Left Atrial Receptor Discharge during Atrial Arrhythmias in the Dog
By Irving H. Zucker and Joseph P. Gilmore

ABSTRACT
Afferent receptor discharge originating in the atria was recorded from slips of the cervical vagus in the open-chest dog. The activity of two types of atrial receptor endings was identified. Type A receptors exhibited a discharge pattern that was synchronous with the a wave of the atrial pressure pulse in the control recordings, and type B receptors discharged only during the v wave of the atrial pressure pulse in the control recordings. Atrial arrhythmias (flutter or fibrillation) were induced by mechanical stimulation of the area around the sinoatrial node. During atrial arrhythmias, there was a moderate rise in mean left atrial pressure (7.5 ± 0.7 cm H₂O to 8.6 ± 0.6 cm H₂O during arrhythmias in which type B receptors were studied, 6.1 ± 0.1 cm H₂O to 7.8 ± 0.4 cm H₂O during arrhythmias in which type A receptors were studied), a fall in aortic blood pressure, and a decrease in right atrial force. Atrial contractions were asynchronous and rapid. Type A atrial receptors showed a relatively greater increase in discharge (184.1%) during fibrillation than did type B atrial receptors (27.5%). These experiments demonstrated that both types of atrial receptors increased their discharge rate during atrial arrhythmias, indicating that they might be involved in a reflex diuresis which occurs during these arrhythmias in humans.

KEY WORDS
reflex diuresis type A receptors atrial fibrillation type B receptors vagal afferents

Receptor endings located in both atria have been described anatomically and electrophysiologically in a variety of species by several workers (1-3). Various investigators (2-4) have described the activity of two types of physiologically distinct atrial receptors; type A atrial receptors have a prominent burst of action potentials synchronous with the a wave of the atrial pressure pulse, and type B atrial receptors show a discharge pattern synchronous with the v wave of the atrial pressure pulse. The function of type A receptors is not known; however, type B receptors are thought to be involved in the reflex diuresis and tachycardia that results from distending the left atrial-pulmonary venous junctions or from increasing left atrial pressure (5-7). Type B receptors exhibit an initial linear relationship between discharge and atrial v-wave pressure followed by a plateau at extremely high atrial pressures (3, unpublished observations).

Type A atrial receptors do not appear to respond to an increase in a-wave or v-wave pressure nor do they respond to changes in the pulse pressure of the a wave (8).

Several workers (9-11) have shown that a water diuresis results in man during atrial arrhythmias such as paroxysmal atrial tachycardia, atrial flutter, and atrial fibrillation. During these arrhythmic episodes, atrial receptor discharge is increased due to a concomitant rise in mean atrial pressure. The output from these receptors is thought to inhibit the release of antidiuretic hormone (ADH) and thus promote the increases in water excretion.

The purpose of the present study was to delineate the activity of both type A and type B atrial receptors during various atrial arrhythmias induced in the dog.

Methods
Mongrel dogs of either sex (11-24 kg) were treated with morphine sulfate (0.5 mg/kg, iv) and anesthetized with alpha-chloralose (100 mg/kg, iv) dissolved in polyethylene glycol (100 mg/ml). Supplemental doses of chloralose were given as required throughout the experiment. The trachea was intubated, and the dog was ventilated using a positive-pressure respirator. To inhibit muscular movements, gallamine triethiodide (1 mg/kg, iv) was administered with supplemental doses of chloralose. The chest was opened...
by a transverse thoracotomy in the third or fourth intercostal space. The pericardium was split, and a metal cannula was placed in the left atrium through the atrial appendage for measurement of left atrial pressure with a Statham P23Db transducer. In some dogs, a transducer-tipped catheter was inserted into the left atrium through a pulmonary vein. A polyethylene catheter was placed in the aortic arch through the right femoral artery with its tip close to the aortic valve. Arterial blood pressure was measured with a Statham strain-gauge arch was sutured to the right atrial appendage and used for a qualitative index of atrial contractile force.

