A STUDY OF RIGHT AND LEFT ATRIAL RECEPTORS

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The satisfactory recording of impulses in afferent fibres from receptors in the great veins and atria has been accomplished by a number of investigators (Amann & Schäfer, 1943; Walsh, 1947; Whitteridge, 1948; Jarisch & Zotterman, 1948; Dickinson, 1950; Neil & Zotterman, 1950), and it has been shown that their frequency of discharge is related to the pressure in the great veins and atria (Whitteridge, 1948; Dickinson, 1950). The receptors so far described are known to arise from the atria and are characterized by the presence of an a volley of impulses in time with the a wave of the venous pressure curve. Hereafter these will be referred to as type A atrial receptors.

The existence of another kind of cardiovascular fibre in the vagus was reported by Walsh & Whitteridge (1944) and confirmed by Whitteridge (1948). It was shown that this fibre differed in many ways from venous and depressor fibres and, for several reasons, it was believed that it arose from receptors in the small vessels of the lung. Later, Pearce & Whitteridge (1951) showed that a linear relationship existed between the activity of these ‘pulmonary vascular’ fibres and the pulmonary arterial pressure. The blocking temperature of these fibres was shown to be about 8 to 4°C (Torrance & Whitteridge, 1948) which corresponded well with their conduction velocity (Paintal, 1952).

However, no experiments with the view to locating these pulmonary vascular receptors had been undertaken with the open chest so far. This was recently achieved, and in this paper the results of these experiments will be described. It will be shown that all such receptors encountered so far arose in the right and left atria of the heart; these will be referred to as type B atrial receptors.

METHODS

Twelve cats anaesthetized with chloralose (80 mg/kg) were used in the present series of experiments; satisfactory results were obtained from ten. The technique of isolating single units and recording their nerve impulses was identical with that described elsewhere (Paintal, 1953). All the experiments were done on the right cervical vagus.

The right venous pressure was recorded by a semi-rigid catheter 20 cm long inserted through the left external jugular vein and connected to a capacitance manometer filled with 0.9% (w/v)

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sodium chloride. In one experiment the right intraventricular pressure was recorded with a similar catheter passed down the left external jugular vein and the catheter recording the venous pressure was inserted down the corresponding vein of the right side. The electronic circuit used was a modification of the one described by Alexander (1951) for an ultramicrometer. Additional amplification was obtained by a direct-coupled pentode which permitted a sensitivity of over 20 V/cm H2O. The manometer was linear over the range of pressures recorded and was stable over long periods. Nevertheless, to obviate any errors arising from base-line shift, each record was calibrated separately with a water manometer. The electronic circuit used was a modification of the one described by Alexander (1951) for an ultramicrometer. Additional amplification was obtained by a direct-coupled pentode which permitted a sensitivity of over 20 V/cm H2O. The manometer was linear over the range of pressures recorded and was stable over long periods. Nevertheless, to obviate any errors arising from base-line shift, each record was calibrated separately with a water manometer. The natural period of the whole recording system filled with saline was about 50 c/s. The positions of the catheters were always checked at the end of each experiment. A constant endeavour was made to identify artifacts due to movements of the heart in the venous pressure records. Provided that the catheter was not blocked at the time of recording the pressure records were, as a rule, free from artifacts; where they were present the pressure records were discarded.

The intrapleural pressure was recorded with a wide bore needle connected to an air-filled mirror membrane manometer.

RESULTS

Location of so-called pulmonary vascular receptors

Altogether, the location of ten such fibres has been achieved with certainty. Experiments were always begun with the animal breathing spontaneously with an intact chest. Single units were dissected until a pulmonary vascular fibre was obtained (Fig. 1) and was then finally identified by the criteria described already (Whitteridge, 1948; Pearce & Whitteridge, 1951). These were, briefly: (1) that the pattern of discharge should be of a late systolic character, without an a burst of impulses in time with auricular systole; (2) the activity should be augmented by an increase in venous return produced by normal or obstructed inspiration, or by suction of air from the trachea; (3) the activity should be decreased or abolished during a sustained positive pressure inflation of the lungs.

