Tachypnea after stimulation of afferent cardiac sympathetic nerve fibers

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UCHIDA, YASUMI. Tachypnea after stimulation of afferent cardiac sympathetic nerve fibers. Am. J. Physiol. 230(4): 1003-1007. 1976. — The role of afferent cardiac sympathetic nerve fibers in the regulation of respiration has been examined. Application of potassium chloride or lactic acid solutions to the left ventricular surface of anesthetized vagotomized dogs resulted in a decrease in the maximum firing rate and shortening in period duration of firing of phrenic nerves. Also, application of the agents caused a decrease in amplitude and an increase in rate of respiratory thoracic movements. The same changes in phrenic nerve activity and respiratory movements were produced by coronary artery occlusion and centrifugal electrical stimulation of the left inferior cardiac nerves. The results indicate tachypnea that can be produced by excitation of afferent cardiac sympathetic nerve fibers.

THE HEART IS INNERVATED by afferent nerve fibers that have their pathways in the cardiac sympathetic nerves (1, 6, 7, 9-12). These afferent nerve fibers have been called afferent cardiac sympathetic nerve fibers in order to differentiate them from afferent cardiac nerve fibers in the vagus (7, 9-12). Although afferent functions as vasopressor and nociceptor have been clarified considerably, the role of the afferent cardiac sympathetic nerve fibers in the regulation of respiration is still unclear. Our study was undertaken to examine the effect of chemical and electrical stimulation of afferent cardiac sympathetic nerve fibers on phrenic nerve activity.

METHODS

Surgical preparation. Experiments were carried out on 15 adult mongrel dogs under intravenous pentobarbital sodium anesthesia (20-25 mg/kg). The trachea was intubated for artificial positive-pressure respiration with air. The upper seven ribs on the left side were removed. The anterior aspect of the left heart was exposed by pericardiotomy. A small branch of the left anterior descending artery that supplied the blood to the apical portion was dissected free of surrounding tissues, and a catheter 1 mm in external diameter was introduced in retrograde fashion into it to monitor the peripheral blood pressure of the coronary artery. Another catheter was introduced into the right femoral artery to monitor the systemic blood pressure. A force-displacement strain gauge arch was sewn to the right thoracic wall to monitor thoracic wall movements caused by spontaneous respiration. The influence of artificial respiration on the thoracic wall was insignificant. The bilateral cervical vago-sympathetic trunks were transected.

Recording phrenic nerve activity. The left phrenic nerve was dissected free of surrounding tissues and was transected at the level of the aortic arch. The cut central end of the nerve was placed on bipolar platinum-iridium electrodes connected to an AC-coupled preamplifier. The action potentials of the phrenic nerve fibers were displayed on the screen of a cathode-ray oscilloscope and were recorded on running films. At the same time, the action potentials were employed to trigger a square-wave generator and the output was integrated by a pulse integrator. Action potentials above the noise level were sampled by the square-wave generator by changing the slice level. The generator was connected to a loudspeaker to monitor whether sampling of the action potentials was accurate. The output of the integrator used in this study had a linear relation to the number of the action potentials per second in the range of 1-500 Hz. The height of the integrated record thus obtained indicated the number of the action potentials per second. The integrated action potentials, coronary blood pressure, systemic blood pressure, and respiratory thoracic movements were recorded on an ink recorder.

It is well known that phrenic nerve fibers fire phasically synchronous to respiratory movements. In this study, the time from the beginning of one phasic firing to the beginning of the next was called period duration. The period duration in the control study was calculated for 1 min and compared to that of following stimulation of afferent cardiac sympathetic nerve fibers. The Student t test was employed for comparison.

Chemical stimulation of afferent cardiac sympathetic nerve fibers. Potassium chloride and lactic acid were used to activate afferent cardiac sympathetic nerve fibers since these agents are potent stimulators of the afferent fibers (10, 12). Potassium chloride and lactic acid were dissolved in physiological saline since this solvent was ineffective in exciting the afferent fibers in our previous study (10). Concentration of potassium chloride was 1 mg/ml (1.32 × 10⁻² mol) and concentration of lactic acid was 1 mg/ml (1.04 × 10⁻² mol). A filter paper 3 x 3 cm² in size was immersed in the solution and was placed on the anterior wall of the left ventricle for at least 1 min. Eight dogs were used for potassium chloride application and five for lactic acid application.
Occlusion of coronary artery. Coronary artery occlusion excited afferent cardiac sympathetic nerve fibers in our previous study (11). Therefore, the proximal segment of the anterior descending branch of the left coronary artery was occluded by a screw clamp for 90-120 s in five dogs that were used for chemical stimulation experiments. Period duration of firing and the maximum firing rate of phrenic nerve fibers and amplitude of respiratory thoracic movements were compared before, during, and after occlusion of the coronary artery.

