

Direct Relationship between Renal Arterial Pressure and Plasma Renin Activity in Conscious Rats

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Much of our knowledge concerning renin secretion and renal perfusion blood pressure is derived from experiments with partial constriction of the renal artery or suprarenal aorta. It is known that lowering renal arterial pressure (RAP) enhances plasma renin activity (PRA) (1–3). However, little is known about the details of the relationship between RAP and PRA in conscious rats; this type of experiment has usually been conducted in larger animals such as dogs. The use of rats in these experiments could, however, offer several advantages. In addition to the obvious economic reason for using rats, the availability of several kinds for experimental hypertension, including some genetic types (4), makes the rat the most suitable species for hypertension research.

The present report describes the relationship between RAP and PRA in conscious rats with graded suprarenal aortic constriction.

Externally adjustable artery constrictors were constructed of a 12 cm piece of polyethylene tube (external diameter of 1.0 mm, internal diameter of 0.5 mm), a 15 cm piece of stainless steel (diameter of 0.3 mm) and a 5 cm piece of silk thread. One end of the polyethylene tube was bent at a right angle. The piece of stainless steel was pierced through the tube, and the tip of the steel was turned back. The thread was looped around the suprarenal aorta. This looped thread was hung on the tip of the steel which was turned back. Therefore, when the other end of the steel was pulled, the thread was also pulled and the suprarenal aorta was constricted. In this manner, suprarenal aortic

constriction was performed.

Twelve male Wistar rats weighing 290–330 g were housed in individual cages. All animals were fed a regular diet and tap water ad libitum. Six to seven days before the experiment, a right nephrectomy was performed under ether anaesthesia; and two days prior to the experiment, a surgical placement of catheters and a constrictor was performed under pentobarbitone anaesthesia. For collecting arterial blood samples, a catheter was inserted into the left carotid artery. Through the right femoral artery, a catheter was introduced into the abdominal aorta to monitor the RAP. The left femoral vein was cannulated to inject saline. These catheters were filled with heparin in advance. The left kidney was exposed via a retroperitoneal approach for indwelling an artery constrictor. This constrictor was passed around the suprarenal aorta as described above. All these catheters and a constrictor were exteriorized through a subcutaneous tunnel at the back of the neck. The rat was given penicillin (30,000 units, i.m.) at the end of the operation. These catheters were flushed daily with heparin.

On the day of the experiment, a femoral artery cannula was connected to a pressure transducer (Nihon Kohden, MPU-0.5) for monitoring RAP. After a 20 min resting period, a blood sample (0.3 ml) was drawn. It was replaced immediately after sampling with the same volume of saline. Ten minutes after blood sampling, the RAP was reduced by 15–25 mmHg with suprarenal aortic constriction. When the reduced RAP was spontaneously increased, further adjustments of the constrictor were made until a steady level of RAP was attained. This reduced RAP

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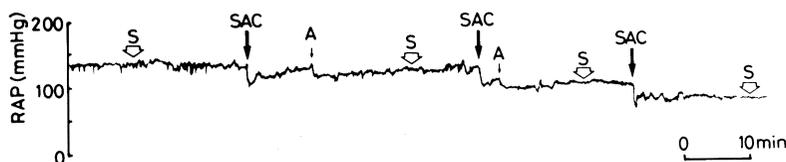


Fig. 1. Changes in mean renal arterial pressure (RAP) following suprarenal aortic constriction (SAC) in a conscious rat. S: Blood sampling, A: Further adjustments of the constrictor.

was kept constant for 20 min. At the mid point of this period, when RAP was stabilized, a blood sample was drawn again. Then, further decrease in RAP, ranging from 15 to 25 mmHg, was performed, and the procedure was repeated. In this manner, the RAP was reduced by 15–25 mmHg steps for three times. A typical experiment is illustrated in Fig. 1.

Blood samples were transferred into chilled tubes containing EDTA and centrifuged. PRA was measured by radioimmunoassay according to the methods of Fyhrquist et al. (5); the results are expressed as nanograms of angiotensin I generated per milliliter of plasma per hour. Regression coefficients were calculated using the method of least-squares. All values are expressed as means and S.E.M.

