Rapid Resetting of Low Pressure Vagal Receptors in the Superior Vena Cava of the Rat

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SUMMARY. The discharge characteristics of mechanoreceptors located in the left superior vena cava were determined in an in vitro preparation developed from the rat. Two classes of receptors with afferent fibers in the vagus were identified on the basis of their response to steps of pressure. Slowly adapting receptors (n = 18) discharged as long as pressure was above threshold and exhibited a biphasic decline in discharge frequency in response to a pressure step. There was a rapid, initial decline in discharge frequency, complete within 15 seconds, followed by a slow, gradual decline complete within 5 minutes. Rapidly adapting receptors (n = 15) discharged irregularly or ceased firing after 5-10 seconds of a step increase in pressure. Following a 15-minute increase in perfusion pressure from 0 to 5 mm Hg, the threshold pressure of the slowly adapting receptors was increased and maximal discharge frequency and slope were decreased, whereas, in the rapidly adapting receptors, the threshold pressure was increased but maximal discharge frequency and slope were unchanged. Additional perfusion of the vessel at 5 mm Hg for up to 60 minutes produced no further increase in the degree of resetting. The resetting was reversible with discharge returning to control levels after a 15- to 25-minute return to 0 mm Hg. To determine whether the resetting of discharge following the acute pressure increase reflected a change within the receptor or an alteration of the vessel wall due to sustained distension, we examined the passive mechanical properties of the superior vena cava. Pressure-radius relationships were determined with an ocular micrometer. A 15-minute increase in pressure had no significant effect upon the mechanical properties of the vessel. Rapid resetting in these low pressure mechanoreceptors occurs with no discernible alteration in the vessel wall. (Circ Res 51:241-249, 1982)

MECHANORECEPTORS that lie in the great veins and atria are involved in several aspects of circulatory control. Electrophysiological studies reveal a variety of receptors based on the conduction velocity of the afferent fiber and the specific stimulus required to activate the receptor. However, in vivo, the complex geometry of the cardiac chambers makes it difficult to control the stimulus parameters and quantitate the discharge characteristics of the receptors. Due to these limitations, quantitative data regarding discharge characteristics, such as threshold pressure, sensitivity to suprathreshold pressure, adaptation, and the relationship between electrical activity and the mechanical properties of the tissue, are lacking.

Of particular interest is the question of the ability of the mechanoreceptors to adapt to prolonged elevations or reductions in pressure. The threshold pressure necessary to elicit discharge from atrial receptors is increased after chronic elevation of atrial pressure in an experimental model of hypertension (Thoren et al., 1979b) and in an experimental model of heart failure (Zucker et al., 1977). Recent reports indicate the threshold pressure necessary to elicit discharge of the high pressure arterial baroreceptors is dependent upon the prevailing pressure (Krieger, 1970; Salgado and Krieger, 1978; Samodelov et al., 1979; Coleridge et al., 1981). Because of the postulated role of low pressure receptors in volume control, it is important to know to what extent and over what time period they are also capable of altering their discharge characteristics in response to acute changes in pressure. Reports indicate that the responses of atrial receptors are reduced after a 20-minute distension (Anyukhovsky et al., 1976) and after exposure to an elevated pressure for 60 minutes (Kappagoda and Padsha, 1981). It would also be of interest to know if any alterations in discharge, which may occur, reflect a change within the receptor or an alteration of the mechanical properties of the vessel wall.

To answer these questions, an in vitro preparation has been developed from the rat in which the discharge of vagal afferent fibers connected to low pressure receptors is recorded. The preparation is a cylindrical segment of the superior vena cava which is composed of cardiac muscle and is an area described in the dog (Coleridge et al., 1957, 1964), in the cat (Gupta, 1977), and in the rat (Thoren et al., 1979a; Kaufman et al., 1981) as being supplied with receptors whose responses are indistinguishable from those of receptors located in the atria. The vessel is perfused to maintain its viability, pressure waves are applied, and the discharge of single mechanoreceptive vagal afferent fibers is recorded. The vessel distends radially in response to a pressure stimulus as it is fixed at its in vivo length. The favorable geometry of the vessel allows analysis of the passive mechanical prop-
erties of the vessel wall. This permits a more complete description of the response characteristics of the low pressure mechanoreceptors.