Electrical stimulation of afferent cardiac sympathetic nerve fibers. In five dogs, the left inferior cardiac nerve was dissected free of surrounding tissues and was transected at the level of the atrioventricular junction. The cut central end of the nerve was placed on bipolar electrodes and a train of square-wave electrical pulses (1 ms, 20 Hz, for 10 s) was applied via the electrodes on the inferior cardiac nerve. The nerve was stimulated with 5 V, which is supramaximal for the myelinated Aβ fibers (7, 9), and thereafter with 20 V, which is supramaximal for the unmyelinated fibers (7, 8). Period duration and the maximal firing rate of the phrenic nerve fibers and amplitude of respiratory thoracic movements were compared before and during stimulation.

RESULTS

Effect of chemically induced excitation of afferent cardiac sympathetic nerve fibers on phrenic nerve activity. Immediately after application of potassium chloride solution to the left ventricular wall, the maximum firing rate of the phrenic nerve fibers was reduced simultaneously with shortening in period duration of firing in all preparations. The decrease in the maximum firing rate and shortening in period duration of firing were always accompanied by a decrease in amplitude of respiratory thoracic movements that was mainly due to reduced inspiration and an increase in rate of respiratory movements (Figs. 1 and 2). Although the filter paper in which potassium chloride was contained was left in place for at least 1 min, phrenic nerve activity and respiratory movements tended to return toward the control states. Both phrenic nerve activity and respiratory movements completely returned to the control states within 1 min after removal of the filter paper (Fig. 3). On application of the agent, a rise in both coronary and systemic blood pressures was observed in all preparations. However, the beginning of the rise in pressure occurred later than the changes in phrenic nerve activity and respiratory movements (Table 1). In three preparations, a transient fall preceded the rise in pressure (Fig. 2). Extension of the limbs was observed immediately after application of the agent in these preparations. The data for these preparations were not included in Table 1 since the beginning of the rise in pressure may have been modified by the somatic movements.

Application of lactic acid solutions also resulted in an abrupt decrease in the maximum firing rate and shortening in period duration of firing of phrenic nerve fibers in all preparations. These changes were also accompanied by a decrease in amplitude and an increase in rate of respiratory movements (Fig. 4). A rise in systemic blood pressure was also observed in all preparations (Table 1). A transient fall prior to the rise in pressure was observed in one preparation.

Effect of coronary artery occlusion on phrenic nerve activity. Decrease in the maximum firing rate and shortening in period duration of firing of phrenic nerve fibers were produced during coronary artery occlusion in all preparations. These changes were always accompanied by a decrease in amplitude and an increase in rate of respiratory movements (Fig. 5). These changes persisted throughout the occlusion period and disappeared within 30 s after the cessation of occlusion. Changes in coronary and systemic blood pressures were inconsistent; the pressures fell in two but rose in the remaining three preparations (Table 1).

Effect of electrical stimulation of afferent cardiac sympathetic nerve fibers on phrenic nerve activity. Central end stimulation of the left inferior cardiac nerves with 5 V, which is supramaximal for the myelinated Aβ fibers (7, 8), resulted in an abrupt decrease in the maximum firing rate and shortening in period duration of firing of phrenic nerve fibers. These changes were always accompanied by a decrease in amplitude
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1 KCl lmg/Kg for 10 sec of electrical pulses of 20 V, which is supramaximal for the unmyelinated fibers (7, 8), the magnitude of the changes in phrenic nerve activity and respiratory movements was augmented. However, no essential difference in modality of the changes was observed.

The latency for the changes in phrenic nerve activity and blood pressure caused by electrical stimulation was shorter than that caused by chemical stimuli and coronary occlusion (Table 1).

Since there was a possibility that the changes in

and an increase in rate of respiratory movements (Figs. 6 and 7). However, phrenic nerve activity and respiratory movements returned to the control states immediately after the cessation of stimulation. A rise in coronary and systemic blood pressures was also produced by stimulation (Table 1). Changes in phrenic nerve activity and respiratory movements had a tendency to occur earlier than the rise in pressure (Table 1). With a train

FIG. 2. Effect of 1 mg/ml in concentration of potassium chloride on phrenic nerve activity and respiratory movements. From top: integrated action potentials of phrenic nerves, coronary blood pressure (CBP), systemic blood pressure (SBP), and respiratory thoracic movements (Resp.). Downward arrow indicates application of potassium chloride solution. Insp. = inspiration. Exp. = expiration.

FIG. 3. Effect of potassium chloride on phrenic nerve activity and respiratory movements. From top: period duration of firing, maximum firing rate of phrenic nerves expressed as percent of control value, and amplitude of respiratory movements expressed as percent of control value; n = number of phasic firings of phrenic nerves or number of respiratory cycles. NS = not significant.

FIG. 4. Effect of 1 mg/ml concentration of lactic acid on phrenic nerve activity and respiratory movements.

