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Peripheral Blood Flow Response to Step-Wise Increase of Arterial Pressure in Conscious Rats

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Iriuchijima, J. *Peripheral Blood Flow Response to Step-Wise Increase of Arterial Pressure in Conscious Rats.* Tohoku J. Exp. Med., 1998, **185** (3), 199-207 —— In conscious rats, changes in renal or superior mesenteric flow were observed when arterial pressure was elevated by occluding the terminal aorta. Blood flow was measured with an implanted electromagnetic flow probe and terminal aorta occlusion (TAO) was induced with an implanted pneumatic occluder. Arterial pressure was recorded with an indwelling catheter in the common carotid. Each TAO lasted for 20 seconds and flow and pressure at the end of this period were noted as those during TAO. After elimination of the reflexive compensation of arterial pressure by ganglionic blockade, the renal flow increase during TAO was slight but significant ($p < 0.01$), although the relative increase in flow was less than that in pressure. In other words, renal autoregulation, constancy of renal blood flow in the face of arterial pressure change, was imperfect. After further pentobarbital anesthesia, however, renal autoregulation was more complete to such an extent that the renal flow increase was insignificant during TAO. In contrast, the relative increase in superior mesenteric flow during TAO was larger than that in pressure with or without anesthesia. ———— pressure-flow relationship; autoregulation; renal flow; superior mesenteric flow

Peripheral blood flow change in response to primary change of arterial pressure would appear to be one of the fundamental questions of circulatory physiology. In the past this relationship was obtained under anesthesia (Thurau and Kramer 1959), in excised preparations (Pourageaud and De Mey 1998), or by an indirect method of flow measurement (Burton and Yamada 1951). In this study changes in renal and superior mesenteric flows were observed with an electromagnetic flowmeter in conscious rats on step-wise increase of arterial pressure induced by occlusion of the terminal aorta.

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Methods

Instrumentation

Male Wistar rats weighing 330±23 (S.D.) g, aged 13±1 weeks, were anesthetized with thiamylal sodium (50 mg/kg, i.v.). Each rat was implanted with an electromagnetic flow probe (type FC, Nihon Kohden, Tokyo) around either the renal or superior mesenteric artery. The diameter of the probe was 1 mm for the renal artery and 1.5 mm for the superior mesenteric artery. A polyethylene catheter (PE10 fused to PE20, Natsume Seisakusho, Tokyo) for recording arterial pressure was inserted into the right common carotid artery. Another catheter was inserted into the right external jugular vein for injection of drugs. The wire from the flow probe ending with a plug and the other ends of the catheters were all passed subcutaneously to the dorsal neck and exteriorized.

A pneumatic cuff occluder (OC2A, ME Service, Takamatsu) was implanted around the terminal aorta. The free end of the tube from the cuff was also exteriorized on the neck.

Observations of flow and pressure

After implantation the rat was kept separately in a white plastic cage measuring 35×30×17 cm, containing wood chips. Two or three days after implantation, after the rat had resumed eating and drinking, occlusion experiments were performed. The cable from the flowmeter circuit (MFV-1100, Nihon Kohden, Tokyo) was connected to the plug of the flow probe and the polyethylene tube (external diameter, 2.5 mm) from a pressure transducer to the arterial catheter. Flow and pressure signals were smoothed with an RC (resistance-capacitance) low pass filter of a time constant of 0.1 second and recorded with a rectangular pen-writer.

Terminal aorta occlusion

The terminal aorta was occluded by sending 3.5–4 ml of air to the occluder with a 5 ml syringe. Each terminal aorta occlusion (TAO) lasted for 20 seconds. Both arterial pressure and blood flows completed their responses to TAO within this period. Deocclusion was done by recovering the air into the syringe. Occlusion and deocclusion could be performed without any behavioral change in the rat.

In each rat TAO was repeated in the following three successive stages: First before any medication, second immediately after intravenous infusion of hexamethonium bromide (C6) (2.5% solution) at a rate of 0.8 mg/min for a total dose of 25 mg/kg for ganglionic blockade, and finally under anesthesia, about 10 minutes after intravenous injection of pentobarbital sodium at a dose of 30 mg/kg as a bolus.

Statistics

The paired t-test was used for the significance of a successive change in a variable. The group t-test was used for the difference in a variable between the two arteries when the difference in the S.D.'s was less than 100%. Otherwise the U-test was used. p-Values of <0.05 were considered to indicate statistical significance.