We have identified two classes of low pressure receptors based on their response to a suprathreshold step of pressure. The threshold pressure necessary to elicit discharge in both types of receptor is increased after a 15-minute perfusion at an increased pressure. This acute resetting is reversible and occurs with no discernible change in the passive response of the vessel wall to distension.

Methods

Adult, male Sprague-Dawley rats weighing approximately 250-350 g and 10-20 weeks of age were anesthetized with ether induction followed by an intraperitoneal injection of pentobarbital (30 mg/kg). The trachea was intubated with PE 200 tubing and the animal was artificially respired by a positive pressure respirator. The second through fifth ribs on the left side were removed. The left lobe of the lung was ligated and removed for better access and visualization of the left superior vena cava (SVC) which is depicted in Figure 1. The left SVC is composed of cardiac muscle to the point where it joins the azygos vein (J. Kraus, unpublished observation) and contracts with the right atrium in vivo. The left thoracic vagus was cut, dissected free of surrounding tissue, and reflected back onto the left SVC. A metal cannula (outside diameter = 2.39 mm) was passed via the inferior vena cava into the left SVC and tied in place at the point where the left SVC enters the right atrium. This cannula served as the outflow in the in vitro setup. Another metal cannula (outside diameter = 2.10 mm) was passed via the subclavian vein into the left SVC and tied in place with the tip of the cannula at the point where the azygos vein joins the left SVC. This cannula served as the inflow in the in vitro setup.

The cannulated segment of the left SVC, with its vagal innervation intact and fixed at its in situ length, 1-2 cm, was transferred to the in vitro perfusion system diagrammed in Figure 2. The inflow and outflow cannulas were fixed and the vessel was placed in a bath filled with mineral oil. The vessel and nerves were covered with oil throughout the experiment. A Haake FJ heater circulated warmed water under the bath to maintain the temperature of the oil between 36 and 38°C. The vessel was perfused with a similarly warmed Krebs-Henseleit solution (NaCl 111 mm; KCl 4.7 mm; MgSO4 1.78 mm; CaCl2 1.25 mm; KH2PO4 1.13 mm; NaHCO3 25 mm; dextrose 11.1 mm) which was gassed with 95% O2-5% CO2 pH 7.4. Flow through the vessel could be varied between 0.15 and 15.0 ml/min by adjusting the rate of a Holter infusion pump. Flow through the isolated vessel was in the same direction as occurs in vivo. Surrounding tissues, primarily fat and any portion of the pulmonary vessels which adhered, were removed. The preparation remained viable for up to 8 hours and single units were studied on the average for 2-4 hours.

Step or ramp increases in pressures were applied by a shaker, an electrodynamic transducer (Ling), and bellows (Robert-Shaw, Inc.) connected to the inflow cannula by a three-way stopcock. A function generator was connected to the shaker driver to produce the desired waveform. When pressure steps or ramps were applied, the outflow stopcock was closed. Pressure was measured from a sidearm of the outflow cannula with a strain gauge pressure transducer (Statham P23Db). By altering the height of the outflow tube, we could vary mean perfusion pressure while maintaining flow. The pressure signal was displayed on an oscilloscope and recorded on an FM tape recorder (Hewlett-Packard 3600).

Slips of nerve fibers were teased from the left cardiac branch of the vagus with sharpened needles. Fibers were split until one or two identifiable mechanoreceptive units could be detected in response to the increase in pressure produced by a brief occlusion of the outflow cannula. Nerve fibers were placed on platinum-iridium electrodes and action potentials recorded with a high gain (10,000X) capacitance coupled amplifier (PAR, model 113). The output of the amplifier was led to the FM recorder and from there to an audio monitor and oscilloscope.

The data analysis system was similar to that previously described by Brown et al. (1976). An off-line computer

![Figure 1](image1.png)  
**Figure 1.** Ventral view of rat heart. RA = right atrium, LA = left atrium, PV = pulmonary vein, PA = pulmonary artery. Arrows indicate where ligatures are tied around the tips of the cannulas. Scale indicates length in centimeters.

