nerve during a progressive step wise reduction of the extramural pressure at a constant intra-aortic pressure of 20 mm Hg. The corresponding graph beneath shows the relationship between the impulse frequency and the transmural pressure (intra-aortic pressure minus the extramural pressure). Reducing the extramural pressure in steps produced a progressive increase in the baroreceptor impulse frequency from 50 to 89 impulses/sec which was similar to the effect obtained in other experiments by progressively elevating the intra-aortic pressure as described previously (Angell James, 1968, 1969, 1971*a*).

The results from five fibres in three experiments are summarized in Table 1 in which the effects of progressively increasing the intra-aortic arch pressure have been compared with the effect of progressively reducing

the extramural (intra-thoracic) pressure, and a typical experiments is shown in Fig. 3. The Figure shows the similarity of the curves relating impulse frequency to transmural pressure obtained by these two methods. It was found (Table 1) that the threshold pressure was slightly higher, though not significantly, in four of the fibres when the effective stimulus to the baroreceptors was the reduction of extramural pressure. Again the frequency of impulses at this pressure was also slightly higher in four fibres.

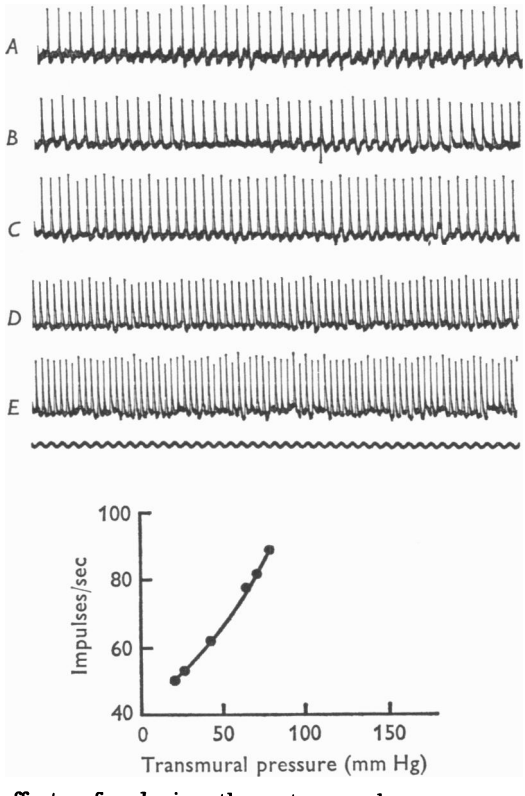

Fig. 2. The effects of reducing the extramural pressure on the impulse frequency of a single fibre from the left aortic nerve of a rabbit (wt., 1·8 kg). Intra-aortic perfusion pressure maintained constant at 20 mm Hg. The graph shows the relationship between impulse frequency and transmural pressure.

Analysis of the impulse frequency at pressures of 80 and 100 mm Hg shows that the frequency was slightly lower (mean $-14{\cdot}6 \pm 10{\cdot}6$ and $-7{\cdot}8 \pm 6{\cdot}6$ impulses/sec respectively) when the extramural pressure was reduced but the difference was not significant ($P > 0{\cdot}2$ and $P > 0{\cdot}3$). Moreover, the gradient of the curves was less by a mean of $0{\cdot}53 \pm 0{\cdot}67$ impulses/sec.mm Hg ($P > 0{\cdot}1$).

In another four fibres from two other experiments the intra-aortic pressure was elevated and the extramural pressure reduced alternately in a stepwise manner and the impulse frequency was plotted against the transmural pressure. It was found that the resultant curves were similar to those produced by raising the intra-aortic pressure alone.

In five other experiments, it was demonstrated that *increasing* the extramural pressure caused a reduction in impulse activity in single fibres of the aortic nerve comparable with that of reducing the intra-aortic pressure by the same amount.