Results

Changes in arterial pressure during TAO

One example each of the experiment for renal (top) and superior mesenteric (bottom) flows is presented in Fig. 1. The recording to the left was made before any medication (BM), in the middle after ganglionic blockade (C6), and to the right under additional pentobarbital anesthesia (PA).

Before ganglionic blockade, the rise in arterial pressure induced by TAO was rapidly offset partially. After blockade, with or without anesthesia, the arterial pressure reached a relatively steady level in the first several seconds and was maintained till the end of the 20 second occlusion period. The renal flow tended to be offset after an initial rise during TAO, while the superior mesenteric flow did

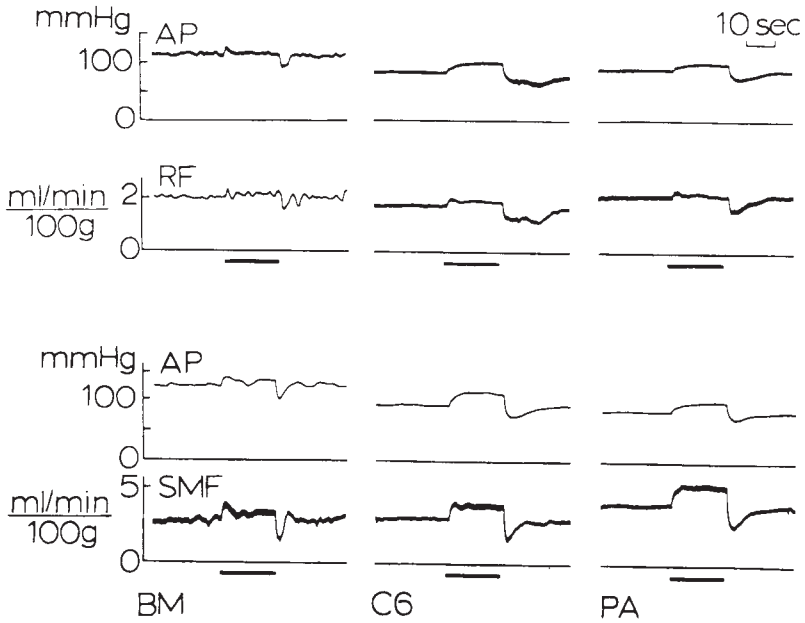

Fig. 1. Simultaneous recording of arterial pressure (AP) with renal flow (RF) in a rat (top) and superior mesenteric flow (SMF) in another (bottom). For the underlined periods (each for 20 seconds), the terminal aorta was occluded with a pneumatic occluder, to induce a step rise of AP. Occlusion experiment was repeated in successive three stages, first before any medication (BM) (left), after ganglionic blockade with hexamethonium bromide (C6) (middle), and after further pentobarbital anesthesia (PA) (left). Terminal aorta occlusion (TAO) induced a marked step rise in AP only after C6. RF increase during TAO was less than proportional to AP, while SMF increase was more than proportional.

not show such a tendency.

The mean values ± S.D. of arterial pressure before and during TAO as well as its absolute and percent changes during TAO from 11 rats are tabulated in Table 1. Pressures observed in rats with the flow probe at the renal artery and in those

TABLE 1. *Increase in arterial pressure (AP) during occlusion of terminal aorta (TAO) in rats in three situations*

	Before C6	After C6	After C6+PA
AP before TAO	117±12 mmHg	92±8	87±13
AP during TAO	126±17 mmHg	110±15	100±15
Increase in AP	9.1±7.6 mmHg	18.0±8.3	12.9±4.2
% Increase in AP	7.5±6.4%	19.1±7.2	14.9±4.5

mean ± S.D. $n=11$, C6, hexamethonium bromide (25 mg/kg, for ganglionic blockade, immediately after infusion); PA, pentobarbital anesthesia (30 mg/kg, about 10 minutes after bolus injection).