The effect of decrease in RAP on PRA is summarized in Fig. 2. These plots show individual values of PRA averaged within a 10 mmHg range of RAP. Clearly, small reductions of RAP below the control pressure (137.4 ± 3.4 mmHg) do not affect the PRA significantly; but below 90–100 mmHg, PRA is a steep and linear function of the RAP. From these data, two straight lines could be approximated and were fitted by standard regression techniques. The equation of a relatively flat line was $(PRA) = -0.034(RAP) + 6.6$, with a correlation coefficient of 0.630 ($P > 0.05$, $N = 5$); and the equation of a much steeper line was $(PRA) = -0.409(RAP) + 42.6$, with a correlation coefficient of 0.991 ($P < 0.01$, $N = 5$). Although the correlation coefficient of the equation of the flatter line was not statistically significant since the number of points was only five, the intersection of these two lines was defined as the threshold pressure which was at approximately 96 mmHg.

Recently, in conscious dogs maintained on

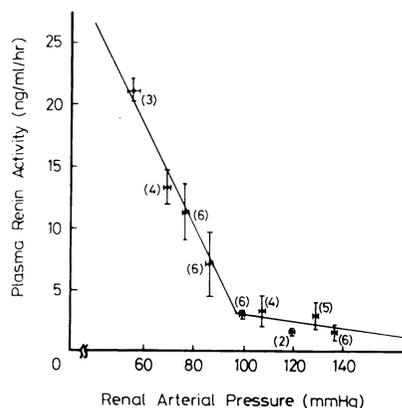


Fig. 2. Relationship between mean renal arterial pressure and plasma renin activity in conscious rats ($n = 12$). The number of data is given beside the plots in the parenthesis. Values are the mean and S.E.M.

a low-salt diet, Farhi et al. demonstrated the direct relationship between RAP and PRA with graded renal arterial constriction. They suggested that a threshold pressure, below which PRA was a steep and linear function of RAP, was approximately 77 mmHg (6). Later, Finke et al. showed that the threshold pressure was approximately 90 mmHg in conscious beta-blocked dogs (7). In the rat, on the other hand, there have been very few experiments of this type. Moreover, the experimental procedures of these studies on the rat were only a one step reduction of RAP such as a renal arterial constriction with approximately 50% reduction of renal blood flow (8) or a reduction of RAP to 40–60 mmHg (9). Therefore, these studies were not designed to estimate the threshold pressure.

We used conscious, chronically prepared rats to circumvent the complication associated with alterations in cardiovascular and renal

function associated with anaesthesia and acute surgery (10), and the present experiment demonstrated the relationship between RAP and PRA with graded suprarenal aortic constriction. In agreement with generally accepted findings, reduction of RAP was associated with the release of renin. However, the relationship was not linear, and the threshold pressure was 96 mmHg. Meanwhile, it was demonstrated that the lowest RAP at which renal blood flow was autoregulated was approximately 100 mmHg in the anaesthetized rat (11). Thus, the threshold pressure demonstrated in the present study is very close to the lowest perfusion pressure of the renal autoregulatory range, although there are some differences between the anaesthetized and unanaesthetized condition, so that some relationship between renal autoregulatory range and threshold pressure may be considered. After all, we feel that baroreceptor-stimulated renin release in the rat is hardly enhanced within the autoregulatory range, while it is markedly increased below it.

On the other hand, in the dog, a previous attempt to characterize the pattern of the renin release with regard to changes in RAP has shown that most of the measurable increments in renin secretion occur either within the lowest 15 mmHg of the range of renal autoregulation (2, 12) or in the lower part of the perfusion pressure curve, which is not accompanied by renal autoregulation (13). Blaine et al. have suggested that renin release is controlled by a vascular receptor within the range of autoregulation while it is controlled by a macula densa receptor below the range (14).

Further, renin release induced by renal arterial constriction is potentiated by beta-adrenergic stimulation in anaesthetized dogs (15). In the anaesthetized cat, renal denervation attenuates the increments in renin release induced by aortic stenosis (16). These results indicate that not only the renal baroreceptor and/or tubular macula densa but the beta-adrenergic component might mediate the renin release during reduction of RAP.

In conclusion, the threshold RAP for renin release in conscious rats was approximately 96 mmHg in our experimental con-

ditions. However, participations of the tubular macula densa and/or beta-adrenergic component on renin release induced by reduction of RAP and relationship between the threshold pressure and renal autoregulatory range in the rat should be examined in further studies.

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