TABLE 1. The relationship of baroreceptor impulse frequency to transmural pressure which was elevated by increasing the intra-aortic pressure (*A*), or by reducing the extramural pressure (*B*). Five fibres in three experiments. Non-pulsatile perfusion of the aortic arch

	A Intra-aortic pressure increase	*B* Extramural pressure decrease	Difference (*B*–*A*)
Threshold pressure (mm Hg)	59·4 ± 12·5 (23–95)	68·4 ± 11·2 (33–102)	9·0 ± 4·0 (−4 to +18) $0{\cdot}1 > P > 0{\cdot}05$
Frequency at threshold (impulses/sec)	24·4 ± 8·8 (2–42)	22·2 ± 7·6 (5–41)	−2·2 ± 4·2 (−19 to +3) $P > 0{\cdot}6$
Frequency at 80 mm Hg (impulses/sec)	63·8 ± 9·8 (40–83)	52·0 ± 8·2 (35–70)	−14·6 ± 10·6 (−45 to 0) $P > 0{\cdot}2$
Frequency at 100 mm Hg (impulses/sec)	59·0 ± 18·6 (7–87)	51·3 ± 17·2 (5–88)	−7·8 ± 6·63 (−27 to +3) $P > 0{\cdot}3$
Gradient (impulses/sec. mm Hg)	1·79 ± 0·30 (1·1–2·77)	1·3 ± 0·83 (0·58–2·7)	−0·53 ± 0·67 (−1·62 to +0·1) $P > 0{\cdot}1$

The open values are the means ± S.E. of mean. The ranges are in parentheses.

It may be concluded that changing the extramural aortic arch pressure is an effective way of altering the activity of the baroreceptors. From the similarity of the curves produced by changing the intra-aortic and extramural pressures in opposite directions by equivalent amounts (Fig. 3) it follows that one of the effective stimuli of the aortic baroreceptors is an increase in transmural pressure.

The effects of phasic changes in extramural pressure

The intrapleural pressure changes which occur during respiration were mimicked by subjecting the isolated perfused aortic arch preparation to phasic changes of extramural pressure in the artificial 'thorax' (Fig. 1). The pressures during 'expiration' were zero mm Hg, and during 'inspira-

tion' were up to −30 mm Hg; and the cyclical changes in pressure were applied at a frequency of 20 or 30 c/min.

Non-pulsatile perfusion of aortic arch

Sixteen tests were performed on eight single- or few-fibre preparations in five experiments in which phasic changes in extramural pressure were applied at a frequency of 20 or 30 c/min. The intra-aortic pressure was

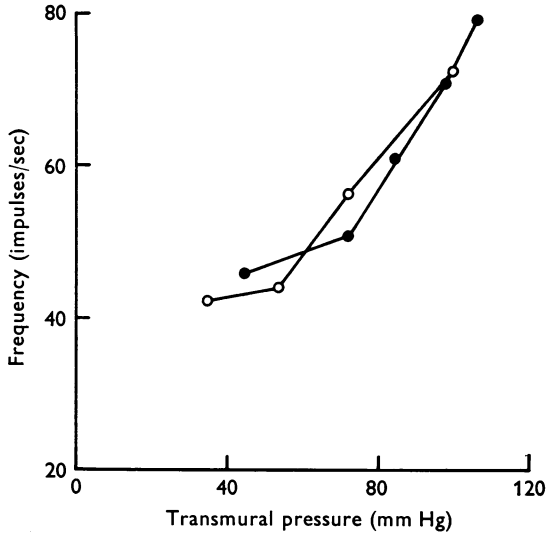

Fig. 3. Graph showing the relationship between the impulse frequency and transmural pressure of a single baroreceptor fibre from the left aortic nerve. Rabbit wt., 2·9 kg. The transmural pressure was elevated by increasing the intra-aortic pressure (*filled circles*, ●), or by reducing the extramural pressure at constant intra-aortic pressure (*open circles*, ○).

TABLE 2. The effect of phasic changes in extramural pressure with non-pulsatile perfusion of the aortic arch. Results of sixteen tests on eight fibres in five experiments

Frequency of 'respiratory' cycle	20–30 c/min
'Respiratory' cycle pressures	0 to −30 mm Hg
Intra-aortic arch mean pressure	Range 30–99 mm Hg
Peak impulse frequency during 'expiration'	Range 47·5–59 impulses/sec
Peak impulse frequency during 'inspiration'	Range 59–83 impulses/sec

maintained at a constant level of 30–99 mm Hg and did not vary by more than 3 mm Hg in any experiment. The results are summarized in Table 2. At zero extramural pressure there was a steady discharge of impulses in fibres of the aortic nerve at a frequency varying from 47·5 to 59 impulses/sec in different tests. It was invariably found that during the negative phase of the 'respiratory' pressure cycle, the discharge increased, the peak impulse