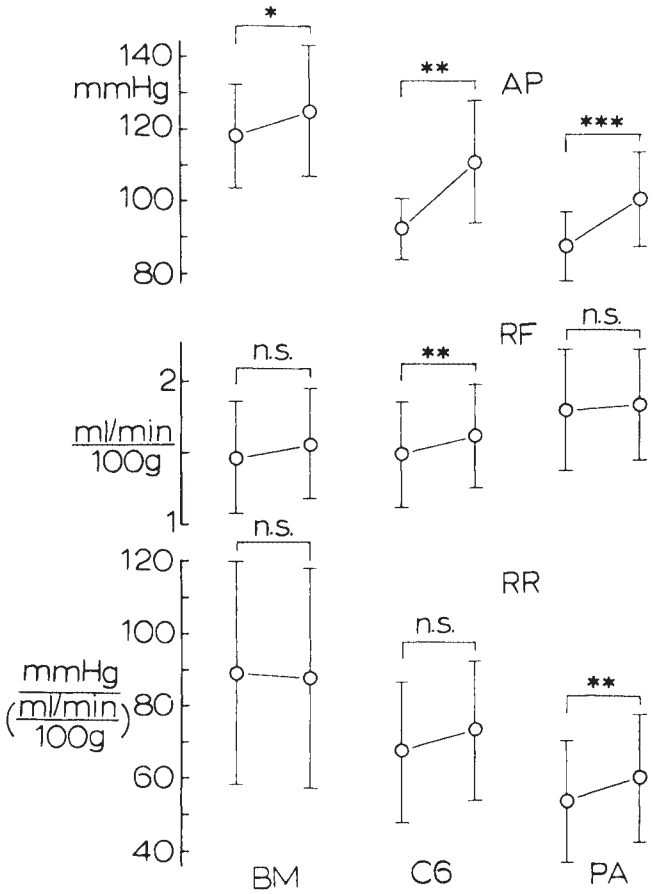

Fig. 2. Changes in arterial pressure (AP), renal flow (RF), and renal peripheral resistance (RR) during terminal aorta occlusion in three successive stages: Before any medication (BM), after ganglionic blockade (C6), and after further pentobarbital anesthesia (PA). $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ by the paired t-test. n.s., not significant; mean ± S.D. $n=6$.

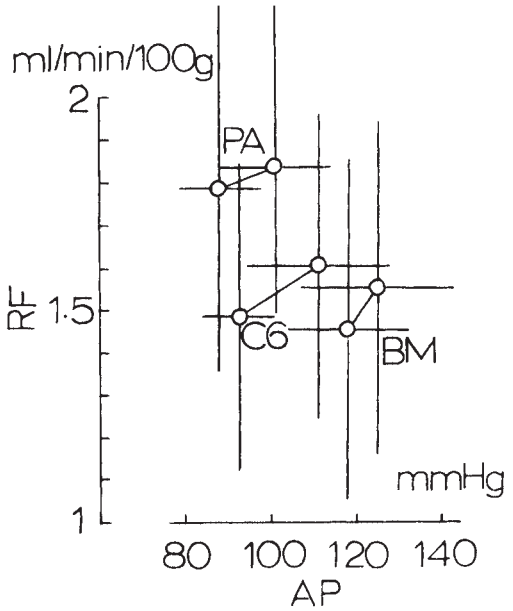

Fig. 3. Two-point (before and during TAO) pressure-flow relationship for renal artery. TAO, terminal aorta occlusion; AP, mean arterial pressure; RF, mean renal arterial flow; BM, before medication; C6, after ganglionic blockade with hexamethonium bromide; PA, after further pentobarbital anesthesia. Horizontal and vertical bars indicate standard deviations.

at the superior mesenteric artery were pooled for this table.

The mean $\pm$ S.D. of arterial pressure, blood flow, and flow resistance before and during TAO are plotted for the renal artery in Fig. 2 and for the superior mesenteric artery in Fig. 4.

Renal flow

The rise in arterial pressure during TAO was significantly greater after C6 than before ($p<0.01$, $n=11$) (Table 1). This may be ascribed to reflex buffering of arterial pressure before C6. Therefore, vascular response to primary change of pressure without neural intervention was observed after the infusion of C6. Under this condition, during TAO, renal flow increased significantly ($p<0.01$) (Fig. 2) with an insignificant change in renal resistance ($9.7\pm10.9\%$, $n=6$).

After further injection of pentobarbital, under anesthesia, the change in renal flow during TAO was insignificant, while renal resistance was increased significantly ($p<0.01$) ($12.4\pm4.7\%$).

The two-point pressure-flow relationships, before and during TAO, are presented in Fig. 3.