![Fig. 1. A type B right atrial fibre. From above downwards, e.g.; impulses in a right atrial fibre; time in sec; intrapleural pressure, inspiration downwards. Activity in the fibres is increasing during inspiration.](image-url)
Identification of the fibre was followed by putting the animal on positive pressure ventilation and opening the chest as quickly as possible. This was done by cutting through the mid-sternal region, taking care that the nerve fibre on the recording electrodes was not disturbed at all. In order to make the necessary observations as quickly as possible no attention was paid to haemostasis as the viability of single unit preparations is very uncertain.

Fig. 2. Effect of occluding the pulmonary artery on the fibre shown in Fig. 1. Records A, B and C are continuous. From above downwards, right intra-atrial pressure; e.c.g.; impulses in a right atrial fibre; time in 1/2 sec. Occlusion of the pulmonary artery was commenced at arrow in A and released at arrow in C.

The pericardium was slit and the pulmonary artery occluded between finger and thumb. In six fibres there was an immediate increase in fibre discharge associated with an increase in venous pressure (Fig. 2) which lasted as long as the compression on the pulmonary artery was maintained. The occlusion initially produced a continuous discharge which then regained the original type of cardiac rhythm with intervals of silence, despite the continued rise
in venous pressures. The silent intervals corresponded to the fall in the venous pressure, and they disappeared when the right auriculo-ventricular (A-v) junction was compressed, which produced a much greater rise in venous pressure. The interval of silence in spite of the raised venous pressure is probably due to the sudden decrease in the stimulus intensity—an explanation provided by Bronk & Stella (1934) for the behaviour of carotid pressure receptors.

Fig. 3. Effect of occluding the pulmonary artery on a type B left atrial fibre. A, B and C are continuous. From above downwards, right intra-atrial pressure; right intraventricular pressure; e.c.g.; impulses in fibre; pulmonary artery was occluded between upper and lower arrows. The calibrations apply to the intraventricular pressure.

In four fibres occlusion of the pulmonary artery abolished the fibre discharge which returned after a variable period on releasing the occlusion. This is illustrated in Fig. 3 which shows the effectiveness of the occlusion by the rise in the right intraventricular pressure. In fibres responding in this way compression of the left A-v junction produced a pronounced increase in fibre activity which always lost its cardiac rhythm and became continuous (Fig. 4). On releasing the occlusions the fibre discharge regained its original character. Compression of the left A-v junction produces a rise in the right intraventricular and the right venous pressures as well, although the rise was never as great as that produced by occluding the pulmonary artery. For this reason occlusion of
Fig. 4. Effect of occluding the left A-V junction on a type B left atrial fibre. The records are continuous. From above downwards, e.g.; impulses in the fibre; time in 1/50 sec. Left A-V junction was occluded between arrows.

Fig. 5. Effect of clamping the pulmonary veins on two type B left atrial fibres. A and B are continuous. From above downwards, right intraventricular pressure (calibrated); right intra-atrial pressure; e.g.; impulses in fibres. The clamp on the pulmonary veins was released at arrow in A and re-applied at arrow in B. Note that, at upper arrow, activity in the fibre with a small impulse ceases and activity in the fibre with large impulses begins. The reverse takes place at the arrow in B. This is presumably due to the two fibres being proximal and distal to the clamp respectively.
the left A-V junction also gives rise to increased fibre activity in right atrial fibres.

Clamping the pulmonary veins produced the results shown in Fig. 5 where the effectiveness of the clamp is shown by the changes in the right intraventricular pressure. From these observations it was provisionally concluded that these four receptors were located in the left atrium. Finally, proof of the location of these receptors, whether on the right or the left side, was obtained after isolating the appropriate atrium by clamping the veins and the A-V junction. Saline was then injected into the atrium through a cannula and a discharge, as shown in Fig. 6, was obtained; removal of saline abolished the discharge.

