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THE CAROTID SINUS—ITS CONTROLLING INFLUENCE ON THE CIRCULATION AND RESPIRATION*

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THE functional importance of the carotid sinus has been recognized since the discoveries of Hering. It is known to govern reflexly a number of respiratory and circulatory phenomena.

The carotid sinus has been admirably studied anatomically by Castro. The anatomical arrangement may be seen from the diagram in Figure 1. The intercarotid nerve terminates as (1) nerve endings, which Castro calls the "glomus caroticum," and which is commonly, though incorrectly, called the "carotid ganglion," and (2) sensory fibers in the bulb of the internal carotid and the entire region of the carotid bifurcations.

When reunited, these two groups of fibers form the nerve of Hering, which then joins the glosso-pharyngeal. Certain nerve fibers, which join the vagus ganglion instead of the glosso-pharyngeal, have been omitted from the diagram. The carotid nerve, or nerve of Hering, therefore, possesses two regions of peripheral perception: one in the arterial walls of the carotid bifurcation, and the other in the glomus caroticum (carotid ganglion). The so-called carotid ganglion is essentially composed of sensory nerve endings and not, as its name would imply, of a relay synapse.

The researches of Hering, C. Heymans, Koch, and their collaborators have demonstrated the part played by variations of the intrasinus pressure in the regulation of the general blood pressure. A hypertension in this region produces a general somatic hypotension with bradycardia, while a reduction of the intracarotid pressure results in general hypertension by means of peripheral vasoconstriction, and in tachycardia. Hering has shown that occlusion of the two common carotids causes a great increase in pulse rate and a marked rise of arterial pressure. On the other hand, when the carotids are reopened and the blood-flow through them is increased, the heart is markedly slowed and the arterial pressure returns to the normal level.

Denervation of the carotid sinus, together with section of the depressor nerves of Cyon, which possess a similar action, produces most of the phenomena of intrasinus hypotension and results in prolonged arterial hypertension. The increase in blood pressure persists as long as the carotids remain closed. The blood pressure returns to its original level only when the carotids are again opened. Tachycardia is marked during the hypertension and groups of extra systoles are common.

The peripheral vasoconstriction may be revealed in different ways. The simplest method of demonstrating it is by means of a spleen oncometer, and noting the changes in volume which follow occlusion of the carotid arteries. When the carotids are closed, the spleen contracts markedly in spite of the increase in blood pressure. The splenic volume returns to the original when the carotids are opened and the general blood pressure falls to its initial level.

The terminations of the nerve of Hering in the sinus are extremely sensitive to pressure. This can be demonstrated by varying the pressure on a fluid bathing the endings of the nerve, and noting changes in the blood pressure recorded from the femoral artery. An increase in sinus pressure causes a fall of blood pressure, and a decrease in sinus pressure is followed immediately by a marked rise in blood pressure.

If now, instead of reducing the pressure inside the sinus, the two carotid sinuses are denervated by section of both the nerves of Hering, the general blood pressure rises instantly. Under these conditions the animal becomes definitely hypertensive (Koch). Similar results can be obtained in animals which have recovered from the operation for denervation. If, in addition, the depressor nerves are severed in such animals, the general arterial pressure remains elevated afterward. At the same time the heart rate is accelerated, sometimes attaining a rate of 250 per minute.

Therefore, it may be concluded that in the terminations of the nerves of Cyon and of Hering there

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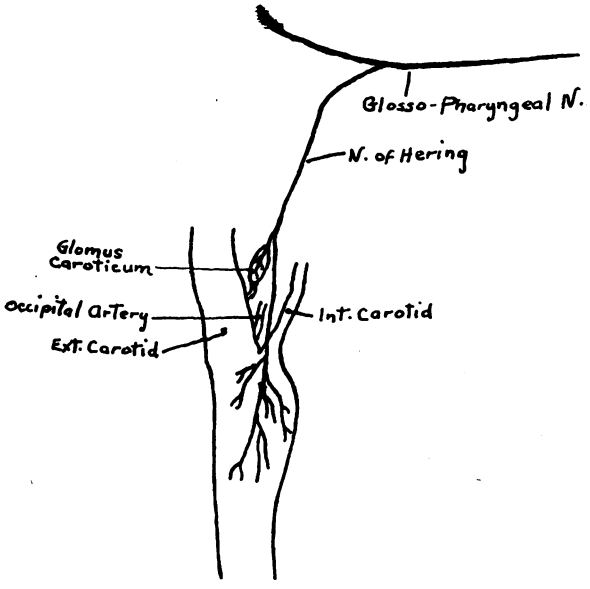

Fig. 1.—Diagram of carotid sinus and innervation.

are areas which constantly control the general blood pressure. Section of these nerves removes the depressor control, and puts the organism in a state of chronic hypertension and of definite tachycardia.