Single units originating in receptors subsequently located in the left atrium were dissected from slips of the left cervical vagus as described previously (2, 12). The activity of atrial receptors was initially identified by the characteristic cardiac rhythm heard when the nerve potentials were appropriately amplified and played through a loud speaker. Identification was verified by the timing relationships of the recorded vagal impulses with the electrocardiogram (ECG), the atrial pressure pulse, and the arterial pressure pulse. These receptors were classified as type A or type B as described by Paintal (3). At the conclusion of each experiment, the receptor ending was located in the nonbeating heart by discrete punctate simulation. All of the left atrial receptors studied in this paper (types A and B) were located at the left atrial-pulmonary venous junctions.

Nerve potential recordings were made using bipolar platinum electrodes and were amplified using a differential amplifier (Tektronix type 3A9). The spikes were displayed with the ECG on a dual-beam oscilloscope (Tektronix type RM565). Pressure recordings were amplified on a recorder (Beckman type R411) and then displayed with the ECG and the spikes on an ultraviolet paper recorder (Honeywell Visicorder model 906). Since atrial receptors exhibit changes in their activity during the respiratory cycle, all recordings were made during the expiratory pause.

After appropriate control recordings had been made, the area about the sinoatrial node was mechanically stimulated to elicit atrial arrhythmias. Atrial fibrillation occurred in most instances; irregular, asynchronous atrial contractions could be identified electrocardiographically as well as visually. In addition to fibrillation, atrial flutter was often seen. For the purpose of simplicity, both types of arrhythmias will be referred to subsequently as fibrillation or as arrhythmia. Ventricular rate was calculated by measuring the R-R interval of several consecutive heart beats during expiration, since the spike discharge was counted during expiration. The number of spikes per minute was calculated by counting the spike discharge over a 4-5-second recording at a paper speed of 100 mm/sec. Mean left atrial pressure was measured by planimetry, taking the area under the left atrial pressure curve for several seconds of each recording. Statistical significance was calculated using a two-tailed Student's t-test based on the number of fibrillations studied.

Results

Three type A and seven type B receptors were analyzed. Figure 1A shows a control tracing from a typical type A left atrial receptor. Two spikes per cardiac cycle occurred at the peak of atrial contraction immediately following the P wave of the ECG. Figure 1B shows the same receptor during atrial fibrillation. During the arrhythmic period, spike discharge was random and asynchronous and its frequency was increased compared with that of the control period. Following the arrhythmic period, a synchronous pattern of discharge with an a burst was resumed (Fig. 1D). Episodes of fibrillation generally lasted only a few seconds, and then the heart reverted spontaneously to a normal sinus rhythm. During fibrillation, left atrial pressure showed rapid increases and decreases in amplitude with none of the characteristic waves attributable to the atrial pressure pulse. Right atrial contractile

![FIGURE 1](http://circres.ahajournals.org/)

**FIGURE 1**

Tracing of an original recording of the activity from a type A left atrial receptor. Spikes = neurogram, ECG = electrocardiogram, RAF = right atrial force, Ao.P. = aortic blood pressure, and LAP = left atrial pressure. All recordings were made during expiration. A: Control. B: Atrial fibrillation. C: Recovery from fibrillation. D: Return to control state.

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force exhibited a dramatic decrease, showing low-amplitude asynchronous activity. Aortic blood pressure fell, and although QRS complexes were seen ventricular contraction was usually not sufficient to open the aortic valve. Figure 1C shows the same receptor as the atrium recovered from an episode of atrial fibrillation. Atrial contractile force was always potentiated for several beats immediately following an arrhythmic episode (Fig. 1C). Figure 1D shows the complete return to the control state.