Fig. 6. Effect of injecting saline into an isolated left atrium on a type B left atrial fibre. From above downward, right intraventricular pressure in a failing heart; e.c.g.; impulses in the fibre. At arrow in A saline was injected. B shows the effect of withdrawing saline.

By observing the effect on the fibre discharge of pressing the atrium, it was found that the receptors were located in the posterior part of the atria, some near the opening of the veins. This is illustrated in Fig. 5 where a clamp near the opening of the pulmonary veins into the atrium produced the opposite effects in two receptors, due presumably, to one receptor being situated distal to, and the other proximal to, the clamp. Later, when the clamp was applied farther away from the atrium both the receptors behaved identically. None were located in the auricular appendage.

No responses could be obtained by pressing near the interauricular septum or the bases of the aorta and pulmonary artery where the supracardial ganglia (Nonidez, 1936) are located. Finally, in three cases, destruction of a localized portion of the atria by a clamp abolished all responses from the receptor, this being preceded by a high-frequency discharge. By these methods all the fibres encountered were definitely located in the atria, six in the right and four in the left. None was found in the small vessels of the lung.
In three fibres it was shown that the conduction velocity of the single active unit before and after opening the chest was identical, thus proving that the active fibre after opening the chest was the same as the one observed with an intact chest.

As all the nerve fibres were dissected from the right vagus it is clear that a considerable number of fibres of the left side cross over to the right vagus, and probably the converse is true as well.

Although the left atrial type B receptors are similar to the right atrial ones in several ways, they have a number of distinctive features. The discharge in right atrial receptors (Fig. 1) increases during the first cardiac cycle after the beginning of inspiration, reaches a peak at the height of inspiration, and falls considerably at the end of it. The increase in activity of left atrial receptors (Fig. 7A) occurs two to three heart beats after the beginning of inspiration; often this is preceded by a small decrease in the number of impulses (Fig. 7A). Peak activity is attained at the end of inspiration or the beginning of expiration. Such differences are fully accounted for by the observation of Cahoon, Michael & Johnson (1941) on the size of the right and left auricles during the respiratory cycle. Similar differences in timing occur during obstructed inspiration (Fig. 7B) or during suction of air from the trachea.

During a sustained positive pressure inflation of the lungs the activity in the atrial receptors of both sides decreases or is abolished. However, on releasing the positive inflation, activity returns within one to two cardiac cycles in the right atrial receptors, but in those of the left side the return is delayed by about five to seven heart beats, usually until the subsequent inspiration. These observations on the difference between right and left atrial receptors are in general agreement with those of Whitteridge (1948) on right- and left-sided type A atrial receptors possessing an α volley of impulses.

With the open chest the late systolic pattern of discharge of these fibres remains unaltered, although an α burst of impulses has often been seen in a number of fibres. This acquisition has always been a temporary feature and is probably brought about by a change in the position of the heart. The right atrial receptors are unaffected by the respiratory changes produced by the positive pressure ventilation. On the other hand, the left atrial fibres show an increase at the beginning of each inflation (Fig. 7C).

The volley of impulses in these receptors begins about 70–210 msec after the Q wave of the e.c.g. and it varies considerably in the same fibre with the respiratory cycle, beginning earlier in the cardiac cycle with increase in activity. However, for any given level of activity its relation to the QRS complex is not appreciably altered by increasing or reducing the heart rate. On the other hand, the relation of the volley to the P wave of the e.c.g. is easily varied by any change in the heart rate. With a normal heart rate of about 130/min the discharge usually ceases at, or a few milliseconds before,
the $P$ wave of the e.c.g. If the heart is slowed as by stimulating the vagus the discharge ceases considerably before the $P$ wave; at rates of 100/min the interval between the last impulse and the beginning of the $P$ wave may be over 100 msec. Conversely, with a rapid heart the discharge may end well after the $P$ wave. The timing of the $v$ wave of the venous pressure curve varies in the same way as the fibre discharge when the heart is slowed or speeded up. The observation (Whitteridge, 1948) that the $v$ wave may run into the next $a$ wave in rapidly beating hearts is confirmed. The cessation of the discharge therefore does not appear to be related to auricular systole, but rather to ventricular activity for reasons which will be discussed later.
Isolated atrial experiments