Not only are the blood pressure, the vasomotor center, and the cardiomoderator center affected by every change of pressure within the sinus, but the respiratory center is also affected. The respiration is increased, both in amplitude and in frequency, simultaneously with the increase in the general blood pressure. Section of the nerves of Cyon and denervation of the carotid sinuses appear equally important for abolishing a permanent inhibitory influence on the respiratory center by removing the depressor tonus of the sensitive areas. For, after section of these nerves, the respiration increases considerably in rate and amplitude. Hence, modifications of the intrasinus pressure may lead to profound changes in the pulmonary ventilation. Occlusion of the carotid arteries provokes a reduction of the intrasinus pressure and so causes a marked increase in the pulmonary ventilation, which disappears when the carotids are again opened. On the other hand, after denervating the sinus, modifications of pressure in the sinus have no effect on the pulmonary ventilation. These responses of the pulmonary ventilation to variations in the intrasinus pressure naturally cause parallel changes in the exhaled carbon dioxid. Typical results may be seen in Table 1.

TABLE 1.—*Dog Anesthetized with Chloralosane*

	Air Exhaled in Five Minutes	CO_2 Per Minute
Normal	30.5 L.	129
Carotids closed	49.8	173
Normal	40.7	122
Carotids closed	52.3	177

TABLE 2.—*Dog Anesthetized with Chloralosane*

		CO_2 Vols. Per Cent
10.19′ 30″	Blood from right femoral artery	43.6
10.31′	Both common carotids closed	
10.46′	Blood from right femoral artery	38.6
10.50′ 05″	Carotids reopened	
10.50′ 10″	Blood from right femoral artery	42.4

Necessarily, also, the changes in ventilation produce modifications in the carbon dioxid tension of the arterial blood. This is illustrated by results in Table 2.

After these matters were settled, we investigated, at first with Heymans and Bouckaert in Ghent, and later in my laboratory in Liège, the actions of different drugs which are known to stimulate the respiratory center, but especially sodium sulphid, potassium cyanid, nicotin, lobelin, hordenin, hexetone, and carbaminocholin.

Extremely small doses (1/1000 to 1/10,000 milligram) of these substances injected into the common carotid artery may produce an enormous hyperventilation, while the same doses injected into the internal carotid artery beyond the sinuses, *i. e.*, directly toward the brain, do not have the slightest action. In fact, large doses of these substances injected in this way have a tendency to produce a depressant action.

On the other hand, if the opposite carotid artery is denervated in the same animal, and the injection of drugs into this denervated carotid is repeated, there is no increase in respiration. Exactly the same results are obtained in unanesthetized dogs, with and without denervated sinuses.

These chemical substances also have an action on the heart rate and on the vasomotor center, effects which are likewise essentially reflex in origin. Injection into the common carotid artery of any of these substances, namely, cyanid, sulphid, lobelin, nicotin, hordenin, and carbaminocholin, produces a bradycardia up to cardiac arrest, while the arterial blood pressure rises. The same substances injected into the denervated carotid artery or vertebral artery, or into the internal carotid beyond the sinus, no longer slow the heart or raise the arterial pressure.

Therefore, it can be said that there exists, at the carotid sinus, a sensitiveness devoted to the perception of changes in blood pressure and to chemical changes in the fluid which bathes this organ.

The vasomotor system is sensitive, through the carotid sinus, not only to drugs but also to one of the most important physiological substances, namely, carbon dioxid. It is known from the work of Severini that carbon dioxid acts locally as a powerful vasodilator. But if it is administered through the lungs, after the vagi are severed, it acts as a stimulant of the vasomotor center. This stimulating action of carbon dioxid can be seen

even when both carotid arteries are occluded, that is, when the arterial pressure is elevated. This can be demonstrated by giving carbon dioxid at the plateau of hypertension, when the blood pressure rises still higher. However, in dogs with the nerves of Hering cut, that is, in chronic hypertension, the inhalation of carbon dioxid is always followed by a sudden and considerable fall of blood pressure.

