Control by the Superior Cervical Ganglion of the State of Contraction and Pulsatile Expansion of the Carotid Sinus Arterial Wall

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The state of contraction and resistance to stretch of the arterial wall of the carotid sinus modulates sensitivity of pressoreceptors to intra-arterial pressure. Experiments show that electric stimulation of efferent sympathetic pathways to the carotid sinus leads to blood pressure fall and decrease of the carotid sinus hypertensive reflex. This effect can be prevented by local application of Regitine to the carotid sinus. These experiments suggest that the state of contraction and resistance to stretch of the barosensitive arterial walls is controlled by sympathetic innervation through local release of norepinephrine and/or epinephrine. Disturbances of this innervation could have a role in development of abnormal relaxation and decreased pulsatile expansion of the barosensitive arterial walls, and, thus, in the pathogenesis of hypertension.

BLOOD PRESSURE is determined largely by a balance between physiologically high central vasomotor and cardiac accelerator outflow and constant, inhibition of this outflow by the buffer or moderator nerves. This regulation or inhibitory action depends, in turn, upon stimulation of pressoreceptors by the intra-arterial pressure itself. Hauss and associates proved the concept that pressoreceptors are stimulated by stretching or pulsatile expansion of the arterial wall. Heymans and co-workers further showed that the state of contraction or resistance to stretch of the barosensitive arterial walls modulates the sensitivity of the receptors to intra-arterial pressure changes. Increased state of contraction and resistance to stretch leads to increased stimulation of pressoreceptors, and, thus, to increased inhibition of central sympathetic outflow. Blood pressure decreases and the blood pressure elevation caused by clamping of the common carotid arteries is lessened. On the other hand, relaxed barosensitive arterial walls and decreased resistance to stretch shifts the balance so that blood pressure is increased and the response to common carotid occlusion is exaggerated. This important new concept of blood pressure regulation was confirmed by Landgren and associates, and by Witzel, who recorded action potentials of the carotid sinus nerves during different states of contraction of the barosensitive arterial walls.

Heymans further suggested that epinephrine and norepinephrine may be normally present in the walls of large arteries and, by regulating intrinsic tone and resistance to stretch of the barosensitive arteries, have a part in the reflex homeostasis of blood pressure.

The large arterial walls are innervated by the sympathetic nervous system. The carotid sinus has an especially strong innervation originating in the superior cervical ganglion. The sympathetic fibers divide and terminate partly around the cells of the carotid body and partly in the arterial wall of the carotid sinus. The structure of the carotid body shows two different cell-groups: chromaffin and nonchromaffin. Developmental studies of Boyd and Watzka revealed that the cells are partly mesenchymal and partly neurogenic in origin. Sympathetic and parasympathetic fibers advance during development into a mesenchymal cell-group which originates from the adventitia of the internal carotid artery and is in close connection with the arterial wall. From sympathetic nerves, chromaffin cells develop, and from parasympathetic nerves, nonchromaffin cells develop. Chromaffin cells can be found not
only in the carotid and aortic bodies but along sympathetic fibers as far as the media of the barosensitive arterial walls, as was shown in some animals by Palme, 8 and Watzka. 9 These findings suggest that the sympathetic innervation of the carotid sinus might play a role in the control of the state of contraction of the carotid sinus wall.

The function of the sympathetic innervation of the carotid sinus was investigated by Palme who found that electrical stimulation of one isolated superior cervical ganglion, with connection to the carotid sinus only, leads to blood pressure fall. Further, previous unilateral disruption of the sympathetic innervation results in exaggerated blood pressure elevation to common carotid occlusion on the denervated side. 8 Palme explained these results through possible influence of the sympathetic innervation on the pressoreceptors by means of epinephrine release which would increase the sensitivity of the receptors directly. Floyd and Neil, however, found that efferent sympathetic stimulation affects only the chemoreceptor action potentials which increase during sympathetic stimulation. 10 Further, blood pressure decrease in the femoral artery following increase of pressure in the isolated carotid sinus is not changed during stimulation of efferent sympathetic fibers.

