Experimental Studies on the Nervous Control of the Renal Circulation—Effect of the Electrical Stimulation of Splanchnic, Vagal and Other Somatic Nerves and of the Carotid Sinus Reflex on the Renal Circulation (II)

Jugoro TAKEUCHI, M.D., Eiichi UCHIDA, M.D., Shosaku NAKAYAMA, M.D., Tadanao TAKEDA, M.D., Yoshitada MIYASATO, M.D., Shigeru YAGI, M.D., Gosuke INOUE, M.D., and Hideo UEDA, M.D.*

The renal blood flow was measured by an electromagnetic flow meter in dogs with the innervated kidney in situ perfused by the donor's blood. This perfusion was designed in order to avoid the possible influence of humoral factors and of prerenal circulatory changes on the nervous control of renal hemodynamics in studied dogs. It was confirmed that stimulation of the distal cut end of the splanchnic nerve resulted in marked renal vasoconstriction. And slight renal vasoconstriction was also observed in the stimulation of the distal end of the divided vagal nerve. By occlusion of carotid arteries, slight renal vasoconstriction was observed. It was in contrast to the independence of renal vascularity when a pressure was given on the carotid sinus. Responses of renal blood vessels were variable and not consistent in the stimulation of the proximal end of the divided femoral and sciatic nerve, as well as in the stimulation of the proximal end of the divided vagal nerve.

In a previous paper,1) we reported some results of the experimental studies on the nervous control of the renal circulation, especially on effects of the electrical stimulation of splanchnic, vagal and other somatic nerves and of the occlusion of carotid arteries in dogs. But with the techniques described previously, the influence of humoral factors and of prerenal circulatory changes, such as in cardiac output, might have been partly responsible for the alteration of renal hemodynamics. Therefore, an improvement for the experimental technique and devices were necessitated in order to measure the neural control on the renal vessels more exactly.

In the present study, the innervated kidney was perfused in situ by the donor's blood which was kept independent of stimulating procedure;
thus effects of such factors as prerenal circulatory changes and of humoral agents could be avoided throughout the experiment.

**Methods**

Experiments were performed on 21 dogs each weighing 9.6 to 15.0 Kg. Anesthesia was made with thiopental sodium (20 to 30 mg./Kg.) in 13 dogs, with pentobarbital sodium (5 to 10 mg./Kg.) in 5, and with chloralose (50 to 80 mg./Kg.) plus morphine chloride (6 to 4 mg./Kg.) in 3. In each experiment, another dog as large as the experimental animal (recipient) was used as a donor to perfuse the recipient's kidney. After a donor was heparinized, its femoral artery was connected with recipient's renal artery and the renal vein of the recipient was connected with donor's femoral vein through an electromagnetic flow meter. The connections were made by polyethylene tubes as closely as possible. Thus in this procedure, which we described in the preliminary reports,^2,^3^ the kidney was perfused completely by donor's blood during the experiment with a stable pressure which was recorded by an electromanometer connected to a side-branch in the perfusing circuit.

The nerve stimulation and the carotid occlusion were carried out in similar fashions as described previously.^1^ In addition, a blind sac was made on the unilateral carotid artery and a high pressure was given thereupon according to the method described by Moissejeff,^4^ and effect of carotid sinus reflex on renal circulation was investigated.

**Results**

Splanchnic Nerve Stimulation—

Thirty-five electrical stimulations of the distal end of the divided greater splanchnic nerve were made on 4 dogs. A rise in systemic arterial pressure and a simultaneous decrease in renal blood flow occurred in all 29 experiments except 6 instance with inadequate stimulating conditions (Fig. 1). The elevation of mean arterial pressure ranged from 7 to 53 mm. Hg with an average of 21 mm. Hg (4 to 41.4%; mean 15%). The decrease in renal blood flow was 11 to 62 ml./min. with a mean of 37 ml./min. (17 to 100%; mean 53%).

Hydergine® was given intravenously prior to nervous stimulations in 2 dogs. The vasoconstrictive responses were inhibited or supressed in all 6 experiments on these dogs. No evidence for the vasodilatatory effect of nervous stimulation was observed (Fig. 2).

Efferent Vagal Nerve Stimulation—

Stimulation of the distal end of the cut cervical vagal nerve produced a prompt fall in systemic arterial pressure with cardiac arrest or brady-
cardia and a slight decrease in renal blood flow in all 5 experiments on 4 dogs (Fig. 3). The decrease in renal blood flow ranged from 3 to 23 ml./min. with an average of 13 ml./min. (21 to 38%; mean 22%). In all experiments except one, decrease in renal blood flow was over 11 ml./min., which could be regarded as significant.