Experiments with the isolated atrium have shown that these type B atrial receptors do not discharge impulses when the atrium is empty but do so when a certain threshold of filling is reached which is usually between 0.5 and 1 ml. Such responses can be obtained for as long as 20 min after the heart has stopped. Injection of a certain quantity of saline into the inactive atrium produces a slowly adapting discharge (Figs. 6 and 8B). If the quantity introduced is small, the discharge ceases after a few seconds. In an atrium showing spontaneous activity the process of adaptation is modified by the muscular contractions; the frequency of discharge rises rapidly with the increase in intra-atrial pressure and falls off during relaxation to a lower level than before (Fig. 8A).
Atrial filling was found to bear a linear relation to fibre discharge (Fig. 9). The injection was performed by means of a 20 ml. syringe which was connected to a wide bore cannula through a piece of polythene tubing. Starting with an empty atrium, saline was then injected in 1 or 2 ml. steps, each subsequent volume being added on to the previous one. The rate of injection was not accurately controlled but attempts were made to make the injections as rapid as possible. The average frequency of discharge over a period of 0·5 sec of the record was determined 1 sec after each injection and the values plotted as shown in Fig. 9. In this figure the values were obtained from two sets of observations on the same fibre.

![Figure 9](https://example.com/atrial-filling.png)

**Fig. 9.** Relation of frequency of discharge in a type B left atrial fibre to various levels of atrial filling in an isolated left atrium. The frequency of discharge plotted was averaged over 0·5 sec of the record 1 sec after each injection. The data were obtained from two sets of observations on the same fibre.

Accurate observations on relation of atrial filling to fibre discharge could only be made in left atrial fibres as the left atrium only could be made sufficiently water-tight—the criterion being that it should be possible to withdraw the same quantity of saline as was injected. This was not possible in the right atrium after clamping off the great veins, vena azygos, and the right A-v junction, presumably because of leakage into the coronary sinus and small cardiac veins.

From the results obtained it seems reasonable to infer that these receptors are stretch receptors responding to changes in the atrial filling.

Plotting the frequency of discharge as the reciprocal of the interval between the impulses shows that it does not bear any relation to the a wave of the venous pressure curve with which the highest pressure and the highest rate
of rise of intra-atrial pressures are nearly always coincident. In this respect these receptors differ from the type A atrial receptors already described (Whitteridge, 1948; Dickinson, 1950) which show a predominant $a$ volley with or without $c$ and $v$ volleys of impulses. On the other hand, the $v$ wave does seem to be related to the fibre discharge in some ways although the relation is not so close as is that of the carotid and aortic pressure receptors to the carotid and aortic pressures respectively (Bronk & Stella, 1932; Whitteridge, 1948). The contour of the frequency curve is at times related to the contour of the $v$ wave but it can deviate considerably from it and it seems, therefore, that the discharge of impulses in atrial receptors is not occasioned by the $v$ wave of the intra-atrial pressure. The beginning of the discharge is always delayed with respect to the $v$ wave and, although peak frequency and peak pressure in the $v$ wave coincided within 5 msec in four fibres, they may deviate from each other by as much as 60 msec.

The general coincidence is of interest as both fibre discharge and the $v$ wave probably owe their origin to atrial filling. However, the contour of the $v$ wave may also depend on other factors such as ventricular systole and the presence of such factors might explain the observed deviation of the $v$ wave from the frequency of discharge. If the gradual elevation of the intra-atrial pressure during ventricular systole is due to atrial filling (Wiggers, 1928) then the slight delay in the beginning of the volley in relation to the $v$ wave is probably due to the receptors having a threshold at which they fire off.