![Figure 2](image2.png)  
**Figure 2.** Schematic representation of the in vitro superior vena cava-vagal cardiac nerve preparation.
The entire series required approximately 10 minutes. The edges of the vessel could be visualized. Changes in external diameter in response to steps of pressure were measured with an ocular micrometer fitted on to a dissecting microscope; at 25X, minor divisions of the ocular micrometer were equal to 39 μm. During the control period, a random series of steps, between 0 and 14 mm Hg, were applied. Each step was maintained for 30 seconds, and the change in external diameter after 30 seconds was measured. At the completion of the step the pressure was returned to 0 mm Hg. There was an interval of 30 seconds between the steps. The entire series required approximately 10 minutes. The test period followed a 15-minute perfusion of the vessel at 5 mm Hg. Random steps between 0 and 14 mm Hg were applied for 30 seconds as in the control period. At the completion of each step, the pressure was returned to 5 mm Hg for 30 seconds to reverse any recovery of the vessel wall elements. The values obtained from the four rats during the test period were averaged, as were the values obtained during the test period for comparison.

To quantify further the mechanical properties of the SVC wall, we calculated the internal radius, wall thickness, stress, and strain by the method described in Andresen et al. (1978). Student’s t-test was performed to determine the significance of any differences which might exist between external and internal radii, wall thickness, stress, and strain.

**Results**

**Types of Vagal Afferent Fiber**

The receptors in this study were determined, by probing with a cat’s whisker, to be concentrated on the dorsal surface of the vessel and toward the junction of the superior vena cava and the right atrium, although many receptors could be localized more distal to the atrium, out to the azygos vein. The responses of these receptors to square wave steps of pressure, rise time less than 150 msec, and ramps of pressure, increasing at a rate of 0.5 mm Hg/sec, were studied. Normal right atrial pressure in the rat ranges from 0 to 6 mm Hg (Ricksten et al., 1981; Kaufman et al., 1981) with an intrathoracic pressure which varies at end expiration between 0 and —2 mm Hg (Noresson et al., 1979). In 37 experiments, a total of 40 receptors were analyzed. These receptors were divided into two classes on the basis of their response to steps of pressure. Both types of receptor were found in the same rat. However, due to splitting of the nerve to obtain a single unit, usually only one receptor was studied in each experiment. We never observed conversion of one type of discharge pattern into another.

To examine adaptation over a longer time scale, the discharge of three slowly adapting fibers was monitored continuously throughout a 15-minute perfusion at 5 mm Hg, as illustrated in Figure 5. Following the initial rapid reduction in discharge, illustrated in Figure 4A, there is a second more gradual decline in discharge. This second phase of adaptation is complete within approximately 5 minutes, fluctuating around a mean by only 1–3 Hz between the 5th and 15th minutes. Between 15 seconds and 5 minutes, discharge frequency decreases by 3–5 Hz, and if the discharge level at 15 seconds is designated as 100% of discharge level, at 5 minutes discharge has fallen to 75–80% of its level at 15 seconds. Over the next 10 minutes there is no significant further reduction in discharge (P < 0.01).

**Rapidly Adapting Receptors**

Rapidly adapting receptors, illustrated in Figure 3B, respond to a suprathreshold step of pressure with a burst of impulses. However, discharge continues very irregularly or ceases approximately 5–10 seconds after the onset of the pressure step even at high (greater than 5 mm Hg) pressures. Figure 4B illustrates that the discharge frequency in the initial 5- to 10-second burst increases with increasing pressure up to a max-
A. Slowly Adapting

B. Rapidly Adapting

FIGURE 3. A: Response of a slowly adapting receptor to pressure steps of 2, 4, and 6 mm Hg. B: Response of a rapidly adapting receptor to pressure steps of 4, 7, and 10 mm Hg.

imum. The highly irregular discharge after the initial 5- to 10-second burst, seen in 15 of the 17 rapidly adapting receptors studied, fluctuated with an instantaneous frequency between 0.1 and 5.0 Hz, and remained irregular as the pressure was increased.

When monitored for 15 minutes following a step increase in pressure, rapidly adapting receptors exhibit an irregular discharge which declines to less than 1.0 Hz within 10 seconds. Discharge remains low frequency and irregular as long as the pressure step is maintained.

