

Carotid Sinus Baroreceptor Control of Arterial Pressure in Renovascular Hypertensive Subjects

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SUMMARY We used the neck chamber technique to study carotid baroreceptor control of blood pressure in 18 renovascular hypertensive subjects. Carotid baroreceptors were stimulated or deactivated for 2 minutes by applying graded reductions or increases in the neck tissue pressure (NTP) outside the carotid sinuses. The sensitivity of the baroreflex was separately calculated for these two conditions by the coefficients of the linear regressions relating the changes in NTP to the resulting changes in mean arterial pressure (MAP, catheter measurement). Baroreceptor deactivation increased MAP, and the sensitivity of the baroreflex was 0.12 ± 0.07 in an early (5 to 15 seconds) and 0.32 ± 0.05 in a late (90 to 120 seconds) phase of the stimulus application. Baroreceptor stimulation reduced MAP, and the baroreflex sensitivity was in this instance 0.66 ± 0.08 and 0.50 ± 0.08 respectively. Both these sensitivities were significantly greater than those obtained for the baroreceptor deactivation. These responses entirely reproduced those of essential hypertensive subjects, but differed from those of normotensive subjects in whom baroreflex sensitivity was greater for carotid baroreceptor deactivation than for stimulation. Our findings indicate that carotid baroreceptor control of blood pressure undergoes a marked resetting in renovascular hypertension. The similarity of the baroreflex between renovascular and essential hypertension suggests a secondary origin of the resetting in man. (Hypertension 4: 47-50, 1982)

KEY WORDS • renovascular hypertension • essential hypertension • neck chamber • carotid baroreflex • arterial baroreflexes • blood pressure • baroreceptor resetting

IN previous studies^{1, 2} we found a major difference in the reflex control of blood pressure (BP) exerted by the carotid sinus baroreceptors in normotensive subjects and in subjects with essential hypertension. In normotensive subjects, the reflex change in BP that followed stimulation of carotid baroreceptors was smaller than the opposite change that follows carotid baroreceptor deactivation, whereas in essential hypertension the reverse was the case.

This phenomenon suggests that: 1) in normotensive subjects the carotid baroreflex has a relatively low threshold and is therefore almost maximally activated at the existing BP levels; and 2) the threshold for the baroreflex activation rises in essential hypertension to such a marked extent that in this condition the baroreflex is slightly rather than markedly engaged by the existing high BP levels. This hypothesis implies that a

pronounced resetting of the carotid baroreceptor control of BP occurs in essential hypertension.¹⁻³

It has often been debated whether the resetting of arterial baroreflexes may be a consequence of essential hypertension, or may precede and initiate it.^{4, 5} Although evidence has favored both possibilities, the data are mostly derived from animal and in vitro studies⁶⁻¹⁰ and not from those in humans.

We investigated carotid sinus baroreceptor control of BP in subjects with renovascular hypertension and compared it with the carotid baroreflex control observed in the previously studied essential hypertensive subjects.¹

Methods

We studied 18 subjects (7 males, 11 females) of different ages (range, 26-63 years; mean, 48.6 years) in whom renovascular hypertension had been diagnosed on the basis of arteriographic visualization of a tight stenosis of either the right or left renal artery, and evidence that the renal arteriovenous renin concentration on the side of the stenosis was at least 50% greater than contralaterally.¹⁰ The patients had no major symptoms and signs of target organ damage

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nor did they have any major disease other than hypertension. They had discontinued antihypertensive drugs at least 3 weeks before the study. Informed consent was obtained.

Carotid sinus baroreceptor control of BP was assessed by the variable pressure neck chamber method, which produces a measurable reduction or increase in the air pressure around the neck, with a resultant increase or reduction in transmural pressure across the carotid sinuses, and consequently a stimulation or a deactivation of the carotid baroreceptors.^{17, 18} The neck chamber used was the same as that used in our previous studies on normotensive and essential hypertensive patients.^{1, 2} This neck chamber reduces or increases the air pressure evenly around the patient's neck, and this change is linearly transmitted to the carotid sinuses in the predictable amount of 64% of the negative, and 86% of the positive, applied pressure. The small variation in these average figures among the different subjects¹⁷ allows us to estimate the loss of pressure occurring through the neck tissues and to calculate more precisely the stimuli imposed on the carotid baroreceptor area. The changes in neck chamber pressure were measured by a strain-gauge transducer connected to the neck chamber interior. In each patient, arterial BP was measured by a femoral artery catheter; mean arterial pressure (MAP) was obtained by electric damping of the pulsatile pressure signal and by integration of the pressure tracing over 10-second periods. Heart rate changes were disregarded in this study, as in previous studies we found them to be mild and transient, in contrast to the BP changes.