The effective venous pressure is related to the number of impulses in a cardiac cycle, which is in agreement with the observations of Dickinson (1950) on the type A atrial receptors. However, as the preceding sections show, the effective venous pressure, though related to fibre activity is not the stimulus for these type B atrial receptors.

**DISCUSSION**

These experiments indicate conclusively that the great majority of so-called pulmonary vascular receptors are located in the right and left atria of the heart since all the ten receptors examined so far were found in that region, none in the small vessels of the lungs.

In view of this finding a distinction is made between these receptors and those (also known to arise in the atria) possessing an $a$ volley of impulses in time with the $a$ wave of the venous pressure curve; they are therefore designated type B and type A atrial receptors respectively.

These results do not imply that there are no receptors in the small vessels of the lung; they only indicate that all the so-called pulmonary vascular receptors so far examined arise elsewhere.

It seems reasonably certain that these type B atrial receptors are not pressure receptors of the type found in the aorta (Whitteridge, 1948) or the
carotid sinus (Bronk & Stella, 1932) since they do not follow the intra-atrial pressure changes. They are inactive at a time when the pressure in the atria is the highest, i.e. during the $a$ wave, and although some relation of the volley to the $v$ wave does exist, the two may deviate quite considerably from each other. On the other hand, it is clear that they are slowly adapting stretch receptors which under normal conditions respond to changes in the atrial volume (Fig. 9). They are no different from stretch receptors in other parts of the body, such as those in the lungs, which are slowly adapting and respond linearly to changes in the volume of air in the lungs (Adrian, 1933). Like other stretch receptors those in the atria are insensitive to anoxia for they continue to be active for as long as 20 min after the heart has stopped. The atria are thin-walled collapsible structures and the tension in their walls increases when they are filled; the greater the filling the greater the stretch.

In the isolated atrium the occurrence of spontaneous atrial contractions gives rise to a volley of impulses associated with a rise in the intra-atrial pressure (Fig. 10). The muscular contraction leads to an increase in the tension in the atrial wall due to the rise in the intra-atrial pressure. The receptors are therefore stretched and are stimulated. Fig. 8A illustrates the effect of injecting saline into an isolated atrium showing spontaneous activity. During each isometric contraction due to the rise in intra-atrial pressure the frequency of discharge rises rapidly owing to an increased stretch on the receptors and falls off during relaxation to a lower level than before, rising again to a new level soon after. This is to be contrasted with the events occurring during atrial systole in a normal heart (see below).

In the relaxed isolated atrium the activity of these receptors would bear some relation to the intra-atrial pressure which would be the same as the relation of volume to pressure under similar conditions. The finding of any such relationship, however, would not mean that the atrial receptors respond to intra-atrial pressure changes because, as shown already, they clearly do not do so normally.

The patterns of discharge of the type B atrial receptors, i.e. the occurrence of a late systolic burst without an $a$ volley of impulses is satisfactorily explained when they are regarded as responding to changes in atrial volume which they do in the isolated atrium. After the closing of the $A-V$ valves following the $QRS$ complex of the e.c.g., the atrium starts to fill gradually and when the threshold of filling for the receptor is reached, it is stimulated and starts firing. Thereafter, the frequency of discharge increases with increasing filling until, at some time during ventricular relaxation (Fig. 4), the $A-V$ valves open and blood flows into the ventricle thereby reducing the atrial volume. The discharge therefore ceases at this point. This relation of the volley to ventricular activity is fairly constant, and it is now easy to see why the relation of the volley to the $QRS$ complex mentioned earlier does not alter significantly
whether the heart rate is raised or lowered by stimulating the vagus. The phase of rapid filling is followed by a variable period of diastasis, provided the heart is slow enough (Wiggers, 1945). During atrial systole the atrial volume is still further reduced and there is therefore no discharge of impulses. This point is illustrated by the fibre shown in Fig. 10C where there is one atrial systole as

