The Response of Atrial Stretch Receptors to Increases in Heart Rate in Dogs

IRVING H. ZUCKER, PH.D., AND JOSEPH P. GILMORE, PH.D.

ABSTRACT The discharge characteristics of type B left atrial receptors were analyzed during alterations in heart rate. Recordings were made from single-fiber preparations of the left atrium of barbiturate-anesthetized, open-chest dogs. The heart was paced following a sinoatrial crush at frequencies ranging from 60 to 240 beats/min. Left atrial transmural pressure was varied at each heart rate by the intravenous infusion of warm isotonic NaCl. As heart rate was increased, there was a progressive decrease in the peak "v" wave left atrial pressure. Concomitantly, the number of spikes per cardiac cycle decreased as did the maximal instantaneous frequency of discharge. A significant positive relationship could be demonstrated with either the discharge per minute [(spikes per cycle) x heart rate] or discharge per cycle vs. the peak "v" wave of the left atrial pressure, regardless of heart rate. The number of impulses that entered the central nervous system per unit of time remained relatively constant at heart rates between 90 and 240/min. It is concluded from these data that the reflex effects which have been attributed to atrial stretch receptor stimulation during clinical episodes of atrial tachyarrhythmias may be better correlated with some aspect of receptor discharge other than frequency or the number of discharges per cycle.

ATRIAL STRETCH receptors have been located in both the right and left atria in a variety of species. Two types of atrial receptors whose fibers traverse the vagus have been identified by Paintal, who termed them type A and type B on the basis of the timing of their discharge in relation to the cardiac cycle. Their discharge characteristics have been investigated by several workers and these receptors have been implicated in reflexes that may be involved in the control of fluid and electrolyte balance, heart rate, and systemic resistance. During clinical episodes of atrial tachyarrhythmias such as atrial fibrillation and paroxysmal atrial tachycardia, a pronounced polyuria is often exhibited, lasting in some cases longer than the paroxysm. Although atrial pressure is often elevated during these episodes, the contribution of increasing heart rate per se to atrial receptor discharge has been investigated by only one group of workers; however, in their study a qualitative analysis of discharge in relation to changes in atrial pressure was not made. Furthermore, the frequency of discharge was not correlated with left atrial pressure (LAP). Therefore, our present study was undertaken to quantify the discharge of type B atrial stretch receptors in response to alterations in heart rate over a wide range in the dog.

Methods

Six mongrel dogs of either sex, weighing between 15 and 25 kg, were anesthetized with pentobarbital sodium.
Atrial receptor discharge was recorded from single-fiber preparations of the left cervical vagus by methods previously described. The receptor was localized by punctate probing until a high frequency burst was elicited. The nerve potentials were recorded on an ultraviolet oscillographic recorder (Honeywell Visicorder 1858) and simultaneously on magnetic tape (Hewlett-Packard 3950). The instantaneous frequency of the receptor discharge was displayed with each cardiac cycle on a storage oscilloscope along with the ECG, aortic pressure pulse, and LAP pulse. At the conclusion of each experiment the animal was bled, the heart was opened, and the receptor was localized by punctate probing until a high frequency burst was elicited. The nerve potentials were recorded on an ultraviolet oscillographic recorder (Honeywell Visicorder 1858) and simultaneously on magnetic tape (Hewlett-Packard 3950). The instantaneous frequency of the receptor discharge was displayed with each cardiac cycle on a storage oscilloscope along with the appropriate atrial pressure pulse by playing the tape-recorded discharge through a rate meter that displayed the reciprocal of the interspike interval (1/t) as a series of intensified dots, as described previously. The discharge was plotted against the peak of LAP "v" wave at the various heart rates. For statistical analysis we used the Student's t-test and least squares linear regression.

Results

Figure 1 illustrates the response of a type B left atrial receptor to increasing heart rates. This animal previously had been given a total of 400 ml of warm isotonic saline intravenously to elevate discharge so that the effects of increasing heart rate would be evident. When heart rate was increased to 120 beats/min (upper right hand panel) LAP fell, aortic pressure rose, and atrial receptor discharge decreased (in terms of discharge per cardiac cycle). With further increases in heart rate, receptor discharge continued to decrease (lower panels). Aortic pressure remained constant and LAP fell at 150 beats/min. Discharge decreased further at 190 beats/min. However, because of the short time available for atrial filling, the peak "v" wave of the LAP pulse is difficult to ascertain in this tracing. In any event, it is clear from this figure that the number of spikes per cardiac cycle fell as heart rate was increased.

In addition to the number of spikes per cardiac cycle, an important component of neural information processing may be the instantaneous frequency of the receptor discharge. (Diabutal, Diamond Laboratories), 35 mg/kg, iv, and supplemental doses of anesthetic administered as needed throughout the experiment. After placing the animal on positive pressure ventilation supplemented with a stream of 100% oxygen, we performed a transverse thoracotomy in the 4th intercostal space and widely retracted the thorax. One catheter-tipped transducer (Millar, Houston, Texas) was placed in the left atrium via a small pulmonary vein and another in the aortic arch via a femoral artery. The dynamics of these transducers have been described previously. The pericardium was opened and the sinoatrial node was crushed between partial occlusion clamps. An effective sinoatrial crush was indicated by a marked decrease in the intrinsic heart rate, often below 60 beats/min. Pacing electrodes were applied to the right atrial appendage and the heart was paced, with a Grass S88 stimulator, at rates ranging from 60 to 240 beats/min. To vary LAP, warm isotonic saline or a mixture of whole blood and saline was infused intravenously for each increase in heart rate.