To establish the role of sympathetic innervation in the control of the state of contraction of the carotid sinus, experiments were carried out that alter activity in the sympathetic innervation of both carotid sinuses simultaneously.

**METHOD**

Both carotid sinuses were isolated and the vago-aortic nerves were cut in dogs anesthetized with sodium pentobarbital (25 mg. per kilogram of body weight). In one group of dogs the superior cervical ganglia were cautiously freed on both sides and their connections, except to the carotid sinus, were cut. In another group, the efferent sympathetic fibers to the carotid sinus were isolated and their connection to the ganglion disrupted centrally. In the first group of dogs the ganglia, in the second group the efferent sympathetic fibers, were put on fine shielded electrodes. Care was taken to prevent spreading of electrical current to other nerves, especially to the carotid sinus nerves. Systemic blood pressure was registered from a femoral artery by a mercury manometer and recorded on a smoked drum.

The response of the systemic blood pressure to occlusion of both common carotid arteries was tested. Next, the sympathetic ganglia, or efferent sympathetic fibers, were stimulated bilaterally by an electronic stimulator producing a low-frequency current of 10 to 60 cycles per minute and an intensity of 1 to 5 volts. The stimulation lasted three to five minutes with constant or increasing intensity. During the stimulation, clamping of the common carotid arteries was repeated once or twice. Five to 10 minutes after the end of the stimulation the occlusion test was repeated. In eight experiments 10 to 20 micrograms of Regitine in 0.5 to 1 ml. physiologic saline was injected in the adventitial and periadventitial tissue of the carotid sinus. A few minutes later electrical stimulation and occlusion of the common carotid arteries were repeated.

**RESULTS**

Clamping of the common carotid arteries caused the usual elevation of systemic blood pressure (figs. 1, and 3, !1 and !2). Bilateral stimulation of the superior cervical ganglion, isolated except for its connection to the carotid sinus, or stimulation of the efferent sympathetic fibers to the carotid sinus, resulted in gradual decline of systemic blood pressure in 10 of 12 experiments (fig. 1, !3). The maximal blood pressure fall, caused by stimulation with an intensity approximately twice the rheobase, was from 40 to 50 mm. Hg of mean pressure. The lowest level was reached about three

![Fig. 1. Femoral arterial blood pressure. A: !1 - !2: clamping and unclamping of common carotid arteries. B: stimulation of both isolated superior cervical ganglia with connection to the carotid sinus only. !3: beginning of stimulation. !4 - !5: clamping and unclamping of common carotid arteries. C: 10 minutes after the end of stimulation blood pressure is back to the starting level and clamping (!6) and unclamping (!7) of common carotid arteries are again effective.](http://circres.ahajournals.org/)

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FIG. 2. Same dog as in figure 1. A: 5 minutes after local application of 20 micrograms Regitine to both carotid sinuses. 1-2: clamping and unclamping of common carotid arteries. B: stimulation of both isolated superior cervical ganglia by the same frequency and intensity as before Regitine application. 3: beginning of stimulation. 4-5: clamping and unclamping of common carotid arteries during stimulation. 6: 20 minutes after Regitine application stimulation of sympathetic ganglia decreases blood pressure. 7-8: clamping and unclamping of common carotid arteries during third minute of stimulation. 9: section of both carotid sinus nerves during stimulation.

minutes after beginning stimulation. Following the end of stimulation the blood pressure rose gradually to its former level.

Lowering the intra-arterial pressure by clamping the common carotid arteries resulted in decreased or no reflex blood pressure eleva-

Fig. 3. Femoral arterial blood pressure. A: 1-2: clamping and unclamping of common carotid arteries. Between A and B: Stimulation of both isolated superior cervical ganglia with connection to the carotid sinus only. 3-4: clamping and unclamping of common carotid arteries during third minute of stimulation. C: 4 minutes after the end of stimulation clamping (15) and unclamping (16) of common carotid arteries still less effective.

tion when performed during the lowest blood pressure level (fig. 1, 4 and 5, fig. 3, 3 and 4). These carotid sinus hypertensive reflexes were still decreased three to five minutes after cessation of stimulation (fig. 3, 5 and 6).