frequency varying from 59 to 83 impulses/sec. The typical response of a few-fibre preparation is shown in Fig. 4 when a phasic extramural pressure of −20 mm Hg was applied at a frequency of 20 c/min to the aortic arch which was being perfused at a pressure of 47 mm Hg. The peak frequency of the smaller fibres increased from 39 to 50 impulses/sec when the extramural pressure was reduced to −20 mm Hg (transmural pressure 67 mm Hg). A second fibre was recruited at 62 mm Hg transmural pressure and reached a peak frequency of 50 impulses/sec at the maximum transmural pressure of 67 mm Hg. The third fibre also increased its frequency to reach a peak at the maximum transmural pressure. Again in Fig. 6*A*, taken from another experiment, a change of extramural pressure from zero to −12 mm Hg increased the discharge frequency of the large action potential from 67 to 95 impulses/sec.

It was observed during the negative pressure cycle that the instantaneous impulse frequency at any given transmural pressure was greater during the 'inspiratory' part of the cycle than at the same pressure during the 'expiratory' part of the cycle. This is illustrated in Fig. 5 in which the impulse frequency is plotted against the transmural pressure for one of the fibres illustrated in Fig. 6*A*. An elliptical shape of the curve is probably due to the alteration of the visco-elastic properties of the aortic wall after previous expansion (Angell James, 1969, 1971*b*).

It was found in different experiments that the transmural pressure at which a fibre was recruited during 'inspiration' was lower, equal to, or higher than that at which the fibre ceased firing during 'expiration'. Thus in Fig. 4, the two transmural pressures are the same in the case of the larger recruited fibre, whereas with the smaller recruited fibre the transmural pressure at which it was recruited during 'inspiration' was higher than that at which the fibre ceased firing during 'expiration'.

These experiments demonstrate therefore that at constant intra-aortic arch pressure a phasic 'respiratory' type change of extramural pressure produces a progressive change of frequency of impulses in aortic baroreceptor fibres. The frequency increases as the transmural pressure increases during the negative phase of the cycle and vice versa. At the same time there is recruitment of other fibres.

Pulsatile perfusion of aortic arch

In vivo the aortic arch of the rabbit is normally subjected to intra-aortic pulsatile pressures of about 20–30 mm Hg amplitude at a mean pressure of about 90 mm Hg and a frequency of 200–400 c/min by the heart beat. At the same time it is subjected by extramural rhythmical negative changes of intrathoracic pressure due to respiration. This situation was mimicked in the excised aortic arch preparation by a combina-

tion of pulsatile perfusion and phasic changes in extramural pressure. Sixteen tests in three experiments were performed on six single- and few-fibre preparations. The aortic arches were perfused with pulsatile pressures of 15–44 mm Hg at mean pressures of 33–105 mm Hg and pulse frequencies of 160 or 210 c/min.

The typical effects of phasic changes of extramural pressure are shown in Fig. 6. In *B* and *C* the mean aortic arch pressure was 97 mm Hg, the

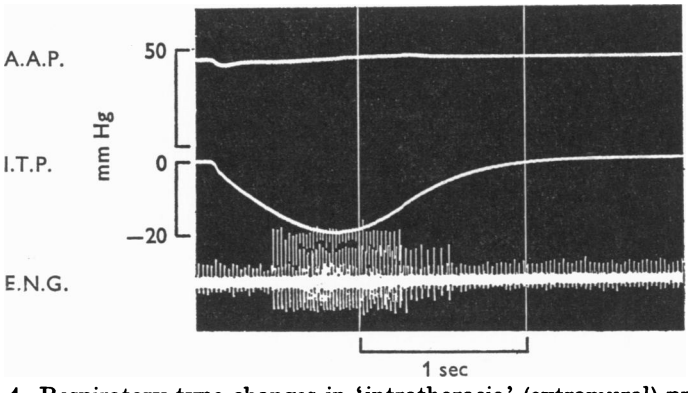

Fig. 4. Respiratory type changes in 'intrathoracic' (extramural) pressure of −20 mm Hg applied at a frequency 20 c/min to an isolated aortic arch perfused with Krebs–Henseleit solution at a pressure of 47 mm Hg (non-pulsatile). E.N.G., electroneurogram from the left aortic nerve. A.A.P., aortic arch pressure (mm Hg). I.T.P., intrathoracic (extramural) pressure (mm Hg).

