Quantitative Studies in Man of the Cardiovascular Effects of Reflex Vagal Stimulation Produced by Carotid Sinus Pressure

I. Localization of an Increased Effect in a Patient with Angina Pectoris

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with the technical assistance of Virginia Marcus, B.S.

In a two year period the effect of carotid sinus pressure on auriculoventricular conduction in a 70 year old man with angina pectoris increased markedly. At first, right carotid sinus pressure gave only P-R interval prolongation. Two years later, pressure on either side produced dropped beats. The maximum effect on the sinoauricular rate remained the same. No other change could be detected in the patient's heart during this period. The site of the cause of the increased vagal effect was either in the intrinsic cardiac nerves to the atrioventricular node or in the node itself.

MARKED cardiac effects due to reflex vagal stimulation are frequently observed following carotid sinus pressure in patients with various diseases, especially coronary artery disease. However, the segment of the reflex arc responsible for hyperactivity of the reflex has not previously been demonstrated, except in the occasional case showing a lesion in the neck near the carotid sinus.

Repeated studies of the carotid sinus reflex over a two year period in a patient with angina pectoris, particularly suitable for such studies, indicated that the site of an increased vagal effect was in the heart; either in the auriculoventricular node or in the intrinsic cardiac nerves to that node. Initially, right carotid sinus pressure had no effect on the auriculoventricular node, whereas left carotid sinus pressure produced P-R interval prolongation; two years later pressure on either side produced dropped beats. During the entire period of observation, the maximum effect on the sinoauricular rate from pressure on either side remained the same.

The presentation and analysis of our observations in this patient form the basis of the present report.

Observations

The patient, N. S. (BIH #17498), a 70 year old man (in 1948), had been known to have attacks of angina pectoris for about 10 years. These attacks were usually precipitated by exertion and were characterized by a squeezing substernal pain radiating down the left arm, relieved by nitroglycerin and by rest. Similar attacks could be brought on readily by a two step exercise test.

The detailed observations reported here were made on six days during a three month period (April to June) in 1948 and on six days during a three month period (June to August) in 1950. With the patient in a sitting position, a continuous electrocardiogram (lead II) was taken immediately before, during and immediately after the application of pressure to either the right or the left carotid sinus. Pressure was applied 24 times in 1948, 11 on the right and 13 on the left; 54 times in 1950, 32 on the right and 22 on the left. At least three or four minutes were allowed to elapse between successive pressure tests on the same day; this interval has been found to be well beyond the time required for the electrocardiographic changes produced by pressure to disappear. In 1948 each pressure was applied for about five seconds; in 1950 for exactly

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three seconds. In 1948 the observer stood behind the patient and, with his fingers over the site of the maximum pulsation, massaged the neck and the carotid sinus vigorously toward the vertebral column. In 1950 manual pressure was applied similarly in some instances; in other instances a measured-pressure device which will be described elsewhere was used. The manual pressures in 1948 and 1950 were of approximately the same intensity; the measured pressures in 1950 varied over a wide range, generally being less intense than the manual ones.

Each P-R interval of the electrocardiogram was paired with the preceding P-P interval; both intervals were measured to the nearest 0.01 second. Five to ten successive P-P intervals immediately before each pressure, varying usually by no more than 0.03 second, and the corresponding P-R intervals, usually showing no variation, were used as controls to determine the changes produced by that pressure. For the purposes of this report only maximum changes in P-P and P-R intervals are considered. Data not included here indicated that the greatest P-R interval prolongation before the occurrence of dropped beats in this patient was 0.10 second. Further increase in this effect could not be measured; dropped beats, therefore, have been grouped as indicating the maximum increase in auriculoventricular conduction time.

On several occasions the patient noted mild, very transient dizziness in association with carotid sinus pressure. This occurred particularly in 1950 when slowing of the sinoauricular rate together with a dropped beat sometimes produced ventricular asystole for as long as three seconds. He gave no his-

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<th>TABLE 1.—Maximum Effects of Right and Left Carotid Sinus Pressure on the P-P and P-R Intervals</th>
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* Control before pressure.
† Maximum during carotid sinus pressure.
‡ Maximum minus control.
§ Dropped beat.

Results

Table 1 shows the maximum effects of right and left carotid sinus pressure on the rate of impulse formation in the sinoauricular node (change in P-P interval) and on the duration of auriculoventricular conduction (change in P-R interval).

In 1948 right carotid sinus pressure slowed the rate but did not increase auriculoventricular conduction time. Left carotid sinus pressure in 1948 produced prolongation of the P-R interval as well as slowing, although dropped beats
were never observed. In 1950, however, dropped beats were readily produced following either right- or left-sided pressure. The maximum slowing of rate, on the contrary, from pressure on either side remained the same in both years.