![Fig. 10. Type B right atrial fibres. In A from above, downwards, e.g.; impulses in a fibre; time in 1/10 sec. In B and C there is an intra-atrial pressure record (uppermost) as well. A shows the discharge in a fibre with open chest. B shows the discharge in the same fibre with the atrium isolated. Each atrial contraction produces a burst of impulses associated with the rise in pressure. C shows the effect of alternation of atrial contractions as indicated by the a wave on the pressure record on the activity in another fibre.](image)

shown by the a wave of the venous pressure curve to every two ventricular systoles. With the alternation of auricular systole there is an associated alternation in the number of impulses per cycle. When auricular systole is absent some blood is retained in the atrium and with the added venous filling in the following cycle there is an increased discharge.

It is conceivable that during atrial systole, although there is a rise in pressure which tends to increase the tension in the atrial walls, this is unable to stretch it sufficiently to stimulate the receptors in the presence of the markedly reduced volume which occurs at this time.

The nerve endings described histologically in this region (Nettleship, 1936; Nonidez, 1937) are chiefly sub-endothelial and they are probably the stretch receptors concerned. It is not difficult to imagine the effect on these endings
when the atria are distended by the inflow of blood. The possibility was considered that the receptors in question might be located near the auriculo-ventricular orifices where appropriate endings are believed to exist (Nettleship, 1936). In the present experiments no receptors were localized near the A-V junction, although a number were definitely localized on the posterior aspect of the atria and near the opening of the veins into the atrium.

It is indeed surprising that these receptors have not been encountered by investigators working on animals with open chests (Jarisch & Zotterman, 1948; Dickinson, 1950). Possibly it is due to the fact that they were mostly recording from multi-fibre strands and the activity of these receptors was therefore masked by the more pronounced activity of type A atrial receptors.

The function of the type B atrial receptors is obscure. Although their pattern of discharge is different from that of type A atrial receptors there is no reason to regard them as being different in function. In fact, being located in the same region and responding in the same way to alterations in the venous return the two types may have the same functions. The possibility of correlating the activity of the right-sided ones with the Bainbridge reflex is rendered difficult owing to the doubt cast on the reflex by the work of Ballin & Katz (1941). They could not be the afferent mechanisms responsible for the doubtful veno-pressor reflex suggested by McDowall (1924), as such a reflex requires that the receptors be stimulated by lowered venous pressure presumably due to a reduction in atrial filling. On the other hand, the position of the left atrial receptors seems more hopeful. It is very likely that they play an important part in the production of a reflex fall in the systemic blood pressure when the left atrium is distended by obstruction to the outflow of blood (Daly, Ludány, Todd & Verney, 1937). The fact that there is a considerable amount of crossing over of afferent atrial fibres into the vagus of the opposite side should be borne in mind in any investigation of their reflex effects.

SUMMARY

1. The pulmonary vascular receptors described by Whitteridge (1948) have been re-investigated with open chests in the cat, and it has been shown that all the ten receptors so far examined were located in the right and left atria of the heart, none in the small vessels in the lung.

2. These receptors have only a late systolic volley of impulses in contrast to other receptors (also located in the atria) which have a predominant presystolic volley in time with the a wave of the venous pressure curve. To distinguish them, therefore, the two types were designated type B and type A atrial receptors respectively.

3. The left atrial type B receptors have a number of characteristic features which distinguish them from the right-sided ones. A good many of their afferents cross over to the right vagus.
4. Experiments performed with the isolated atrium have shown that these receptors adapt slowly to a maintained stimulus. They respond linearly to changes in atrial filling.

5. It is concluded that the type B right and left atrial receptors do not respond to intra-atrial pressure changes. They are stretch receptors responding to change in atrial filling.

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