Rapid Resetting of the Baroreceptors in Renal Hypertensive Rats

Edson D. Moreira, Fumio Ida, Vera Lucia L. Oliveira, and Eduardo M. Krieger

The characteristics and extent of rapid or acute resetting of the aortic baroreceptors were studied in long-term renal hypertensive rats during 30 minutes of sustained hypertension produced by phenylephrine infusion. The aortic baroreceptors of hypertensive rats exhibited complete resetting to hypertension because during the control period the systolic threshold pressure for activation of the baroreceptors was similar (137±5 vs. 142±4 mm Hg) to the control diastolic pressure. Five minutes after onset of hypertension, a resetting of 32% (percent change of mean pressure threshold divided by total change of mean pressure) was demonstrable. The extent of resetting was 39%, 38%, and 41% after 10, 20, and 30 minutes of hypertension, respectively. When the percent change of systolic threshold pressure divided by total change of control diastolic pressure was used to calculate the extent of resetting, similar results were obtained. The extent of displacement of the entire baroreceptor pressure-response curves was similar to that of pressure thresholds. Reversibility of the resetting process was not complete within 30 minutes of pressure normalization after the administration of phenylephrine was interrupted. These data indicate that the characteristics and extent of rapid resetting of the baroreceptors of renal hypertensive rats, which were reset to operate at hypertensive levels, are similar to those previously described in normotensive rats. (Hypertension 1990;15(suppl I):I-40–I-44)
when submitted to a short-lasting increase in pressure. The present experiments were undertaken to study the characteristics and extent of rapid resetting within the first 30 minutes of hypertension produced by phenylephrine infusion in long-term renal hypertensive rats.

Methods

Long-term (2 months) one-kidney, one clip, male renal hypertensive rats (RHR) (n=16) weighing 200–250 g were used. The procedure for recording whole nerve activity of the aortic baroreceptors in rats anesthetized by pentobarbital anesthesia (30 mg/kg) was similar to that used in previous studies.4,10 The pressure threshold at which the aortic baroreceptors initiated firing and the pressure-nerve activity relations changed from low to high pressure levels was measured during rapid (10–15 seconds) changes of pressure produced by withdrawal and infusion of blood into the femoral artery. Arterial pressure (carotid artery) and baroreceptor activity were continuously monitored on an oscilloscope (5115 Tektronix Storage Oscilloscope, London, England) and recorded on a tape recorder (3960 Hewlett-Packard, Hewlett-Packard Co., Atlanta, Georgia) for analysis. The data presented are the average of two or three consistent measurements made during each experimental situation. To quantify the whole nerve activity, the nerve traffic was amplified, full wave rectified, and integrated with a time constant of 3.9 msec. (The electronic circuit was built by the Division of Bioengineering of the Heart Institute, Faculty of Medicine, University of São Paulo, São Paulo, Brazil.) The integrator output provided the averaged nerve activities used to study the pressure-nerve activity relation on a beat-to-beat basis (by computer, 120 Hz). To permit comparison of results in different rats, the baroreceptor discharges were normalized (percent of the maximal discharge at higher pressure). Changes in the position of the electrodes during long recording sessions can alter the stability of the pressure-nerve activity relation but not the pressure-threshold values for activation of the baroreceptors, as shown in previous studies.10 Thus, the pressure-nerve activity relation was analyzed in only eight of 16 rats in which displacement of the pressure thresholds was studied.

To calculate the extent of resetting, the ratio of mean threshold pressure changes divided by total mean pressure changes (ΔMAPth/ΔMAP×100) was used as suggested by Munch et al9 with an in vitro preparation of the aortic arch of rats. Additionally, the ratio of systolic threshold pressure changes divided by total control diastolic pressure changes (ΔSth/ΔCDP×100) was used. The latter criterion was chosen because in previous studies we observed that an exact coincidence exists between Sth that initiates baroreceptor firing and CDP of conscious rats. Also, whenever pressure is constantly changed to hyper- or hypotensive levels, complete resetting occurs when baroreceptors again begin to fire at Sth similar to the new CDP.3 Direct arterial pressure was measured in freely moving rats by means of a plastic cannula inserted into the abdominal aorta through the femoral artery under ether anesthesia 1 day before the acute experiment. The cannula emerged through the back of the rat and was connected to a strain-gauge transducer (P23Db, Gould-Statham, Oxnard, California) from which the signals were fed into a multichannel recorder (model 7754A, Hewlett-Packard). The level of anesthesia was adjusted to maintain the arterial pressure at the same values existing in conscious rats before recording the first baroreceptor function curve during the control period. Thereafter, infusion of phenylephrine (2–4 μg/kg/min) into the femoral vein was adjusted to produce a sustained rise of 40 mm Hg in MAP during a 30-minute period. Measurements of the baroreceptor function curves were repeated 5, 10, 20, and 30 minutes after the beginning of the pressure rise. When the administration of phenylephrine was interrupted, measurements of the pressure-nerve activity relation were again repeated 5, 10, 20, and 30 minutes after pressure normalization.