Semple and Wardener (1959) introduced autoregulation index (AI):

$$AI=(\Delta q/q)/(\Delta p/p),$$

where q = blood flow and p = arterial pressure and Δ refers to the change. In other words, AI is the ratio of the relative change of flow to that of pressure. For

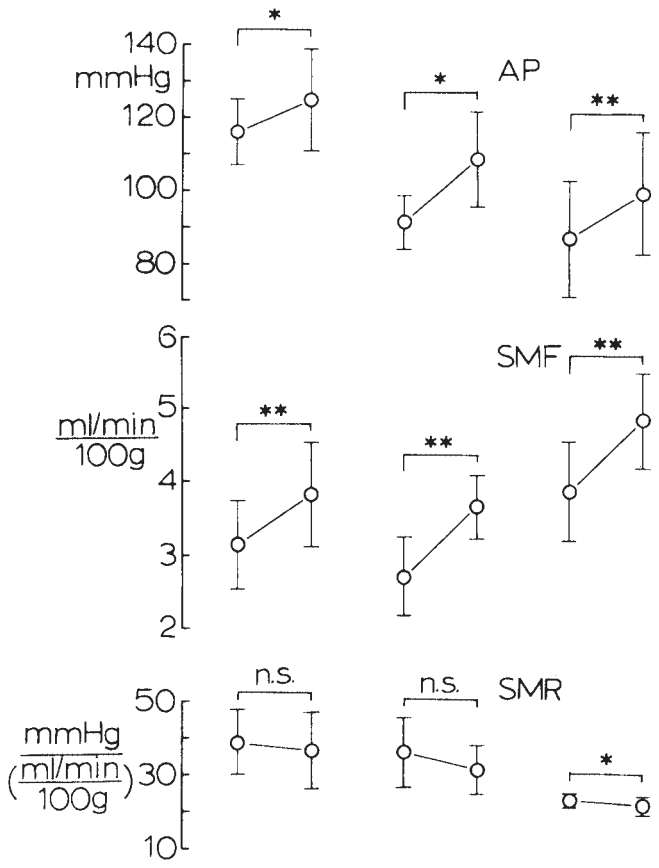

Fig. 4. Changes in arterial pressure (AP), superior mesenteric flow (SMF), and superior mesenteric peripheral resistance (SMR) during terminal aorta occlusion in three successive stages: Before any medication (BM), after ganglionic blockade (C6), and after further pentobarbital anesthesia (PA). $*p<0.05$, $**p<0.01$ by the paired t-test. n.s., not significant; mean$\pm$S.D. $n=5$.

TABLE 2. *AI (autoregulation index) for two arteries in three situations*

	Before C6	After C6	After C6+PA
Renal artery	1.20$\pm$0.53	0.588$\pm$0.352	0.138$\pm$0.212
Sup. m. artery	2.57$\pm$1.32	2.25$\pm$1.44	1.86$\pm$0.67

AI$=(\Delta q/q)/(\Delta p/p)$, where q = blood flow and p = arterial pressure and Δ refers to the change on occlusion of the terminal aorta.

$n=6$ for renal artery and $n=5$ for superior mesenteric artery. mean$\pm$S.D. C6, hexamethonium bromide (25 mg/kg, used for ganglionic blockade); PA, pentobarbital anesthesia (30 mg/kg, about 10 minutes after bolus injection).

complete autoregulation AI should be 0. For a relative flow change which is equal to the relative pressure change, in other words, for proportionality between pressure and flow, AI = 1. If AI > 1, the relative flow change is greater than the relative pressure change: When pressure increases, resistance is decreased.

AI was calculated for the changes in pressure and flow during TAO for renal

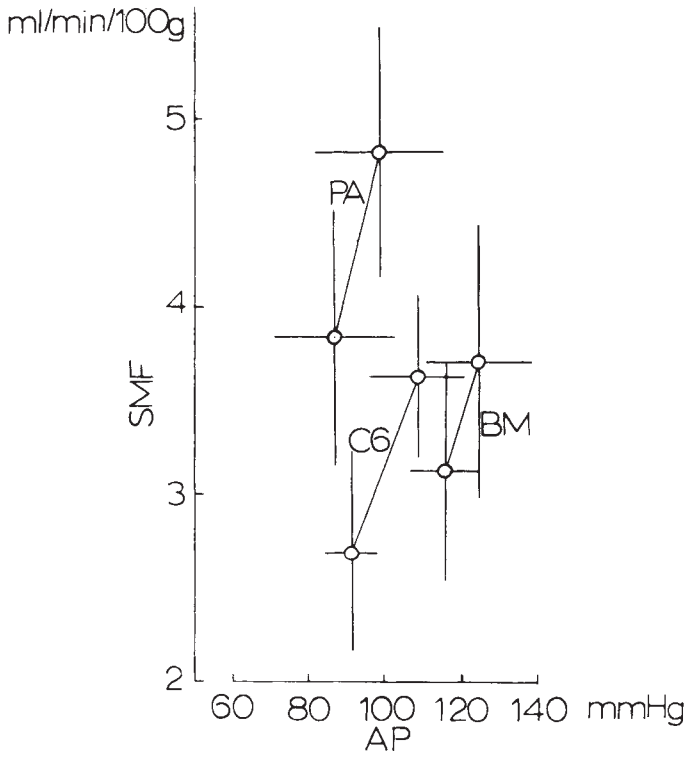

Fig. 5. Two-point (before and during TAO) pressure-flow relationship for superior mesenteric artery. TAO, terminal aorta occlusion; AP, mean arterial pressure; SMF, mean superior mesenteric arterial flow; BM, before medication; C6, after ganglionic blockade with hexamethonium bromide, PA, after further pentobarbital anesthesia. Horizontal and vertical bars indicate standard deviations. Note that gradients are steeper than in Fig. 3.