Fig. 1. Dog No. 95, Exp. 9: Stimulation of distal end of divided greater splanchnic nerve (100 c/s, 3 v).

Fig. 2. Dog No. 95, Exp. 17: Stimulation of distal end of divided greater splanchnic nerve (30 c/s, 5 v) after intravenous injection of 0.9 mg. of hydergine.

Fig. 3. Dog No. 93, Exp. 3 and Exp. 4: Stimulation of distal end of divided cervical nerve (30 c/s, 3 v and 50 c/s, 5 v).
Occlusion and Giving Pressure on Carotid Artery—

The occlusion of bilateral or unilateral common carotid arteries was followed by an elevation of systemic arterial pressure, ranging from 11 to 35 mm. Hg, with an average of 22 mm. Hg (9 to 26%; mean 17%). In 9 of 12 experiments on 5 dogs, pressor responses accompanied by more or less decrease in renal blood flow, ranging from 3 to 9 ml./min. with an average of 5 ml./min. (3 to 23%; mean 12%). But significant decrease was found in only 4 experiments among them (Fig. 4).

![Fig. 4. Dog No. 133, Exp. 14: Occlusion of unilateral common carotid artery.](image1)

![Fig. 5. Dog No. 132, Exp. 3: Giving pressure unilaterally on blind sac prepared from carotid artery including carotid sinus.](image2)

When a high pressure (160 to 220 mm. Hg) was given into a blind sac, prepared on a common carotid artery, a fall of systemic arterial pressure was observed in association with bradycardia but the renal blood flow remained unchanged. Decrements of systemic arterial pressure in 11 experiments on 3 dogs were 9 to 62 mm. Hg with a mean of 36 mm. Hg (Fig. 5).

Afferent Stimulation of Sciatic or Femoral Nerve—

Stimulation of the proximal end of the divided sciatic or femoral nerve in 12 dogs caused both hypertensive and hypotensive responses. Significant decrease in renal blood flow was observed in 13 experiments on 6 dogs. Blood pressure responses in these 13 experiments were hypertensive in 5 experiments, hypotensive in 5, and no significant change in blood pressure was observed in the remaining 3. Fig. 6 and Fig. 7 show a decrease in renal blood flow with hypotensive response in sciatic nerve
stimulation and with hypertensive response in femoral nerve stimulation respectively. Among other 25 experiments with significant alterations in systemic blood pressure, renal blood flow decreased merely slightly (3 to 7 ml./min., not significant) in 18 and did not change in 7. Increase in renal blood flow (8, 9, 12 and 21 ml./min., respectively) occurred in 4 experiments, 2 of which were repeated in the same dog and resulted in slight hypertensive responses (Fig. 8); 2 experiments in another dog produced hypotensive responses.
Afferent Cervical Vagal Nerve Stimulation—

A total of 86 experiments were performed on 14 dogs. Systemic arterial pressure responses produced by stimulation of the central end of the divided cervical vagal nerve were not consistent, that is, hypertensive in 46, hypotensive in 8 and biphasic in 2 experiments. The alteration in renal blood flow was also variable. In 46 hypertensive responses, the renal blood flow significantly increased in 7 (8 to 14 ml./min.), decreased in 11 (8 to 51 ml./min.) and did not change in 28 experiments. In 8 hypotensive responses, the renal blood flow significantly increased in 4 (8 to 18 ml./min.), decreased in one (8 ml./min.) and did not alter in 3 experiments. Fig. 9 is an example which shows a decrease in renal blood flow with a hypertensive response and Fig. 10 shows a slight increase in renal blood flow accompanied by a hypertensive response. No significant change in renal blood flow occurred in experiments with biphasic blood pressure responses. One significant decrease and one significant increase in renal blood flow were observed in 30 experiments without significant alteration in blood pressure.

In 3 of the 14 dogs, stimulation in low voltage (2 to 5 volts) appeared to produce an increase in renal blood flow with a hypotensive response, whereas that in high voltage (5 to 20 volts) resulted in a decrease in renal blood flow with a hypertensive response.
DISCUSSION

We have been interested in the experimental studies on the regulatory mechanisms of renal circulation under the nervous control. In a previous paper,\(^1\) we reported some results of our experimental studies in which effects of the electrical stimulation of splanchnic, vagal and other somatic nerves and of the carotid occlusion on renal circulation were observed in dogs. Changes in renal blood flow were measured by an electromagnetic flow meter which was set between renal and femoral veins of the studied dog. But with the techniques described previously, possibility remained that renal hemodynamics might have been influenced by humoral factors such as epinephrine\(^5,6\) released from any parts of the body and by prerenal circulatory changes\(^7,8\) such as in cardiac output.