FIGURE 1. An original recording of a type B atrial receptor at varying heart rates. The horizontal lines are time markers. The numbers above each panel denote the heart rate. At heart rates of 120–190 a pacing artifact is evident in the ECG trace. Horizontal line at lower left indicates 1 second. Ao.P. = aortic pressure; LAP = left atrial pressure.

Figure 2 illustrates the instantaneous response of a left atrial type B receptor to increasing heart rate. The upper tracing in each panel is the LAP pulse. The lower tracing represent the output of the rate meter (1/t). Several features of the instantaneous frequency are noteworthy: First, at all heart rates (except extremely rapid heart rates, i.e., 240 beats/min) the peak frequency was achieved at the peak of the "v" wave of the LAP pulse. Second, although there appeared to be a tendency for the peak frequency of the discharge to fall as heart rate was increased, it was not marked until high heart rates were reached (e.g., 210 beats/min and greater).

The relationship between atrial receptor discharge in spikes per cardiac cycle and left atrial peak "v" wave pressure is shown in Figure 3. This figure shows the results from one animal at heart rates ranging from 90 to 240 beats/min. Figure 4 shows a plot of the discharge per minute [heart rate x (spikes per cycle)] plotted against left atrial peak "v" wave pressure for the same receptor shown in Figure 3. The relationship is similar to that shown for discharge per cardiac cycle. Figure 5 shows the relationship between the pipe in discharge per minute and the change in left atrial peak "v" wave pressure for all the receptors studied. For any given heart rate, discharge closely follows the level of peak "v" wave LAP. That the input to the central nervous system in terms of the number of discharges per minute does not vary with heart rate is shown in Figure 6. There is no significant difference between the discharge at 90 beats/min and that at any of the higher heart rates.
Discussion

The present experiments indicate that there is an inverse relationship between the activity of type B atrial receptors and heart rate so that over a broad range of heart rates the discharge per minute does not change significantly. In association with the increase in heart rate, both LAP and the time for atrial filling decreased. Our hemodynamic observations are consistent with the recent report of Stone, who demonstrated a decrease in left atrial end diastolic diameter with increases in heart rate of up to 50 beats/min in conscious dogs. That the duration of atrial filling influences atrial receptor discharge is substantiated by the recent work of Arndt and co-workers, who used isolated strips of atrial tissue in the cat with the receptors still intact. While keeping the amplitude of stretch constant they demonstrated a hyperbolic relationship between spikes per cycle and stimulus frequency between 1 and 10 Hz for both type A and B receptors, but the average discharge rate (spikes per second) remained constant over this range of frequencies. These results are essentially in agreement with those of our present study although, unlike Arndt et al., we found no influence of stimulation frequency on the peak instantaneous frequency.

Figure 2. The instantaneous frequency of receptor discharge (lower trace) is exhibited along with the left atrial pressure (LAP) (upper trace) at the heart rates indicated above each panel.

Figure 3. The relationship between discharge in spikes per cardiac cycle and left atrial peak "v" wave pressure at the heart rates indicated by the different symbols.
of type B receptor discharge except at extremely high frequencies of stretch. Previous work from our laboratory indicated that at moderate heart rates left atrial type B receptor discharge did not show a significant velocity component but did correlate with the peak "v" wave of LAP and with atrial segment length. However, other workers have demonstrated velocity components of varying intensity, particularly when they used intense forcing functions. In a recent study Recordati et al. concluded that atrial type B receptors in the cat exhibited a substantial velocity component. Their conclusions were based largely on the observations that receptor discharge correlated better with the rate of change of tension developed during atrial filling than with the mean tension, and that the frequency of discharge was higher during dynamic pressure and length changes than during static changes. Since they used the mean discharge rate per burst for assessing dynamic length and pressure changes instead of the instantaneous frequency, it is not possible to conclude whether the slope of the length and pressure changes or the level of peak length and pressure change is the predominant determinant of discharge rate. In our present study the instantaneous frequency of discharge was maximal at the peak of the "v" wave of the LAP pulse. As heart rate was increased the rate of change of filling pressure increased while peak "v" wave pressure decreased, yet the maximal frequency remained constant or decreased slightly (Fig. 2). These results would indicate that if there is a velocity component to atrial receptor discharge it seems to be negligible, a finding in agreement with our previous results.

Lloyd has shown that stimulation of pulmonary venous...
The response of atrial stretch receptors to increases in heart rate in dogs.
I H Zucker and J P Gilmore

doi: 10.1161/01.RES.38.1.15

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1976 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circres.ahajournals.org/content/38/1/15

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation Research_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation Research_ is online at:
http://circres.ahajournals.org/subscriptions/