Pressure-Frequency Curves

The pressure-frequency relationship can be characterized by three parameters. Threshold pressure is designated as the pressure necessary to produce a sustained discharge. Maximal discharge frequency ($F_{\text{max}}$) is the asymptotic frequency reached at high pressures. Between the threshold pressure and $F_{\text{max}}$ is an approximately linear pressure-frequency region. The slope of the region between threshold pressure and 50% of $F_{\text{max}}$ was calculated using a least squares

FIGURE 4. A: Instantaneous frequency of a slowly adapting receptor as a function of time during pressure steps of 2, 4, and 9 mm Hg. B: Instantaneous frequency of a rapidly adapting receptor as a function of time during pressure steps of 4, 7, and 11 mm Hg.
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adapting receptors. The threshold pressure of the

Table 1. The Fmax, of the slowly adapting receptors

tors, 15 rapidly and 18 slowly adapting, following a

slope of the pressure-frequency curve were examined

was significantly greater than that of the rapidly

due to time limitations imposed by the acute resetting experimental protocol, pressure-frequency curves were determined in response to ramps of pressure, increasing from 0 to 15 mm Hg at a rate of 0.5 mm Hg/sec. Due to time limitations imposed by the acute resetting experimental protocol, pressure-frequency curves were determined in response to ramps of pressure, increasing from 0 to 15 mm Hg at a rate of 0.5 mm Hg/sec. As shown in Figure 6, pressure-frequency curves generated by a 0.5 mm Hg/sec ramp increase in pressure are similar to curves constructed by plotting discharge frequency during the 5th-6th second, slowly adapting, or the 3rd-4th second, rapidly adapting, of a pressure step as a function of the amplitude of the pressure step. For both types of receptor, threshold pressure and the slope of the pressure-frequency curve are similar whether the pressure-frequency curve is obtained from a 0.5 mm Hg/sec ramp increase in pressure or using the discharge frequency during the 5th-6th second, slowly adapting, or the 3rd-4th second, rapidly adapting, following a series of steps increases in pressure. However, for both types of receptor, ramp elicited Fmax is 10-15% greater than Fmax obtained in response to pressure steps.

The results of an analysis of 33 low pressure receptors, 15 rapidly and 18 slowly adapting, following a control perfusion of 0 mm Hg are summarized in Table 1. The Fmax of the slowly adapting receptors was significantly greater than that of the rapidly adapting receptors. The threshold pressure of the rapidly adapting receptors was significantly greater than that of the slowly adapting receptors.

In one experiment on each type of receptor, a control pressure-frequency curve was obtained and then the flow of perfusate was stopped for 5 minutes. This period of zero flow had no significant effect on the pressure-frequency curve.

Rapid Resetting

The pressure-frequency curves of receptors were obtained in response to ramps of pressure increasing from 0 to 15 mm Hg at a rate of 0.5 mm Hg/sec. Pressure-frequency curves obtained after a 15-minute perfusion at 0 mm Hg were compared to curves obtained following a 15-minute perfusion at 5 mm Hg. Figure 7 shows such curves for slowly and for rapidly adapting receptors. A total of 18 slowly and 15 rapidly adapting fibers were analyzed, and the data are summarized in Table 1.

After the acute increase in pressure, the threshold pressures of both slowly and rapidly adapting receptors were increased. Threshold shifts were quantitatively similar in all receptors, ranging from 1.2 to 2.5 mm Hg (mean = 1.6 ± 0.02 mm Hg). Rapidly adapting receptors experienced a 10% decrease in Fmax (range = 8-13%) and a 9% decrease in slope (range = 7-12%), neither change being significant (P < 0.35). Slowly adapting receptors experienced a significant 23% decrease in Fmax (range = 15-37%) and a significant 31% decrease in slope (range = 17-70%).

Additional perfusion of the vessel for up to 60 minutes at 5 mm Hg produced no further increase in the degree of resetting or the changes seen after the initial 15-minute perfusion in four slowly and three rapidly adapting receptors. Figure 7 illustrates that the
TABU

Table 1
Discharge Characteristics of Slowly and Rapidly Adapting Receptors during a Control Perfusion at 0 mm Hg and after a 15-Minute Perfusion at 5 mm Hg

<table>
<thead>
<tr>
<th></th>
<th>Slowly adapting</th>
<th>Rapidly adapting</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>Threshold pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2.6 ± 0.4</td>
<td>4.1 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>15 min at 5 mm Hg</td>
<td>4.2 ± 0.5</td>
<td>5.6 ± 0.7</td>
</tr>
<tr>
<td>F_max (Hz)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>48.4 ± 3.1</td>
<td>26.3 ± 3.2</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>15 min at 5 mm Hg</td>
<td>36.9 ± 3.6</td>
<td>23.5 ± 2.9</td>
</tr>
<tr>
<td>Slope (Hz/mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>13.3 ± 1.8</td>
<td>11.3 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>15 min at 5 mm Hg</td>
<td>9.1 ± 1.1</td>
<td>10.3 ± 1.3</td>
</tr>
</tbody>
</table>

All values expressed as mean ± se.

resetting was readily reversible as discharge returned to control levels after a 15- to 25-minute return to 0 mm Hg.