Results

Displacement of the Pressure Thresholds

The control baroreceptor function curve was measured at a control MAP similar to that existing in RHR during the awake state (166±5 vs. 163±4 mm Hg). Phenylephrine produced an immediate increase in pressure that remained stable during the 30 minutes of infusion (Figures 1 and 2). Five minutes after the onset of hypertension, a significant displacement of 13 mm Hg was already observed in MAPth in response to an MAP increase of 41 mm Hg. This represents a resetting of 32% (%ΔMAPth/total ΔMAP). The extent of resetting was 39%, 38%, and 41% after 10, 20, and 30 minutes of hypertension, respectively (Figure 1). When the percent change of systolic pressure threshold (ΔSth) divided by total control diastolic pressure (ΔCDP) was used to calculate the extent of resetting, similar results were obtained. The magnitude of resetting was 27%, 30%, 30%, and 32% after 5, 10, 20, and 30 minutes of hypertension, respectively (Figure 2).

Displacement of the Baroreceptor Function Curves

Shifts in the entire pressure-nerve activity relation compared with shifts in the pressure thresholds for activation of the baroreceptors were analyzed 5 and 30 minutes after the onset of hypertension (Figure 3). The resetting of Sth (Figure 3A) was 21% and 25% after 5 and 30 minutes, respectively; whereas resetting of MAPth (Figure 3B) was 36% and 42%,
respectively. A parallel displacement of the curves was observed with a tendency for slope to decrease when the baroreceptors were exposed to elevated pressure, especially after 30 minutes of hypertension.

Reversibility of the Resetting

MAP returned immediately (3–5 minutes) to pre-infusion values when the administration of phenylephrine was interrupted (Figure 1). The recovery of MAPth, however, was slower. Maximal reversibility was only 38% during the 30 minutes of pressure normalization (Figure 1). Reversibility was greater when changes in SPth and CDP were analyzed (Figure 2) although reversibility was still only partial because the maximal recovery of SPth was 74%.

Discussion

The most salient feature of the present study is that the characteristics and extent of rapid resetting observed in RHR with the baroreceptors reset to operate at hypertensive levels are identical to those described for normotensive rats. Complete resetting of the baroreceptors of RHR was registered during the control period because the systolic pressure threshold (137±5 mm Hg) for the activation of the baroreceptor was similar to the control diastolic
pressure (142±4 mm Hg), an indication of complete resetting.\textsuperscript{3,11} Despite complete resetting of the baroreceptors, the RHR exhibited normal, rapid resetting, that is, a partial resetting of 30–40% that appeared a few minutes after the onset of hypertension and remained stable up to the end of the 30-minute period of phenylephrine infusion. Analysis of the entire baroreceptor pressure-response relation indicates that the extent of displacement was similar to that of the pressure threshold, suggesting that no significant difference exists in the time course for resetting of low and high threshold baroreceptors. Reversibility of resetting was only partial (74%) in RHR, which is similar to that observed previously\textsuperscript{10} in normotensive rats (63%).

Several lines of evidence\textsuperscript{5,11} indicate that, during the onset and maintenance of hypertension, there are two distinct phases of baroreceptor resetting: phase 1, a rapid or acute resetting (i.e., a partial resetting of approximately 40% that reaches its maximum within the first few minutes and remains relatively constant up to 6 hours) and phase 2, a complete resetting (100%) when the displacement of the pressure threshold for activation of the baroreceptors matches the total pressure rise. Studies of aortic behavior in freely moving rats showed that during transient pressure increases, the displacement of the aortic diastolic caliber is much greater than the increase in pulsation, indicating that, under physiological conditions, sustained distention of the diastolic caliber is an important factor in aortic baroreceptor distortion. Moreover, a pronounced direct relation was observed between the time taken for the diastolic caliber to reach maximal dilation (2 days) and the time taken for complete resetting, suggesting that complete resetting occurred in hypertension when the increased stress on the arterial wall is matched by a proportional permanent increase in diastolic caliber.\textsuperscript{5,11} At the new operational level of resting diastolic caliber, the increased pressure no longer strains the diastolic caliber effectively, and the baroreceptors are only stimulated by pulse pressure. After 2 months of hypertension, the RHR had aortas 20% larger than control rats as opposed to the increases of 6.8% seen after only 48 hours of sustained hypertension; the aortic pulsation was twice as great in response to increased dynamic stress, even when dynamic distensibility remained normal.\textsuperscript{12} RHR exhibited normal rapid resetting during an additional hypertension of short duration. A similar degree of acute resetting (30%) was observed in the entire baroreceptor reflex control of lumbar sympathetic activity in RHR.\textsuperscript{13} In spontaneously hypertensive rats, the extent of rapid resetting of the aortic baroreceptors was also similar but took longer to develop, and the extent of reversal tended to be smaller.\textsuperscript{14} More recently, in vitro studies with an aortic arch–aortic nerve preparation in spontaneously hypertensive rats showed a rapid resetting with the extent of 25%.\textsuperscript{15} Rapid resetting in normotensive animals has been attributed to a slight viscoelastic relaxation of the arterial wall with progressive lengthening of viscous elements that results in decreased force exerted on the baroreceptor.\textsuperscript{16} In addition to viscoelastic relaxation, ionic alteration\textsuperscript{17} and alteration of the receptor ending itself\textsuperscript{18} have been suggested as mechanisms responsible for the development of rapid resetting of the baroreceptors. Because the characteristics of rapid resetting in RHR are identical to those in normotensive rats, the same mechanisms probably act in both groups.

References


**KEY WORDS** • baroreceptors • phenylephrine • renal hypertensive rats
Rapid resetting of the baroreceptors in renal hypertensive rats.

Hypertension. 1990;15:I40
doi: 10.1161/01.HYP.15.2_Suppl.I40

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1990 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/15/2_Suppl/I40

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in
Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/