pulse pressure 34 mm Hg and pulse frequency 210 c/min. In *B* the extramural pressure was zero and the impulse frequency was in time with the pressure pulse, the maximum frequency occurring during systole. During diastole there was a pause in the discharge of 12·3 msec duration. Fig. 6*C* shows the effects of a single 'respiratory' cycle, during which the extramural pressure fell to −12 mm Hg. The following points may be observed. When the 'inspiratory' phase of the 'respiratory' cycle coincides with the systolic phase of the pulse pressure cycle there is an increase of peak frequency in the largest action potential from 140 to 167 impulses/sec, and in two other fibres. At the same time there is recruitment of additional fibres. The period of no discharge during the diastolic phase of the intra-aortic pressure cycle is reduced from 12·3 msec to 6·3 msec. During 'inspiration', therefore, there is an increase in the total number of impulses/pulse pressure cycle and also in the total number of impulses per unit time.

A similar result was obtained in fifteen tests on five fibres in three other experiments. At zero extramural pressure the peak frequency of individual

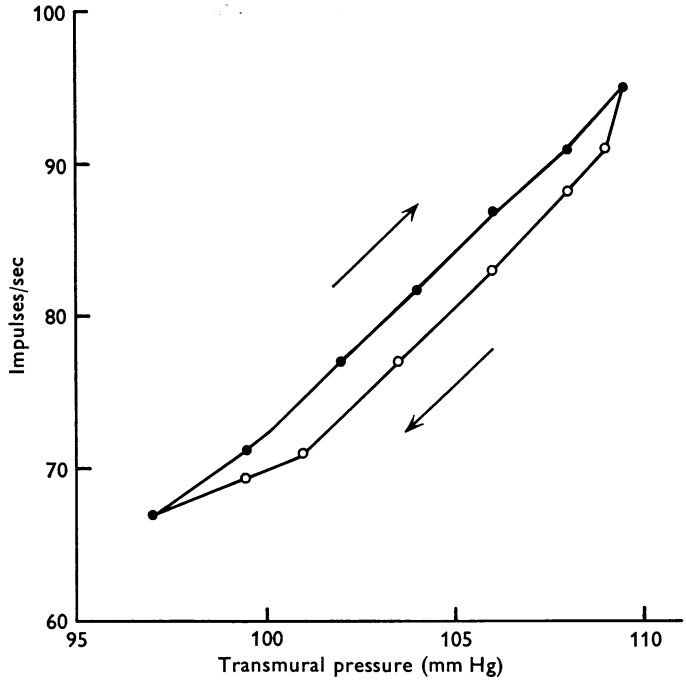

Fig. 5. Graph of the relationship of the instantaneous impulse frequency and transmural pressure (mm Hg) during one cycle of a 'respiratory' type extramural pressure change during non-pulsatile perfusion of the aortic arch. The arrows indicate the direction of the pressure cycle. Single fibre from the left aortic nerve of a rabbit, 2·55 kg. The aortic arch was perfused with a non-pulsatile pressure of 97 mm Hg. Cyclical negative extramural (respiratory type) pressure of 0 to −12 mm Hg applied at a frequency of 30 c/min. The impulse frequency varied from 67 impulses/sec at a transmural pressure of 97 mm Hg to 95 impulses/sec at a transmural pressure of 109 mm Hg.

Legend to Fig. 6.

Fig. 6. Stimulation of aortic arch baroreceptors by changes of intra-aortic 'cardiac' type pulse pressures combined with 'respiratory' type extramural changes of pressure. Recordings from the left aortic nerve of an isolated arch perfused with Krebs–Henseleit solution at a mean aortic pressure of 97 mm Hg. *A*. Non-pulsatile perfusion of aortic arch. Application of a phasic change of 'intrathoracic' pressure of 0 to −12 mm Hg at a frequency of 20 c/min. Impulse frequency increases from 67 to 95 impulses/sec. *B*. Pulsatile perfusion. Pulse pressure, 34 mm Hg. Pulse frequency, 210 c/min. Impulse frequency: systole 140, diastole 0 impulses/sec. *C*. Combination of pulsatile perfusion with extramural phasic 'respiratory' type changes of pressure. Maximum peak systolic impulse frequency increases from 140 impulses/sec during 'expiration' to 167 impulses/sec during 'inspiration'. A.A.P., aortic arch pressure (mm Hg). I.T.P., intrathoracic (extramural) pressure (mm Hg). E.N.G., electroneurogram.