artery in the three stages: before any medication, after C6, and after further pentobarbital anesthesia (Table 2, first line). The tendency for autoregulation in renal flow is represented by the values of AI being smaller than 1 after C6.

Superior mesenteric flow

The response to TAO of superior mesenteric flow was different from that of renal flow (Fig. 4). After C6 the increase in superior mesenteric flow during TAO was more marked ($p<0.01$) than that in renal flow. (The increase was $45.9\pm 22.0\%$ for superior mesenteric flow, while it was $9.0\pm 5.0\%$ for renal flow. The difference was significant at $p<0.01$ by the U-test.) Superior mesenteric resistance was decreased by TAO by $-11.9\pm 12.2\%$, $n=5$, although this change was not statistically significant. Superior mesenteric flow increased during TAO also after further anesthesia, superior mesenteric resistance being decreased significantly ($-9.0\pm 6.3\%$, $p<0.05$, $n=5$).

In Fig. 5, the two-point pressure-flow relationships for superior mesenteric flow are presented. The gradients are steeper than those in Fig. 3.

The tendency of superior mesenteric flow to increase more than proportionally to the increase in arterial pressure is represented by the values of AI over 1 (Table 2, second line).

Discussion

Autoregulation is the tendency for blood flow to remain constant in the face of changes in arterial pressure to the organ. Since Verney and Starling (1922) and Rein (1931) renal flow has been known to be autoregulated. In the rat, however, autoregulation is not so efficient as in the dog (Hope and Clausen 1982).

In the present study renal autoregulation was found to be imperfect in conscious rats in the pressure range covered by the method adopted in this study: Renal flow was increased significantly during TAO after ganglionic blockade (Figs. 1 [top] and 2). However, under additional pentobarbital anesthesia, renal autoregulation was observed to take place typically, with an insignificant change of flow accompanied by an increase in resistance. The reason why renal flow autoregulation is facilitated after pentobarbital anesthesia is unknown. In the superior mesenteric artery, on the contrary, flow increased more than proportionally to pressure with or without anesthesia (Figs. 1 [bottom] and 4).

The tendency of superior mesenteric flow to increase more than proportionally to an increase in arterial pressure should attenuate the increase in arterial pressure without the participation of neural compensatory mechanisms.

Previously, we assumed that the renal vascular bed in the rat in the conscious state had a substantial amount of sympathetic vasoconstrictor tone because renal resistance was decreased about 20% by ganglionic blockade with C6, when arterial pressure was lowered about 20% (Iriuchijima and Sakata 1985). One might argue that such a decrease in resistance does not necessarily indicate the presence of sympathetic tone and may as well be ascribable to renal autoregulation. Our contention has been that such a decrease in renal resistance was not observed after renal denervation (Iriuchijima and Sakata 1985). In the present study it is further shown that the increase in renal resistance ascribable to autoregulation was statistically insignificant and only about 10% on the average when arterial pressure was increased about 20% by TAO. We may assume that what occurs on an increase in arterial pressure should occur in the same absolute amount in the opposite direction on a decrease in arterial pressure of the same magnitude. The observed decrease in renal resistance on ganglionic blockade, which was as large as 20% (Iriuchijima and Sakata 1985), was far greater than can be ascribed to autoregulation alone.

Our previous conclusion that the vasoconstrictor tone in the superior mesenteric area is nil (Iriuchijima and Sakata 1985) should also be reviewed in the light of the present result. However, since about a 20% change of arterial pressure automatically induces only about a 10% change of superior mesenteric resistance in the opposite direction, sympathetic vasoconstrictor tone in this area, if present at all, should be at best sufficient to increase the regional resistance by 10%.

In summary, on step-wise increase of arterial pressure induced by occlusion of

the terminal aorta, in conscious rats after ganglionic blockade, autoregulation of renal flow was imperfect while superior mesenteric flow increased more than proportionally to pressure.

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