Baroreceptor Resetting During Pressure Recovery from Hypotension

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SUMMARY In a previous study we showed that aortic baroreceptors of rat fully reset to hypotensive levels 48 hours after a single injection of reserpine (2 mg/kg, i.p.). In the present experiments the reversibility of the resetting from hypotension during pressure recovery was analyzed in the same model. Direct mean arterial pressure (MAP) was measured daily in eight conscious unrestrained rats whose MAP varied from 71 to 84 mm Hg 24 to 48 hours after the reserpinization. In these animals the recovery of at least 20 mm Hg (96 to 117 mm Hg) from the lowest hypotensive level took 1 to 4 days. Electroneurographic analysis of the aortic baroreceptors was performed under pentobarbital anesthesia (30 mg/kg i.p.) in treated animals and in a group of 12 normotensive control rats. The anesthesia at the dose employed did not significantly alter the control pressure of conscious treated rats (105 ± 2 before and 92 ± 6 mm Hg after anesthesia). There was no lag between the firing range (threshold pressure of 107 ± 4/74 ± 4 mm Hg; “normal” firing of 131 ± 2/102 ± 3 mm Hg) and the exhibited control pressure (142 ± 2/106 ± 4 mm Hg) of the treated animals. A similar relationship was also observed for the control group (107 ± 4/74 ± 4 and 131 ± 2/102 ± 3 mm Hg, respectively, for the firing range indices and 142 ± 2/106 ± 4 mm Hg for the control pressure).

The data showed that, even when the arterial pressure of treated rats had not completely reverted to normotension, the baroreceptor firing range had an upward displacement very close to that of blood pressure normalization, with no lag between these variables. This indicates that the process of baroreceptor resetting from hypotension is faster than baroreceptor resetting to hypotension, as shown previously for the resetting to and from chronic renal hypertension. (Hypertension 3 (suppl II): II-147–II-150, 1981)

KEY WORDS • reserpine • hypotension • baroreceptor resetting

REVERSAL of baroreceptor resetting from hypertensive levels in the rat is a very rapid process that takes only 6 hours if the arterial pressure is acutely reduced.1 This contrasts with the slower rate observed during the onset of an acute aortic coarctation hypertension when complete resetting is achieved after 48 hours.2,3 The difference in time course of baroreceptor resetting was also observed in dogs by direct4 or indirect methods.5,6 In a previous study,7 we showed that the baroreceptors of the rat were completely reset to operate at hypotensive levels after 48 hours of reserpine-induced hypotension. Thus, the time for resetting to hypotension is similar to that for resetting to hypertension. Since the baroreceptors are completely reset after reserpinization when the arterial pressure is maintained at hypotensive level for at least 2 days, the purpose of the present study was to determine whether there is a reversal of this resetting during the spontaneous recovery of pressure. The baroreceptor firing range of each rat was analyzed 3 to 6 days after a single reserpine injection when the arterial pressure had recovered at least 20 mm Hg.

Material and Methods

Male and female Wistar rats weighing 200–250 g were used. Direct arterial pressure was measured daily in conscious animals with an indwelling catheter (PE-10 connected to PE-50) implanted into the femoral artery and exteriorized through the back under light ether anesthesia. Arterial pressure recordings were made with a multichannel recorder (Hewlett-Packard model 7858A) with a Statham (P23-Dd) strain-gauge transducer.

Baroreceptor Analysis

The method used for determining the baroreceptor firing range has been described.8 Briefly, the whole nerve activity of the aortic baroreceptors was recorded under pentobarbital anesthesia (30 mg/kg i.p.). The firing range of the baroreceptors was measured continuously during controlled bleeding and reinjection of blood through the femoral artery to produce large variations of pressure ranging from hypotension to hypertension. The carotid pressure and baroreceptor

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potentials were displayed simultaneously on a dual beam oscilloscope (Tektronix, 502-A) and photographed. An AC differential preamplifier (Grass, P-15) was used for the electroneurographic recordings. Two indices were used to characterize the firing range of the aortic baroreceptor: 1) threshold pressure (pressure at which the baroreceptors cease firing); 2) "normal" pattern of discharge (highest pressure at which the baroreceptor discharges occur only within the systolic interval of the pulse pressure contour).