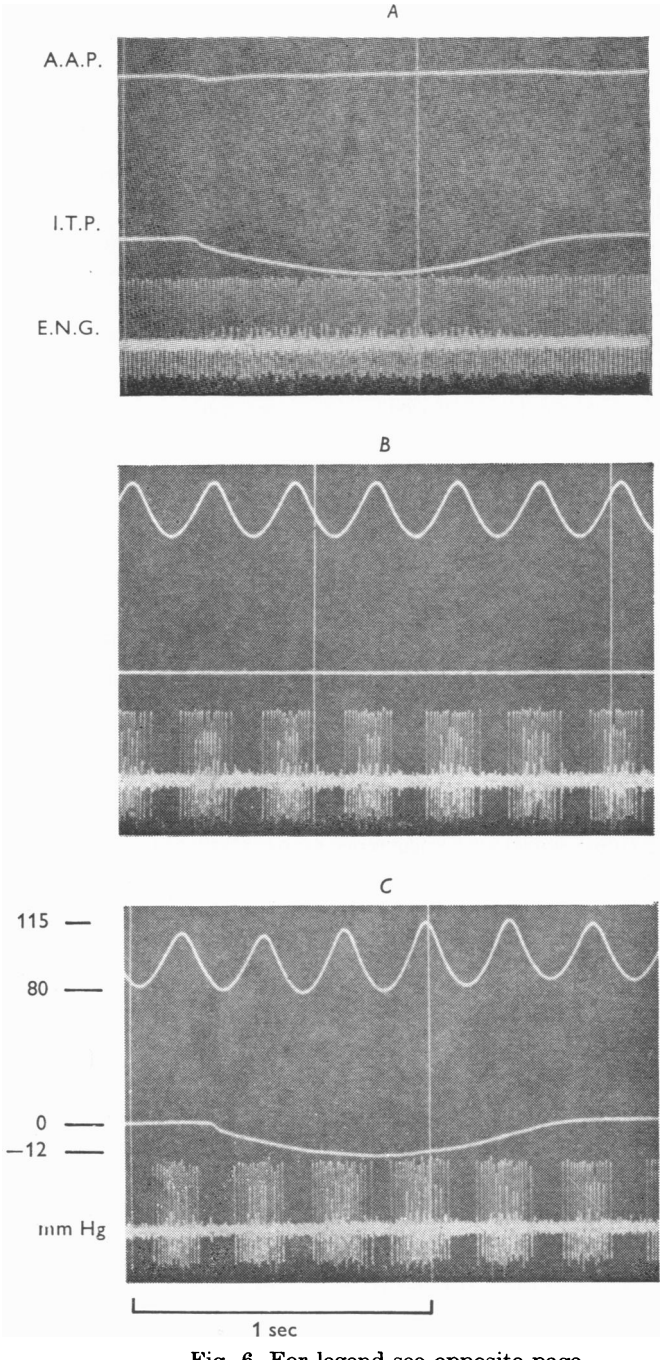

Fig. 6. For legend see opposite page.

fibres during systole varied from 43·5 to 143 impulses/sec and during diastole from 0 to 50 impulses/sec. There was recruitment of other fibres during systole and absence of impulse activity in some preparations during diastole. During the negative phase of the extramural pressure change, which varied from -7 to -38 mm Hg at a frequency of 20 or 30 c/min, the peak impulse frequency increased to 50–167 impulses/sec during systole and to 0–67 impulses/sec during the diastole.

These experiments show that during aortic systole the peak frequency of impulses is greater in 'inspiration' than in 'expiration' and recruitment of additional fibres takes place. When a discharge continues in diastole, the peak frequency also increases during 'inspiration'. But in the absence of a diastolic discharge, the diastolic period during 'inspiration' is shortened. Thus during 'inspiration' there is an increase in the total number of impulses/pressure cycle and in the number of impulses per unit time.

DISCUSSION

These experiments indicate that transmural pressure is a factor affecting the activity of the aortic arch baroreceptors. The evidence for this is the similarity of the curves relating impulse activity in single aortic baroreceptor fibres and aortic arch pressure whether the change in pressure is produced by altering the intra-aortic or the extramural pressure. In some cases, however, the impulse frequency was slightly less for any given transmural pressure when the extramural pressure was progressively lowered than when the intra-aortic pressure was raised. Findings consistent with these were also observed when the reflex vasomotor changes produced by changes in intra-aortic and intrathoracic (extramural) pressures were compared in the dog (Angell James, 1969). The explanation for this discrepancy, and for the small elevation of the threshold pressure which sometimes occurred when the transmural pressure was elevated by reduction in the extramural pressure, may be related to mechanical effects in the arterial wall which differ depending on whether the distending force is acting from the internal or external surface of the aortic arch.