The same protocol was followed as in the carotid baroreflex study on normotensive² and essential hypertensive patients.¹ After each patient had been instructed on the use of the neck chamber, he or she lay supine while the arterial catheter was inserted. Twenty minutes later random sequences of four to six different reductions and four to six different increases in neck pressure were applied, each subsequent change starting no less than 4 minutes from the end of the preceding one. Neck pressure changes were applied rapidly (90% of the total change accomplished in less than 1 second) and were maintained constant for 2 minutes, at the end of which period neck pressure was returned to atmospheric level at a rapid rate.

Analysis of the data was identical to that in the previous studies.^{1, 2} Stimuli imposed on the carotid baroreceptors were evaluated by calculating the increases and reductions in neck tissue pressure outside the carotid sinuses (subsequently referred to as neck tissue pressure); these values were obtained by multiplying the measured changes in neck chamber pressure by the known correction factors for the loss of positive and negative pressure occurring through the neck tissues. The reflex BP responses were measured by taking a control value for MAP (the average value of the 30 seconds preceding the change in neck tissue pressure) and comparing it with values measured between 5 and 15 seconds, and during the last 30 seconds, from the beginning of the change in neck tissue pressure. In this

way we assessed separately the early and late (or steady-state) reflex effects that followed a change in carotid baroreceptor activity induced by the neck chamber.^{1, 2} The carotid sinus responsiveness was evaluated by calculating the linear relationship between the alterations in MAP (the reflex responses) and the changes in neck tissue pressure (the baroreceptor stimuli). Separate regressions were obtained for the early and the steady-state responses, and for the responses to increased and reduced neck tissue pressure. For each condition, the slope of the regression was taken to indicate the sensitivity of the baroreflex.

Statistical evaluation of the data was performed by first testing whether individual regression coefficients differed significantly from zero, a condition that was preliminary to use of the regression slopes as a measure of the baroreflex sensitivity. Then the slopes calculated for each subject were averaged to obtain the average slope characterizing the whole group of 18 patients. Separate averages were calculated for the early and steady-state responses, and for responses to reduced and increased neck tissue pressure. Student's *t* test for paired observations was used to compare in each subject the slopes of the early vs steady-state responses and of the responses to increased vs reduced neck tissue pressure. Data from renovascular hypertensive patients were compared with those of essential hypertensive subjects reported in a previous study,¹ by Student's *t* test for nonpaired observations. A *p* value of at least 0.05 was taken as the level of statistical significance; values were expressed as means \pm the standard error of the mean.

Results

The average effects of decreases and increases in neck tissue pressure (carotid baroreceptor stimulation and deactivation) on MAP in the 18 renovascular hypertensive patients are shown in figure 1 and table 1. When neck tissue pressure was reduced, the MAP was reduced and the reduction was significantly greater in the early than steady-state phase. When neck tissue pressure was increased, the MAP was increased and the increase was significantly less in the early than steady-state phase. When the responses to reduction and increase in neck tissue pressure were compared, the reduction responses turned out to be significantly greater both for the early and the steady-state phase.

Table 1 also compares the renovascular hypertensive patients with the essential hypertensive patients of the earlier study in whom the carotid baroreceptor control of BP was investigated in an identical fashion. Age and control MAP of these two groups were not significantly different. The MAP responses were similar in the two groups of patients: both in the early and steady-state, they were greater after reduced than increased neck tissue pressure, and the magnitude of the reflex effects of both maneuvers was slightly but not significantly less in renovascular than essential hypertension.

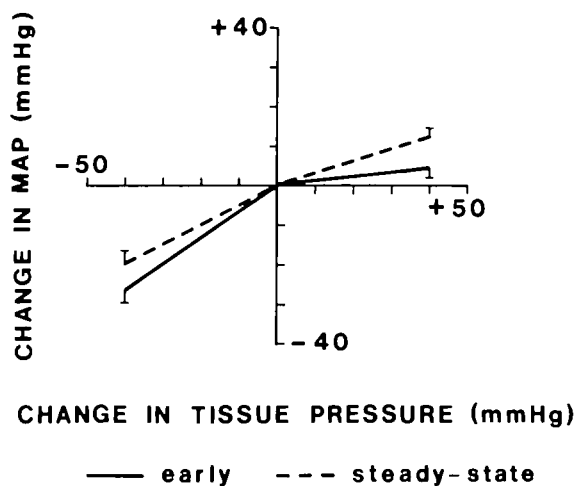


FIGURE 1. Changes in mean arterial pressure (MAP) induced by changes in tissue pressure outside the carotid sinuses (neck tissue pressure). Data are shown as means (\pm SE) of individual regression coefficients for 18 patients with renovascular hypertension. The continuous lines represent the early response and the dashed line the late or steady-state response.