Some 15 to 20 minutes after stimulation, when blood pressure had again reached the starting level, the adventitial and periadventitial tissue of the carotid sinuses was infiltrated with 10 to 20 micrograms Regitine in 0.5 to 1.0 ml. physiologic saline. Following infiltration, blood pressure gradually increased above the original level. If the efferent sympathetic fibers or the isolated superior cervical ganglia were stimulated by the same frequency and intensity current as in the control test 5 to 10 minutes after the Regitine application, no blood pressure fall occurred in seven of eight experiments (figs. 2, and 4, 13).* In these seven, clamping the common carotid arteries during stimulation caused the same rise in systemic pressure as during control tests (fig. 2, and 4, 14, and 15). Direct stimulation of one carotid sinus nerve, however, resulted in sudden and marked blood pressure fall and bradycardia (fig. 4, 16).

* In one experiment the blood pressure decreased and the carotid sinus hypertensive reflex was lessened following sympathetic stimulation even after repeated Regitine application, although the effect was not as marked as in the control test.
The carotid sinus nerves were consequently intact.

The effect of Regitine lasted 15 to 20 minutes. Toward the end of this period, electrical stimulation of the sympathetic efferent pathways gradually became more effective, as shown in figure 2 (C: |0 and |7). However, disruption of both carotid sinus nerves in this phase of the experiment resulted in sudden and marked blood pressure elevation (fig. 2, |8).

**Discussion**

These experiments provide evidence that the sympathetic innervation of the carotid sinus participates in the reflex homeostasis of blood pressure. It was shown by Heymans and associates that local application of epinephrine and norepinephrine to the carotid sinus, which increases the state of contraction and resistance to stretch of the arterial wall, leads to increased stimulation of the pressoreceptors.2 Electrical stimulation of most sympathetic fibers causes release of norepinephrine at the nerve endings. However, stimulation of sympathetic fibers to chromafrin tissue is known to cause epinephrine release. Since chromaffin tissue is present in the carotid body and probably in the adventitia of the carotid sinus, epinephrine probably participates in the effect of stimulation on the carotid arterial wall.

Regitine is a sympatholytic drug. Thus, following Regitine block, electrical stimulation of the sympathetic fibers to the carotid sinus elicits no change in either systemic blood pressure or the carotid sinus hypertensive reflex. Direct stimulation of the carotid sinus nerves, however, results in a prompt and abrupt blood pressure fall, proving that the gradual blood pressure fall following sympathetic stimulation was not caused by spread of electrical impulses to the carotid sinus nerves. If such spread had existed, it would not be altered by Regitine.

It is likely that under normal conditions the state of contraction of the carotid sinus wall is relatively constant. However, the role of pathologically disturbed sympathetic innervation in development of abnormal relaxation and decreased pulsatile expansion of the carotid sinus arterial wall deserves further and intensive study. This may be a factor in essential hypertension.

**Summary**

Continuous electrical stimulation of the isolated sympathetic fibers, or superior cervical ganglia, with connection to the carotid sinuses only, leads to gradual decrease of systemic blood pressure and to decrease of the carotid sinus hypertensive reflex. Blood pressure and carotid sinus hypertensive reflexes return gradually to the control level after cessation of stimulation.

Infiltration of the adventitial and periadventitial tissue of the carotid sinuses with small amounts of Regitine prevents the effect of sympathetic nerve stimulation on blood pressure and carotid sinus hypertensive reflex.

The effect of stimulation of efferent sympathetic fibers to the carotid sinus probably occurs by means of norepinephrine release at the nerve endings in the arterial wall and/or epinephrine release from chromaffin cells of the carotid body, which increases the state of contraction of the barosensitive arterial wall, as suggested by Heymans and associates.

It is suggested that the superior cervical ganglion controls, at least partially, the state of contraction of the carotid sinus arterial wall and thus has a role in the reflex homeostasis of blood pressure. Disturbances of this innervation could have a role in the development of abnormal relaxation and decreased pulsatile expansion of the carotid sinus, and thus participate in the pathogenesis of hypertension.

**References**

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