The procedure of reducing the extramural pressure as a means of stimulating the carotid sinus baroreceptors has been used previously in man. A reduction in pressure in a box enclosing the neck results in reflex cardiovascular changes (Ernsting & Parry, 1957; Bevegard & Shepherd, 1966; Thron, Brechmann, Wagner & Keller, 1967; Wagner, Wackerbauer & Hilger, 1968). A diminution of pressure surrounding the aortic arch at constant intra-aortic pressure also causes a reflex fall in systemic vascular resistance which is dependent on the integrity of the cervical vagosympathetic nerves (Angell James, 1969).

The present experiments provide further evidence that stretch is a factor determining the activity of the aortic baroreceptors. It was found that the increased aortic baroreceptor activity produced by elevation of the intra-aortic pressure can be prevented by simultaneously increasing the extramural pressure by the same amount. Under the latter conditions the wall is presumably prevented from distending. This is in agreement with the findings of Hauss, Kreuziger & Asteroth (1949) who showed that the reflex fall of blood pressure produced by an increase in carotid sinus pressure is abolished if the sinus is prevented from stretching by a plaster cast applied to the outside. These experiments also indicate that squeezing the receptors by increasing the pressure equally inside and outside the vessel is not a stimulus to the baroreceptors.

In some experiments changes of pressure were used to simulate those occurring in normal breathing in the rabbit and were accompanied by changes in frequency of impulse activity. Not only did the frequency of impulse activity in single fibres increase during the negative phase of the cycle, but there was recruitment of additional fibres as well. The curve relating impulse activity to transmural pressure during one 'respiratory' cycle was elliptical so that the frequency of discharge was higher during the 'inspiratory' phase of the 'respiratory' cycle than during the 'expiratory' phase at the same pressure (Fig. 5). This is comparable to the elliptiform curve observed during phasic changes of intra-aortic pressure (Angell James, 1968, 1969, 1971*b*) and is probably related to changes in the visco-elastic properties of the vessel wall as discussed in previous papers (Angell James, 1971*a*, *b*).

When phasic changes of intra-aortic pressure at a frequency similar to that produced by the rabbit's heart and of extramural pressure at a 'respiratory' frequency are superimposed on each other, the effects on baroreceptor fibre impulse activity depends on the phase relation of the two cycles. The transmural pressure, and hence the impulse frequency, is greatest when the systolic intra-aortic pressure coincides with the nadir of the extramural pressure during the 'inspiratory' phase of the cycle.

The question now arises as to whether changes in intrathoracic pressure in the intact animal influence the activity of the aortic baroreceptors primarily by altering the extramural and hence transmural pressure, and to what extent the results of the present experiments are pertinent to this problem. The complexity of the mechanisms involved in the haemodynamic events due to changes of intrathoracic pressure have been reviewed by Sharpey-Schafer (1965) and a discussion of the possible role of the aortic baroreceptors appears in the same article in relation to the Valsalva manoeuvre (Sharpey-Schafer, 1965, see editorial comments pp. 1876–1877). In considering the effects on aortic baroreceptors of changes in

intrathoracic pressures in the intact organism, the distinction must be drawn between those effects due primarily to the change in intrathoracic pressure, with which this paper is concerned, and those occurring secondarily as a result of alterations in cardiac output and peripheral vascular resistance. When the intrathoracic pressure changes, transmural aortic pressure is affected not only by altering the extramural aortic pressure but also by altering the intra-aortic pressure by virtue of the intrathoracic pressure acting as a force on the blood in the left ventricle, which is transmitted throughout the arterial tree. This latter force and the extramural pressure affect transmural pressure in opposite directions, so that the immediate effect within a few heart beats of an alteration of intrathoracic pressure is to produce no change in the aortic transmural pressure and presumably, therefore, there will be no effect on the aortic baroreceptor discharge. It is apparent that the method used in the present study to assess the effects on the aortic baroreceptors of changes in 'intrathoracic' pressure has certain limitations when considering the responses in the intact animal because the changes of 'intrathoracic' pressure were not simultaneously imposed on the arterial perfusion head of pressure. Further studies are therefore required to evaluate the possible role of the aortic baroreceptors during phasic changes of intrathoracic pressure in the intact animal.

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