Discussion

The BP changes induced by stimulation and deactivation of the carotid sinus baroreceptors in renovascular hypertensive patients showed clearcut similarities with the changes induced in essential hypertensive patients. The first similarity concerned the time-course of the BP changes. It is clear from our data that these changes decreased from the early to the steady-state phase during carotid baroreceptor stimulation and increased from the early to the steady-state phase during carotid baroreceptor deactivation. It is also clear, however, that these changes occurred

in a similar fashion in the renovascular and essential hypertensive patients and that no difference could be observed between these two pathological conditions.

The second similarity is related to the sensitivity of the carotid sinus baroreceptor control of BP. The reflex BP responses in the renovascular hypertensive patients averaged slightly smaller than those obtained in the essential hypertensive patients (table 1) but the difference was small and not significant. This was the case both for the responses to increased and reduced baroreceptor activity, and for both the early and steady-state stages of baroreceptor manipulation.

The third and perhaps most important similarity is related to the relative magnitude of the pressor and depressor responses. The pressor responses to carotid baroreceptor deactivation were significantly smaller than the depressor responses to carotid baroreceptor stimulation for both the renovascular and essential hypertensive patients. The carotid baroreflex in both types of hypertension drastically differed from that of the normotensive subjects in whom the depressor responses were smaller than the pressor ones.³ This difference is likely to express a marked resetting of the carotid baroreflex, a resetting that seems identical in direction and magnitude for renovascular and essential hypertension as well.

It should be emphasized that this resetting refers to the overall baroreceptor-BP response and that it is impossible from our data to determine which function of the reflex arch is responsible for this phenomenon. The resetting may occur at the level of the baroreceptors themselves,^{6-8, 10-12} but changes at the central level or in the vascular responsiveness to autonomic stimuli may also be involved.

Our study provides information that is relevant to the question whether resetting of the arterial baroreflexes is a secondary phenomenon in hypertension or can only occur as a primary event that precedes the pressure rise.^{4, 5} In this context, our observation that the resetting occurs in a hypertension of renal origin demonstrates that a secondary type of resetting does

TABLE 1. Mean Arterial Pressure Responses to Carotid Baroreceptor Stimulation and Deactivation Induced by Decrease and Increase in Neck Tissue Pressure

Hypertension	Age (yrs)	Control MAP (mm Hg)	Decreased neck tissue pressure			Increased neck tissue pressure			Decreased vs increased neck tissue pressure	
			Early	Steady-state	<i>p</i>	Early	Steady-state	<i>p</i>	Early <i>p</i>	Steady-state <i>p</i>
Renovascular (n = 18)	48.6 \pm 2.6	148.4 \pm 3.9	0.66 \pm 0.08	0.50 \pm 0.08	< 0.01	0.12 \pm 0.07	0.32 < 0.05	< 0.02	< 0.01	< 0.05
Essential (n = 35)	45.4 \pm 1.6	147.7 \pm 3.3	0.78 \pm 0.05	0.56 \pm 0.05	< 0.01	0.12 \pm 0.04	0.38 \pm 0.05	< 0.01	< 0.01	< 0.01
<i>p</i>		NS	NS	NS		NS	NS			

Data from 18 patients with renovascular hypertension in the present study, and from 35 patients with essential hypertension from a previous study.¹ The responses are shown as means \pm SE of individual regression coefficients of changes in mean arterial pressure (mm Hg) on changes in neck tissue pressure (mm Hg). The coefficients are always positive because blood pressure decreased when neck tissue pressure decreased and vice versa. From left to right, the first two columns of *p* values refer to differences between regression coefficients of early vs steady-state changes, and the last two vertical columns to differences between regression coefficients of decreased vs increased neck tissue pressure. The horizontal line of *p* values refer to differences between regression coefficients of renovascular vs essential hypertensive patients.

take place in humans. However, this does not deny the possibility of primary resetting in essential hypertension, as has been suggested by several investigators.^{9, 13, 20, 21} Andresen et al.,¹³ in particular, have demonstrated in spontaneously hypertensive rats with regard to the afferent element of the reflex arch that a resetting of the aortic baroreceptors may take place before any change in the aortic wall can be measured. Thus a primary resetting may indeed occur, although the similarity of baroresetting in essential and renovascular hypertension suggests that in an established form of human hypertension it is the secondary resetting that is likely to predominate.

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