Reserpine-Induced Hypotension

Conscious rats previously implanted with an indwelling catheter in the femoral artery had direct mean arterial pressure (MAP) measured daily after a single injection of reserpine (2 mg/kg i.p.). This dose produced maximum reduction in arterial pressure 6 to 9 hours after administration, which was maintained for about 48 hours after reserpinization. During the period of spontaneous recovery from hypotension, the rats that showed an increase of at least 20 mm Hg in MAP were anesthetized with pentobarbital and baroreceptor analysis was carried out.

Statistical Analysis

Results are presented as means ± standard error (SE) of the mean. The unpaired Student t test was used for comparing the data. Changes were considered to be significant for \( p < 0.05 \).

Results

Arterial Pressure Measurements

Direct arterial pressure of eight conscious rats was monitored daily after injection of a single dose (2 mg/kg i.p.) of reserpine until baroreceptor analysis was performed. The lowest level of mean arterial pressure was achieved 1 to 2 days after reserpinization, whereas spontaneous recovery of at least 20 mm Hg was observed from the third to the sixth day.

![Figure 1. Spontaneous recovery of the mean arterial pressure (MAP) of eight conscious rats (solid circles) treated with a single injection of reserpine (2 mg/kg i.p.). Hatched area = normal range defined by the average (mean ± 2 SD) 120 ± 14 mm Hg obtained for 10 conscious rats. Clear area = hypotensive range defined by the average (mean ± 2 SD) 82 ± 2 mm Hg obtained for 21 conscious reserpine-treated rats.](image-url)
Since the resetting process is secondary to pressure change, the fact that no lag was observed between the recovery pressure to normotension and the resetting of the baroreceptors indicates that reversal from hypotension was very fast.

Discussion

Evaluation of the threshold pressure for baroreceptor activation, which is the best single indication of shifts in the range of baroreceptor function, showed that there is no lag between the level of pressure during the reversal to normotension and the upward shift of baroreceptor discharge. These data not only demonstrate that there is a reversal of the resetting from hypotension but also suggest that this process is very rapid and similar to that observed during the reversal from Goldblatt one-kidney, one clip hypertension. When the baroreceptors were studied during the reversal of hypertension, the arterial pressure was lowered suddenly and maintained at normal levels for 6 hours. Since it was not possible to restore the pressure of reserpinized rats rapidly by subdiaphragmatic aortic constriction, we monitored baroreceptor resetting during spontaneous recovery from hypotension. The data obtained 3 to 6 days after reserpine injection, when the sympathetic system could not have returned entirely to normal, it appears that its contribution is not crucial for resetting.

Reversibility of morphological alterations has been correlated with partial or complete reversal of resetting in spontaneously hypertensive rats. However, recent observations from our laboratory (M. Sumitani and E.M. Krieger, unpublished results) indicate that, even though reversal of the baroreceptor firing range was complete after 6 hours of pressure normalization, the aorta exhibited permanent morphological alterations (hypertrophy of the middle layer accompanied by atheromatous plaques) in long-term (6 months) Goldblatt one-kidney, one clip hypertensive rats. On the other hand, since the lowest systolic pressure at which the baroreceptors cease firing is almost the same as the diastolic pressure exhibited by the rats in a conscious state, it seems that below the resting diastolic caliber there is no effective strain of the aortic wall to stimulate the receptors. Furthermore, complete resetting occurs to and from hypertension and to and from hypotension as shown in the present paper when the baroreceptors are again activated by systolic threshold pressures higher than the existing diastolic pressures. All of these observations emphasize the importance of alterations in diastolic caliber that follow permanent changes in the level of distending pressure of the aorta until a new state of equilibrium is achieved.

Regarding the validity of the method of whole nerve recording used in this study, it is well to remember that Sleight et al. have compared it with single-fiber recording in chronic renal hypertensive dogs and found no differences in the information they provided for the analysis of baroreceptor resetting.

The fact that no appreciable lag was observed between the recovery of arterial pressure and the displacement of the baroreceptor firing range might have
important physiological implications since the baroreceptors will not oppose the mechanisms trying to normalize the arterial pressure after the subject has been submitted to a sustained period of hypotension. Similarly, the rapid recovery of baroreceptor resetting from hypertension\(^1\) can be very useful, since overactivity of the sympathetic nervous system promoted by the baroreceptors will only counteract the normalization of arterial pressure during the first few hours.\(^{11}\)

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**References**

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