Figure 2A shows a typical type B atrial receptor with its characteristic burst during the η wave of the atrial pressure pulse which ended just prior to atrial contraction. Figure 2B shows the pattern of discharge of the same receptor during atrial fibrillation. During fibrillation, the spike discharge appeared to come in discrete bursts of 1–6 spikes/burst throughout the cardiac cycle. Receptor discharge was silent during the intervals in which gradual decreases in atrial pressure occurred, a pattern that was not seen in the type A receptor response during flutter or fibrillation. Table 1 compares the response of type A receptors and type B receptors before and during atrial fibrillation or flutter. Although the increase in spike discharge was significantly different from control for both type A and type B receptors, the discharge rate of type A receptors increased considerably more than did that of type B receptors (184.1% vs. 27.5%). In every case there was an increase in ventricular rate (deduced from the frequency of QRS complexes) during fibrillation. Mean ventricular rate for the six type A receptor fibrillations was 185.3 ± 9.7/min during the control period and 268.5 ± 10.1/min during fibrillation (P < 0.001). For type B fibers, the mean ventricular rate was 165.7 ± 15.3/min during the control period and 229.4 ± 8.7/min during fibrillation (P < 0.001). The difference in control ventricular rate when type A and B fibers were compared was strictly fortuitous and was not significant (P < 0.40); it probably reflects the fact that fewer type A fibers were studied.

**TABLE 1**

Comparison of Type A and Type B Atrial Receptors during Atrial Fibrillation or Flutter

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean left atrial pressure (cm H₂O)</th>
<th>Spikes/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Fibrillation*</td>
</tr>
<tr>
<td>A</td>
<td>6.1 ± 0.1 (6)</td>
<td>7.8 ± 0.4 (6)</td>
</tr>
<tr>
<td>B</td>
<td>7.5 ± 0.7 (6)</td>
<td>8.6 ± 0.6 (6)</td>
</tr>
</tbody>
</table>

All values are means ± se. The number of fibrillations used for each measurement is given in parenthesis.

*Fibrillation includes those experiments in which atrial flutter was present.

†P values are for comparison with control.


**Discussion**

The present study illustrates the differential response of the two types of atrial receptor endings. The discharge rate per minute of both type A and type B receptors increased during induced, acute atrial flutter or fibrillation. Because atrial contraction was random and asynchronous during these arrhythmias, it was not possible to analyze the receptor discharges in terms of spikes per cardiac cycle. Therefore spike activity was expressed in terms of spikes per minute.

Even when discharge was expressed per cm H$_2$O of left atrial pressure, the percent increase in mean discharge was greater for type A receptors during fibrillation than it was for type B receptors (123.3% vs. 11.2%). Although mean left atrial pressure was higher for type B receptors (7.5 ± 0.7 cm H$_2$O) than it was for type A receptors (6.1 ± 0.1 cm H$_2$O), this difference was not significant ($P < 0.05$). The higher control discharge of the type B receptors probably resulted because they fired during the longer filling phase of the atria as opposed to the shorter period of atrial contraction during which the type A receptors fired. Thus, there were usually more spikes per cardiac cycle from type B receptors than there were from type A receptors. There are several possible explanations for this finding. First, of the ten receptors studied only three were identified as type A fibers. Although this ratio of A to B receptors is larger than that reported by other investigators in the dog (2, 13), it is not representative of the true proportion of A to B receptors, since not every type B receptor found was subjected to fibrillation. Ideally this comparison should be made in the cat during atrial fibrillation because the ratio of type A to type B receptors in this species is one to one (13, 14). Second, because of the sparse number of spikes per cardiac cycle for type A receptors during the control period compared with that for type B receptors (Fig. 1A and 2A), there was a relatively greater increase in type A receptor discharge; however, the increase in the absolute number of spikes was also greater for type A receptors than it was for type B receptors (628 spikes/min vs. 453 spikes/min).