Wall Properties of SVC

To determine whether the resetting of discharge following the acute pressure increase reflects a change within the receptor or an alteration of the vessel wall due to sustained distension, the passive mechanical properties of the SVC were examined. In four rats, the SVC was isolated, perfused, and external diameter measured in response to steps of pressure as described in Methods. External diameter of the vessel was measured midway between the tips of the cannulas. Distension was uniform in the region between the cannulas; however, extension was less at the ligatures since end-diameter was fixed. Data are summarized in Table 2. A t-test revealed no significant difference, at P < 0.05, between the control and test conditions for external and internal radii, stress, strain, and wall thickness, defined as the difference between the external and the internal radius. There also was no difference in the zero pressure radius of the vessel between the control and test condition.

Figure 7. Pressure-frequency curves of a slowly (A) and rapidly (B) adapting receptor during perfusion at 0 mm Hg (filled circles), after a 15-minute perfusion at 5 mm Hg (open circles), and after a 15-minute return of 0 mm Hg (filled squares).
### TABLE 2

**Mechanical Properties of the Superior Vena Cava**

<table>
<thead>
<tr>
<th>Pressure (mm Hg)</th>
<th>Volume (μl)</th>
<th>External radius (mm)</th>
<th>Internal radius (mm)</th>
<th>Stress (×10⁴ dy/cm²)</th>
<th>Strain</th>
<th>Volume (μl)</th>
<th>External radius (mm)</th>
<th>Internal radius (mm)</th>
<th>Stress (×10⁴ dy/cm²)</th>
<th>Strain</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>0.892</td>
<td>0.633</td>
<td></td>
<td></td>
<td>24</td>
<td>0.899</td>
<td>0.647</td>
<td></td>
<td></td>
</tr>
<tr>
<td>±2</td>
<td>±2</td>
<td>±0.043</td>
<td>±0.095</td>
<td>±2</td>
<td>±2</td>
<td>±0.039</td>
<td>±0.095</td>
<td>±6.613</td>
<td>±0.018</td>
<td>±0.06</td>
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<td>0.753</td>
<td>1.16</td>
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<td>0.770</td>
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<td>±2</td>
<td>±2</td>
<td>±0.042</td>
<td>±0.084</td>
<td>±0.02</td>
<td>±0.020</td>
<td>±2</td>
<td>±0.037</td>
<td>±0.077</td>
<td>±0.02</td>
<td>±0.018</td>
</tr>
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<td>4</td>
<td>36</td>
<td>1.139</td>
<td>0.958</td>
<td>3.34</td>
<td>0.390</td>
<td>35</td>
<td>1.171</td>
<td>0.998</td>
<td>3.63</td>
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<td>±3</td>
<td>±3</td>
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<td>±0.069</td>
<td>±0.07</td>
<td>±0.060</td>
<td>±2</td>
<td>±0.049</td>
<td>±0.060</td>
<td>±0.04</td>
<td>±0.81</td>
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<td>6</td>
<td>40</td>
<td>1.220</td>
<td>1.080</td>
<td>6.16</td>
<td>0.549</td>
<td>41</td>
<td>1.247</td>
<td>1.087</td>
<td>6.23</td>
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</tr>
<tr>
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<td>±0.061</td>
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<td>±0.136</td>
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<tr>
<td>8</td>
<td>43</td>
<td>1.313</td>
<td>0.163</td>
<td>9.33</td>
<td>0.659</td>
<td>44</td>
<td>1.310</td>
<td>1.160</td>
<td>9.31</td>
<td>0.623</td>
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<td>±3</td>
<td>±3</td>
<td>±0.075</td>
<td>±0.074</td>
<td>±0.10</td>
<td>±0.181</td>
<td>±2</td>
<td>±0.077</td>
<td>±0.077</td>
<td>±0.10</td>
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<tr>
<td>10</td>
<td>47</td>
<td>1.338</td>
<td>1.191</td>
<td>11.91</td>
<td>0.697</td>
<td>47</td>
<td>1.347</td>
<td>1.201</td>
<td>12.21</td>
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<td>±3</td>
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<td>±0.076</td>
<td>±0.12</td>
<td>±0.191</td>
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<td>±0.080</td>
<td>±0.13</td>
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<td>1.212</td>
<td>14.97</td>
<td>0.722</td>
<td>53</td>
<td>1.362</td>
<td>1.218</td>
<td>15.10</td>
<td>0.695</td>
</tr>
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<td>±3</td>
<td>±0.083</td>
<td>±0.083</td>
<td>±0.16</td>
<td>±0.194</td>
<td>±2</td>
<td>±0.084</td>
<td>±0.084</td>
<td>±0.16</td>
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<tr>
<td>14</td>
<td>57</td>
<td>1.362</td>
<td>1.218</td>
<td>17.60</td>
<td>0.729</td>
<td>55</td>
<td>1.365</td>
<td>1.221</td>
<td>17.69</td>
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<tr>
<td>±5</td>
<td>±5</td>
<td>±0.084</td>
<td>±0.084</td>
<td>±0.19</td>
<td>±0.192</td>
<td>±5</td>
<td>±0.085</td>
<td>±0.085</td>
<td>±0.19</td>
<td>±0.171</td>
</tr>
</tbody>
</table>