**DISCUSSION**

Various factors relevant to the interpretation of these data are considered below. The conclusion is reached that the increased effects of carotid sinus pressure in 1950 as compared to 1948 must have been due to an increased sensitivity to reflex vagal stimulation of the auriculoventricular node or of the postganglionic fibers to that node.

There was no variation in the intensity of the pressure in the two periods to account for the increased effect. The maximum pressure applied in 1950 was of about the same intensity as in 1948. The fact that the maximum effect on the rate was the same in both years confirms the fact that the intensity of maximum vagal stimulation reaching the heart from right and left carotid sinus pressure remained the same.

Since the change in our patient between 1948 and 1950 involved only the auriculoventricular node, it was undoubtedly not related to a difference in sympathetic inhibition accompanying the reflex vagal stimulation. Variations in this mechanism would be expected to affect the sinoauricular node as well as the auriculoventricular node.

Local alteration in either one or both carotid sinususes can similarly be excluded because the increased effect involved only the auriculoventricular node and not the sinoauricular node.

It is likewise clear that slowing of the sinoauricular rate had no causal relation to the increase in auriculoventricular conduction time. The lack of correlation between the P-P and the P-R intervals has been described by Schlamowitz.\(^8\) Our observations confirm this; following right-sided pressure in 1948, with P-P intervals ranging from 0.78 to 1.42 seconds, the length of the P-R interval was constant at 0.15 second.

The possibility of crossing of stimuli from either right or left carotid sinus can be excluded as a factor in the increased vagal effect in this patient. The data obtained in 1948 indicate that there was no significant crossing of stimuli to the auriculoventricular node from the right to the left. Left-sided pressure produced a marked effect on this node, that is, definite P-R interval prolongation. However, no effect on the P-R interval was produced by right-sided pressure at that time. This indicates that, if any stimuli did cross from right to left, their intensity was below the threshold of the auriculoventricular node. Our data permit no conclusions regarding crossed effects on the rate.

However, even if stimuli of sufficient intensity to affect the sinoauricular node did cross, equally in both stimuli and to the same extent in both periods, the following interpretation of our data is not altered.

On the basis of the above considerations, it must be concluded that the observed increase from 1948 to 1950 in the effects of right and left carotid sinus pressure on the auriculoventricular node were due to alterations in that part of the reflex are common to the two sides: the cardiac postganglionic fibers going to that node, or the node itself.

Localization of the increased effects of carotid sinus pressure on the heart, frequently observed in older individuals, particularly those with evidence of coronary artery disease,\(^1\)\(^2\) has not heretofore been definitely established. Nathanson\(^7\) reasoned that the cause must be somewhere on the efferent side of the reflex arc, because of the variation in the relative magnitude of the cardioinhibitory and vasodepressor effects of carotid sinus pressure from one individual to another. Sigler\(^8\) suggested, without supporting data, that changes in the cardiac ganglia might explain the reflex hyperactivity.

Increases in the cardiac effects of carotid sinus pressure have been described in association with a number of conditions, including exacerbation of angina pectoris,\(^9\) congestive heart failure,\(^10\) acute myocardial infarction,\(^11\)\(^12\) and the administration of several drugs, particularly digitalis glycosides.\(^13\) None of these were involved in our patient, whose clinical condition over the two year period remained unchanged. A number of electrocardiograms taken between 1948 and 1950 were identical and, except for left axis deviation, were within normal limits. The blood pressure ranged between 130/70 and
190/90 with no constant trend. Red blood cell counts, hemoglobin determinations and urine examinations were repeatedly normal, and the Hinton test was negative.

Increased sensitivity as a result of anoxia may offer an explanation of the observations made in our patient. Coronary arteriosclerosis, undoubtedly the cause of his angina pectoris, is associated with diminished blood flow to the heart and localized anoxia. Changes in sensitivity have been seen in nerves subjected to anoxia and, accordingly, in this patient, the threshold of the intrinsic nerves to the auriculoventricular node may have been lowered. Other studies in this patient and in other patients have shown that only a small increase in sensitivity may be required to increase markedly the effect of a given stimulus. It is of interest that degenerative changes have been described, most recently by Hermann, in the intrinsic cardiac ganglions of patients with coronary artery disease.

Similar considerations could apply to the nodal tissue. In this connection it should be noted that the control P-R interval, the same in 1948 and 1950, was within normal limits.

SUMMARY

In a two year period the effect of carotid sinus pressure on auriculoventricular conduction in a 70 year old man with angina pectoris increased markedly. At first, right carotid sinus pressure had no effect, whereas left carotid sinus pressure gave some P-R interval prolongation. Two years later, pressure on either side produced dropped beats. The maximum effect on the sinoauricular rate from pressure on either side remained the same. No other change could be detected in the patient's heart during this period.

The data indicate that the site of the increased vagal effect was either in the intrinsic cardiac nerves to the auriculoventricular node or in the node itself.

ACKNOWLEDGMENT

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