Because it is difficult to differentiate the various components of the atrial pressure pulse during fibrillation, we used the mean left atrial pressure as an index of atrial distention. Although there was only a modest increase in mean left atrial pressure during fibrillation, this rise in pressure was sufficient to increase substantially type B receptor discharge (14). Paintal (14) has shown that an increase of approximately 2 cm H$_2$O in mean left atrial pressure in the cat can increase the number of impulses per cardiac cycle for type B receptors by about 7 spikes/cycle. In the dog, increases in left atrial peak u-wave pressure of approximately 2 cm H$_2$O increase type B receptor discharge by about 10 spikes/cardiac cycle (unpublished observations). In most experiments the time the dog was in fibrillation was relatively short (4–5 seconds), and this condition might have precluded a larger increase in mean left atrial pressure. However, in one experiment fibrillation lasted for approximately 30 seconds, but mean left atrial pressure did not increase beyond the level obtained during the first 5 seconds.

Although there are no reports in the literature about changes in atrial pressure during these arrhythmias in clinical situations, several workers (8–10) have implicated atrial stretch receptors in the diuresis that occurs during atrial arrhythmias. The proposed mechanism by which these receptors induce a diuresis is as follows: as a result of activating atrial receptors during periods of increased atrial pressure or distention, an inhibition of ADH secretion occurs which in turn leads to a water diuresis. Indeed Johnson et al. (15) have shown that small increases in left atrial pressure can substantially decrease ADH titers in blood. However, the role of ADH in decreasing urine flow following decreases in atrial pressure remains controversial (16–18). Recently, Karim et al. (19) have reported that factors other than humoral ones may be involved in the diuresis that results from atrial distention. They (19) found a significant decrease in sympathetic activity to the kidney following left atrial distention. This finding was essentially confirmed by the work of Clement et al. (20) in the rabbit. Strong evidence against the role of atrial receptors and ADH in the diuresis that has been described in humans during periods of paroxysmal atrial tachycardia (9) has been presented by Goetz and Bond (21). They induced atrial tachycardia for 60 minutes in conscious dogs and found no change in plasma ADH titers.

Little is known about the function of type A receptors (especially in the dog), although it has...
been proposed (8) that they may signal heart rate. Arndt et al. (8) have shown that the discharge of type A receptors clearly does not show any relationship to the amplitude or the slope of the a wave or to the pressure at the foot of the a wave. It is difficult from the data presented in this paper to correlate the activity of either type A or type B atrial receptors with instantaneous changes in either atrial pressure or atrial force. However, there was a distinct difference in the discharge pattern of the two receptors during fibrillation. Type B receptors (Fig. 2B) showed much more bursting activity than did type A receptors (Fig. 1B). Furthermore, from a qualitative examination of the records, it appears that there might be some relationship between the receptor discharge and the small rapid atrial contractions that are observed during fibrillation. A change in atrial compliance might have contributed to the increase in atrial receptor discharge during atrial fibrillation. However, under the conditions of the present experiments, it was not possible to assess the pressure-volume relationship of the atrium during the brief period of fibrillation encountered.

Paintal (22) has postulated that type A receptors are functionally in series with atrial muscle but that type B receptors are in parallel. Although there is no anatomical evidence to support this view, it seems reasonable based on the firing pattern of these receptors. If type A receptors are indeed in series with atrial muscle and if a given receptor lies in an area of intense asynchronous contractions during fibrillation, one might expect the discharge to increase in proportion to the number and the intensity of the contractions surrounding the receptor. In contrast, type B receptors that fire only during atrial filling would not be expected to fire as rapidly as type A receptors. Such a mechanism could have caused the relatively greater increase in type A receptor discharge compared with that of type B endings which might only fire occasionally.

The results of the present study indicate that receptor endings located in the left atrium increase their discharge rate per minute during atrial arrhythmias in the anesthetized dog. Although type A receptor discharge increased during fibrillation to a greater extent than did type B receptor discharge, it is not possible to determine which of these two receptors are responsible for the afferent input that might initiate the diuretic response to atrial fibrillation. However, since there is no change in type A receptor discharge during volume expansion in the nonarrhythmic state, these receptors might be the ones involved in the afferent limb of the diuretic reflex during fibrillation. It seems reasonably clear that atrial receptors of both types can inform central structures of the ongoing atrial activity during arrhythmic states.

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References
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