* Measured during a control perfusion at 0 mm Hg and after a 15-minute perfusion at 5 mm Hg. Values are means ± SE determined from four rats.

Utilizing the stress, strain, and pressure data, plots of discharge frequency as a function of stress or strain were constructed. Figure 8A illustrates the relationship between discharge frequency and stress. If discharge frequency is plotted as a function of strain, as shown in Figure 8B, the relationship correlates with a linear function (r² = 0.99 for the slowly adapting receptor; r² = 0.93 for the rapidly adapting receptor).

### Discussion

Low pressure receptors have been localized, by probing, in the superior vena cava of dogs (Coleridge et al., 1957, 1964; Kappagoda et al., 1972), cats (Gupta, 1977), and rats (Thoren et al., 1979a; Kaufman et al., 1981), and the responses of these receptors are similar to those of receptors located in the atria. We were unable to obtain conduction velocities of the afferent fibers studied due to the short length, less than 1 cm, of nerve available even before splitting to obtain single units. In an in vivo study of atrial receptors in the rat (Thoren et al., 1979a), all fibers studied conducted at less than 1.2 m/sec, placing them in the C-fiber group.

Slowly adapting receptors, reported in response to balloon inflation or pressure increases in in vivo studies of atrial receptors in the rat (Thoren et al., 1979a), cat (Paintal, 1953), and dog (Kappagoda et al., 1972), are quantitatively similar to those in the present study. The threshold pressures for discharge are in the low to midrange of right atrial transmural pres-
sures reported in unanesthetized rats (Ricksten et al., 1981). Pressure-frequency curves with similar slopes and maximal discharge frequencies have been reported in in vivo studies of atrial receptors in the rat (Thoren et al., 1979a, 1979b).

Rapidly adapting vagal afferent fibers were reported in two in vitro studies of atrial receptors (Langrehr, 1960; Chapman and Pankhurst, 1976). Irregular and low frequency discharge was a characteristic of a group of unmyelinated atrial receptors in the rat (Thoren et al., 1979a). This class of receptors responded to increases in atrial pressure with a \( F_{\text{ma}^*} \) of less than 25 Hz. It is possible that these low frequency, irregularly discharging receptors described by Thoren et al. (1979a) are the rapidly adapting receptors reported in this study, as the \( F_{\text{ma}^*} \) of the rapidly adapting receptors was 26.3 ± 3.2 Hz and discharge was irregular. Also, in the study of Thoren et al. (1979a), a significant difference was found in the threshold pressures between the low and high frequency groups with the low frequency receptors having a greater mean threshold pressure. In the present study, the mean threshold pressure of the rapidly adapting receptors was significantly greater than that of the slowly adapting receptors, 4.1 ± 0.4 mm Hg vs. 2.6 ± 0.4 mm Hg (\( P < 0.01 \)).