In the present study, the renal blood flow was measured on the innervated kidney in situ perfused by donor's blood. Since a donor dog was kept independent of any stimulating procedures, the perfusing pressure was maintained constant throughout the experiment. Thus, effects of such factors as prerenal circulatory changes and of humoral agents could be avoided. Then, alterations in the recorded renal blood flow could be considered as indicating the attitude of renal vessels more directly and exactly.

On splanchnic nerve stimulation, the results reported previously were confirmed in this perfusing method; the elevation in systemic arterial pressure and the marked reduction in renal blood flow indicated vasoconstriction of the renal blood vessels. The result supports the previously presumed conclusion that the decrease in renal blood flow might be attributed to a direct neural effect rather than to a humoral effect, since the perfused kidney was isolated from the recipient's blood.

In the previous study, the renal blood flow decreased by stimulating the distal end of the cut subdiaphragmatic vagal nerve. But changes in the calculated renal vascular resistance were not significant. In the present study, the renal blood flow decreased in all experiments. This fact indicates that the renal vasoconstriction due to neural impulses occurs by stimulation of the distal end of the cut cervical vagal nerve, because the perfusing arterial pressure was constant during experiment. It is not clear, however, whether this renal vasoconstriction was due to direct stimulation of cervical vagosympathetic trunks or due to a reflex secondary to a cardiac effect.

On carotid occlusion, the slight decrease in renal blood flow which is considered to be due to renal vasoconstriction was observed, although significant decrease in renal blood flow was recorded in 4 among 12
significant hypertensive responses. This appears to support our previous findings that the calculated renal vascular resistance increased slightly in all cases.

Sollmann and Brown\textsuperscript{10) observed a diminution in volume of the perfused innervated kidney by means of onometric tracing on traction of the common carotid. But Unna\textsuperscript{11) described no detectable influence on the renal blood flow in a 30 to 50 mm. Hg fall in arterial pressure due to distention of one carotid sinus. In our study in which a high pressure was given on a carotid sinus, the renal vascular vessels appeared to have no change in spite of a marked fall in systemic arterial pressure.

Stimulation of the central end of the cut femoral or sciatic nerve generally produced more or less renal vasoconstriction unrelated to the alteration of systemic blood pressure. This was in accordance with the result of our previous observation. But in 4 of the 42 experiments, a slight increase in renal blood flow was observed, which indicated vasodilatation of renal blood vessels. It is of interest that afferent impulses from these nerves could, unexpectedly, produce vasodilatation in the kidney, although it was elicited in merely exceptional cases.

On stimulation of the proximal end of the divided cervical vagal nerve, alteration in systemic blood pressure and responses in renal blood vessels were various. The renal vessels responded with no significant change in many experiments but occasionally either vasoconstriction or vasodilatation was observed. The hypotensive response accompanied renal vasodilatation more frequently. In 3 dogs, vasodilatation occurred with hypotensive response in low voltage stimulation and vasoconstriction with hypertensive response in high voltage. But it is still not clear whether a correlation between the systemic arterial pressure and the attitude of renal vessels is present or not, because in hypertensive response the latter was as various in the present study as observed in our previous report.

In general, stimulating procedures in the present study produced fewer significant alterations in renal blood flow in comparison with the results obtained from our experiments reported previously. These findings implicate following possibilities: (1) the nervous reflexes actually have less influence on renal vascularity; (2) the resistance intervening in the perfusing circuit was large enough to interfere the recorded results; and (3) operative manipulations during arterial canulation were apt to make more damage on the nervous tissue surrounding the renal artery. Further improvement in experimental conditions will be required to confirm the above-postulated hypotheses.
Summary

The renal blood flow was measured by an electromagnetic flow meter in dogs with the innervated kidney in situ perfused by donor's blood. Following results were obtained:

1. In electrical stimulation of the distal end of the divided splanchnic nerve, renal vasoconstriction was produced.
2. On stimulation of the distal end of the divided cervical vagal nerve, slight renal vasoconstriction occurred.
3. By occlusion of common carotid arteries, slight renal vasoconstriction was produced.
4. Giving a high pressure on the carotid sinus caused no alteration of renal vascular response.
5. On stimulation of the central end of the divided sciatic or femoral nerve, the renal blood vessels showed generally vasoconstriction but rarely vasodilation.
6. On stimulation of the central end of the divided cervical vagal nerve, the attitude of renal blood vessels was various.

References