Consequently, it seemed to me that the current explanation of the action of carbon dioxid on the vasomotor center might not be correct, and that the rise of pressure obtained by inhalation of carbon dioxid might be due to a chemical action through the carotid sinus. In other words, carbon dioxid might act on the vasomotor center reflexly, and not directly, as is currently believed.

In order to test this theory, it was necessary to arrange an experiment in which carbon dioxid was prevented from coming in contact with the carotid sinus during the time it was acting everywhere in the body and especially on the vasomotor center itself. Using the technique of Moisejeff, I closed all the arteries from the carotid sinus (internal carotid, external carotid, occipital and pharyngeal arteries), and left unchanged the nerves of Hering. Under these conditions, the sinuses were isolated and blood could not reach them through the circle of Willis, although they remained sensitive to changes of pressure. Then, at the crest of hypertension, the animal was made to inhale carbon dioxid, and there was obtained a fall of pressure absolutely identical with the fall after the nerves of Hering were cut, instead of a rise of pressure as under normal conditions.

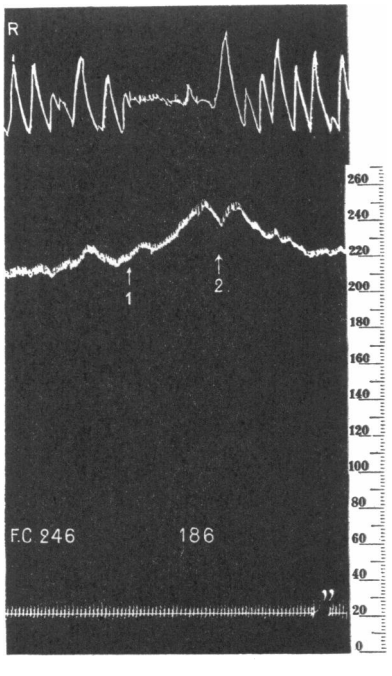

Fig. 2.—Dog, hypertensive for nine months. From 1 to 2, inhalation of twenty drops of amyl nitrite through the nose. At top, respiratory record; below, blood pressure record. F.C., heart rate.

Therefore, it may be concluded that carbon dioxid does not act on the vasomotor center directly, but acts chemically as a reflex stimulant through the carotid sinus.

Very interesting are some results which I have obtained with drugs in chronic experimental hypertension. These results were obtained on three dogs, with the nerves of Hering and Cyon cut and blood pressures for six months of 190, 200, and 220 millimeters of mercury, respectively. The dogs were healthy, and trained to lie quietly for hours for use in the experiments. Their arterial pressures were estimated once weekly by introducing a large needle into the femoral artery, without anesthesia. The drugs tested were chloral hydrate, papaverin, nitroglycerin, and sodium nitrite. The results were entirely negative. Neither papaverin (100 milligrams daily), chloral hydrate (1 to 3 grams daily), nitroglycerin (10 drops daily), nor sodium nitrite (200 to 500 milligrams daily) produced the slightest fall of pressure in these three dogs. Moreover, one of the most common drugs used in treating hypertension, namely, amyl nitrite, always showed the opposite effect in more than three hundred unanesthetized dogs. That is, amyl nitrite always caused a rise of blood pressure under the conditions (Fig. 2). This rise of pressure was also due to a reflex action, as the result of stimulation of the fifth nerve in the nose.

Thus, if the results on unanesthetized dogs are applicable to man, it may be concluded that amyl nitrite causes hypertension, and that none of several chemical substances tried appears to have any demonstrable effect on chronic hypertension under these conditions.

CONCLUSIONS

From these different results, and from others which I have not discussed here, it would appear that the region of the carotid sinus, the anatomical existence of which was ignored only a few years ago, is of great importance, not only for the physiological regulation of respiration, but also for that of the circulation. Rhythm and amplitude of respiration, pulmonary ventilation, elimination of carbon dioxid, and the responses to many chemical substances are subordinate to it, as also are the regulation of the blood pressure, and, to a great extent, the depth and rate of systole. On it depends also the distribution of blood to the muscles and the viscera, through effects on peripheral vasomotor states.

These facts, briefly stated, show that in the carotid sinus there is an organ essential for normal and pathological regulation of two of the most important functions in the body, namely, respiration and circulation. They illustrate, also, the importance of physiological and pharmacological studies, which, if properly applied, may be of value in clinical work.

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