Experimental Studies on the Nervous Control of the Renal Circulation—Effect of the Electrical Stimulation of the Spinal Cord on the Renal Circulation

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An attempt was made to investigate the changes in blood pressure and renal blood flow induced by electrical stimulation of the spinal cord in 48 anesthetized dogs and to map the spinal cord in relation to the control of renal circulation. To avoid possible influences of the upper centrum such as the hypothalamus and medulla oblongata, prior to the stimulation complete transection of the spinal cord was performed in 23 dogs. An increase in renal blood flow accompanied by the pressor response was often seen upon stimulation in the lateral column and lateral border of the anterior column of the upper dorsal segments. This change was inferred to occur due in part to an increase in cardiac output. Stimulation of the lateral column, the lateral border of the anterior column and surface of the transitional zone between the anterior and the posterior column from D₅ to D₁₂ segments resulted in an increase in blood pressure and a decrease in renal blood flow, which were attributed to renal vasoconstriction. Upon stimulation in the spinal cord from D₁₃ to L₃ segments, there usually occurred little change in both blood pressure and renal blood flow, but in some cases a decrease only in renal blood flow was observed, suggesting the existence of nerves affecting mainly the renal blood vessels. Upon stimulation in the posterior column from D₁ to L₃ segments, no changes were usually observed in blood pressure and renal blood flow. After the complete transection of the spinal cord, the changes in blood pressure and renal blood flow were usually decreased in degree but the results of stimulation in the spinal cord from D₅ to L₃ segments were almost similar to those of the experiment in which transection of the spinal cord was not performed. Biphasic and triphasic responses observed in the latter experiment were never seen in the former.

ALTHOUGH the nervous control of renal circulation has been studied by many investigators, it has not been clarified in detail yet. Previously Takeuchi, one of the authors, reported the results of experimental studies of the nervous control of renal circulation, especially the effects of electrical stimulation of the splanchnic, vagal and other somatic nerves^{1), 2)} and of the

diencephalon^{3), 4)} and medulla oblongata.⁵⁾

Anatomical studies of the autonomic center of the spinal cord⁶⁾⁻¹⁰⁾ and physiological and anatomical studies on the descending and ascending pathways mediating the autonomic actions in the spinal cord¹¹⁾⁻¹⁸⁾ have been reported by several authors, but work on the role which the spinal cord plays in the control of renal circulation has not been published. In this study, an attempt was made to investigate the changes in blood pressure and renal blood flow induced by direct stimulation of the spinal cord from D₁ to L₃ segments and to elucidate the significance of the spinal cord in the regulation of renal circulation.

METHODS

Experiments were performed on 48 adult mongrel dogs weighing 9 to 20 Kg. Anesthesia was induced with a combination of morphine chloride (6mg./Kg., subcutaneously) and chloralose (70 to 80mg./Kg., intravenously). The systemic arterial pressure was continuously recorded by means of an electromanometer connected to the cannulated femoral artery. The renal blood flow was simultaneously recorded by an electromagnetic flow meter which was inserted in a circuit between the renal vein and femoral vein. The details of this procedure were described in a previous paper.¹⁾ The renal vascular resistance was calculated by the same equation as described previously.¹⁾

The stimulation of the spinal cord was carried out in the following manner. After the spine was fixed with the stereotaxic instrument devised by the Institute of Brain Research, Faculty of Medicine, University of Tokyo, several segments of the spinal cord were exposed at appropriate levels by laminectomy, and then an electrode was inserted into the spinal cord.

In 23 dogs, a complete transection of the spinal cord was performed at the 2nd or 3rd segment above the stimulated segment in order to avoid possible influences of the upper centrum such as the hypothalamus and medulla oblongata. Of these 23 dogs, only 16 animals could be recovered within 1 hour from spinal shock due to the complete transection of the spinal cord and these 16 dogs were used in the stimulating experiment, the others not being used.