TABLE 1. Effect of stimulation of afferent cardiac sympathetic nerve fibers on systemic blood pressure and phrenic nerve activity

<table>
<thead>
<tr>
<th></th>
<th>Electrical Stimulation</th>
<th>KCl, 1 mg/ml</th>
<th>Lactic Acid, 1 mg/ml</th>
<th>Coronary Occlusion</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>5 V</td>
<td>20 V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control mean systemic blood pressure, mmHg</td>
<td>116</td>
<td>108</td>
<td>118</td>
<td>129</td>
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<td>Latency for changes in systemic blood pressure, s</td>
<td>5.2</td>
<td>5.4</td>
<td>11.8</td>
<td>19.0</td>
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<tr>
<td>Latency for changes in phrenic nerve activity, s</td>
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<td>0.5</td>
<td>5.6</td>
<td>7.5</td>
</tr>
<tr>
<td>P*</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.005</td>
</tr>
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<td>Latency for changes in phrenic nerve activity, s</td>
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<td>3.4</td>
<td>5.2</td>
<td>8.4</td>
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<tr>
<td>P*</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Changes in mean systemic blood pressure, mmHg</td>
<td>6.7</td>
<td>11.7</td>
<td>18.9</td>
<td>12.6</td>
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<tr>
<td>P*</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.005</td>
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<tr>
<td>Changes in mean phrenic nerve activity</td>
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<td>4.9</td>
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<td>P*</td>
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<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

Values are means ± SD. NS, not significant. * Obtained from electrical stimulation with 5 V and chemical stimulation and coronary occlusion experiments. † Obtained from systemic blood pressure and phrenic nerve activity.
phrenic nerve activity and respiratory movements were secondary to the rise in blood pressure, the descending thoracic aorta was constricted by a pair of forceps to observe the effect of a rise in blood pressure of the upper half of the body on phrenic nerve activity and respiratory movements in four preparations. In these preparations, coronary blood pressure was monitored as an indicator of blood pressure changes. The rise in pressure thus produced ranged from 30 to 80 mmHg. On constriction of the aorta, the maximum firing rate became larger and period duration of firing became longer than the control values (Fig. 8). Also, an increase in amplitude and a decrease in rate of respiratory movements were produced by constriction.
The results in this study indicate tachypnea (rapid and shallow respiration) caused by activation of afferent cardiac sympathetic nerve fibers. Since bilateral cervical vagi had been transected, it is unlikely that the afferent cardiac nerve fibers in the vagi caused this reflex respiratory change. Also, it is unlikely that tachypnea was secondary to a rise in systemic blood pressure and/or coronary blood pressure since tachypnea occurred before the beginning of rise in pressure and elevation of systemic blood pressure by aortic constriction caused bradypnea (slow and deep respiration).

It has been established that the stimulating action of potassium chloride and lactic acid on afferent cardiac sympathetic nerve fibers is due to K+ and H+ (10, 12). Therefore, the changes in phrenic nerve activity and respiratory movements caused by these two agents can be attributed to K+ and H+. Phrenic nerve activity and respiratory movements tended to return to the control states before the removal of the filter papers containing the potassium chloride or lactic acid, probably due to tachyphylaxis or dilution of the agents with tissue fluids. Excitation of afferent cardiac sympathetic nerve fibers also tended to cease before the removal of these agents in our previous studies (7, 9).

Occlusion of the coronary artery leads to excitation of afferent cardiac sympathetic nerve fibers (11). The latency for tachypnea caused by coronary occlusion was close to that required for excitation of the afferent nerve fibers (11).

Stimulation of the left inferior cardiac nerves with a train of electrical pulses of 5 V, which is supramaximal for the myelinated afferent nerve fibers, caused tachypnea. The magnitude of tachypnea was increased with electrical pulses of 20 V, which is supramaximal for the unmyelinated afferent fibers (7, 8); however, no obvious difference in modality of respiratory changes was produced. This result indicates participation of both myelinated and unmyelinated afferent fibers in tachypnea.

A rise in systemic blood pressure was produced by chemical and electrical stimulation of afferent cardiac sympathetic nerve fibers. Vasopressor action of the afferent cardiac sympathetic nerve fibers has been demonstrated by several workers (1, 6, 9). In three potassium chloride experiments, a transient fall preceded the rise in pressure. Since extension of the limbs occurred simultaneously with the fall, the fall in pressure may have been secondary to somatic reflexes (9). Tachypnea preceded or tended to precede the rise in blood pressure. This difference in latency may have been due to the difference in conduction time of the reflex arcs and the difference in response time of the target organs.

Carotid chemoreceptors and aortic chemoreceptors with their pathways in the vagi cause reflex hyperpnea (deep and rapid respiration) (2, 5, 14). A certain group of pulmonary receptors with their pathways in the vagi cause apnea when stimulated by veratrum alkaloids but cause tachypnea when stimulated by trichlorethylene (3, 4, 5, 13). Afferent cardiac sympathetic nerve fibers always caused tachypnea in this study, irrespective of the character of the stimuli. Therefore, it can be concluded that afferent cardiac sympathetic nerve fibers have a role in the regulation of respiration that is different from those of the carotid, aortic, and pulmonary chemoreceptors.

It is well known that tachypnea occurs in patients during an attack of angina pectoris. It has been generally considered that tachypnea in these patients is due to acutely induced congestive heart failure. However, the results in this study suggest participation of afferent cardiac sympathetic nerve fibers in the clinically observed respiratory changes.

Received for publication 5 August 1975.

REFERENCES