**Wall Properties of the SVC**

The pressure-volume curve is similar to those observed in other collapsible vessels (Moreno et al., 1970) and reported for isolated left atria in rats (Ricksten et al., 1980). The assumption that this segment of vessel is a right cylinder appears to be justified on the basis of the volume data presented in Table 2. At 14 mm Hg, the radius of the vessel is 1.53 times the radius at 0 mm Hg (1.36/0.89 = 1.53 from Table 2). Assuming a right cylinder, the volume at 14 mm Hg should be (1.53)\( ^3 \) times the volume at 0 mm Hg or \( 2.34 \times V_o \) (\( V = \pi r^2 h \)). The volume at 14 mm Hg is 2.28 \( \times V_o \) (57/25 = 2.28 from Table 2). This justifies the measured values of external radii used for the calculation. The calculated wall thickness is identical to that measured directly from histological sections of left atrial strips of rats, and the values for stress and strain reported here are consistent with those reported in length-tension curves of left atrial strips of rats (Ricksten et al., 1980). For these reasons, the optical method is believed to reflect accurately the gross passive mechanical properties of the vessel wall. The linear relation between discharge frequency and strain indicates that these low pressure receptors are distortion receptors, the distortion being expressed as a stretch in the circumferential direction.

**Rapid Resetting**

The resetting of mechanoreceptor discharge in response to chronic elevations of pressure (Thoren et al., 1979b) and in heart failure (Zucker et al., 1977) has been reported in atrial mechanoreceptors. The discovery that the threshold pressure of arterial baroreceptor discharge is acutely dependent on the pressure to which the receptors are subjected (Krieger, 1970; Salgado and Krieger, 1978; Samodelov et al., 1979, Coleridge et al., 1981) has only recently been extended to atrial receptors (Kappagoda and Padsha, 1981) where the responses of atrial receptors to balloon distension were found to be decreased after a 60-minute increase in atrial pressure. This is supported by the present study, and we have found alterations in discharge within 15 minutes of an increase in pressure. In a study of aortic receptors in the dog (Coleridge et al., 1981), where stimulus-response curves of individual fibers were constructed, the authors report no decrease in maximal discharge frequency or in slope. This is contrary to what we have observed in the slowly adapting atrial receptors. Whether or not this represents an inherent difference between arterial and this class of atrial receptors remains to be seen. Nonetheless, rapid resetting would seem to be a general phenomenon among cardiovascular mechanoreceptors, as suggested by Anyukhovsky et al., (1976).

The mechanism of the rapid resetting process has not been studied previously. Analysis of wall properties is simplified in this atrial preparation due to the cylindrical shape of the vessel, so that alterations in receptor discharge can be ascribed to changes in the neural or the mechanical determinants of receptor discharge. A 15-minute increase in pressure might alter the elastin, collagen, muscle, and connective tissue in the vessel wall in such a way as to decrease discharge. However, such an acute increase in pressure produces no significant changes in any of the wall properties studied. Of course, this method measures only the gross mechanical properties of the whole vessel wall and cannot reveal any local changes which might occur where the receptors are coupled to the vessel wall elements.

In the absence of any alteration in the passive mechanical properties of the vessel wall, an alternative explanation is that acute resetting results from a change within the receptor itself. The effects of reduced sodium on atrial receptor discharge suggests the receptor potential may be due to an increase in sodium permeability (Kunze and Orlea, 1979). The sodium influx produced by an increase in pressure could then increase the internal sodium concentration (Na\(^+\)). The elevated (Na\(^+\)) might stimulate the sodium-potassium pump. Alterations in pump activity have been shown to occur over a period of 10 minutes (Thomas, 1972; Kunze, 1977). The pump, if electrogenic, would hyperpolarize the receptor membrane; therefore more stretch would be required to reach the threshold level of depolarization. There is evidence indicating a similar sequence of events produces post excitatory depression in aortic baroreceptors (Saum et al., 1976). The elevated (Na\(^+\)), could also decrease the gradient for Na\(^+\) influx in response to stretch, thereby decreasing the discharge of the receptor.

The fact that atrial receptors are altered by acute increases in pressure might have important consequences, considering the role of atrial receptors in the
reflex regulation of the cardiovascular system and the kidney. Slowly adapting receptors operate within an elevated pressure range as their threshold pressure is increased. The slope of the stimulus-response curve and Fmax are decreased; therefore, their ability to buffer fluctuations is decreased. Rapidly adapting receptors operate within an elevated pressure range as a result of an increase in threshold pressure. Their ability to buffer fluctuations within this range is not compromised, as there are no significant changes in the slope of the stimulus-response curve or in Fmax.

Low pressure mechanoreceptors appear suited to the ability to buffer fluctuations around a mean level determined elsewhere, possibly the kidney or the central nervous system.

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