The electrodes consisted of 2 dental broaches made of piano wire, 0.13 mm. in diameter. Only a minute scratch was made at the tip of both electrodes with a distance of less than 0.2 mm. between the 2 tiny exposed tips.

The electrical stimuli were rectangular voltage pulses: their duration was 1 msec.; their frequency 100 cycles per sec.; their voltage 3 to 10 volts. Each stimulus was applied for 10 to 30 sec. The location of each stimulated point in the spinal cord was determined by histological examination. Both hematoxylin-stain (Carrazi's method) and myelin-stain (Weil's method) were used.

RESULTS

Ellenberger et al.¹⁹⁾ and Hirt²⁰⁾ showed that in dogs the stellate ganglion received rami communicantes coming from C₆ to D₄ spinal nerves, and

that the greater splanchnic nerve was usually formed by branches from the 5th to 10th thoracic sympathetic ganglia to which spinal nerves from D_5 to D_{12} sent rami communicantes, and that in addition, the lesser and least splanchnic nerves sprang forth from the 11th and 12th thoracic ganglia. According to these facts, the authors conveniently divided the spinal cord into 3 groups: $D_1 \sim D_4$, $D_5 \sim D_{12}$, and $D_{13} \sim L_3$, respectively. Consequently, the results obtained in this experiment are described with reference to these sections.

Experiment 1.

Stimulations were given 385 times at 121 points in the spinal cord from D_1 to L_3 segments in 25 dogs (Table I). Various responses in blood pressure

Table I. Number of Stimulation Points and Experiments
in the Spinal Cord (Experiment 1)

Segment of Spinal Cord	No. of Points	No. of Exper.	Segment of Spinal Cord	No. of Points	No. of Exper.
D_1	2	7	D_9	8	27
D_2	5	12	D_{10}	5	17
D_3	11	31	D_{11}	11	37
D_4	7	22	D_{12}	13	52
D_5	8	25	D_{13}	8	27
D_6	8	23	L_1	16	46
D_7	4	15	L_2	6	16
D_8	8	26	L_3	1	2
			Total	121	385

and in renal blood flow were obtained depending on the stimulated sites and here changes in both above 10% of the prestimulating states were regarded as significant. Typical response patterns are demonstrated in Fig. 1 A-F.

Fig. 1. A-J. Various patterns of responses in blood pressure and in renal blood flow observed in Exp. 1. Stimulation of the spinal cord with 100 cps, 1 msec., at 10 volts for 10 sec. excluding I in which stimulation was carried out for 30 sec.

Fig. 1 A-type response was one in which renal blood flow was abruptly decreased coincident with the onset of a rise in blood pressure, and in Fig. 1 B-type response, it was observed that a marked and rapid fall of renal blood flow was preceded by a transient increase in blood pressure. The former was seen at 18 points and the latter at 9 points. Both of these responses were mainly observed upon stimulation in the lateral column, the lateral border of the anterior column and surface of the transitional zone between the anterior and the posterior column from D_5 to D_{12} segments. Usually in these parts renal vascular resistances increased markedly.

Fig. 1 C-type response: A rise in blood pressure and little or no change in renal blood flow. This response was seen upon stimulation at 8 points that were mainly located in the lateral column of the upper dorsal segments.

Fig. 1 D-type response: A rise in blood pressure and an increase in renal blood flow. It was observed at all 18 points and was mainly seen upon stimulation in the lateral column and lateral border of the anterior column from D_1 to D_8 segments. Renal vascular resistances of these parts were either slightly increased or unchanged.

Fig. 1 E-type response: Little or no change in blood pressure and a decrease in renal blood flow. It occurred at 10 points and was observed upon stimulation in the lateral column and surface of the transitional zone between the anterior and the posterior column from D_5 to L_3 segments. The decrease of renal blood flow in all these responses was less in degree than that of Fig. 1 A- or 1 B-type responses, as was the increase in renal vascular resistances.

Fig. 1 F-type response: Little or no change in either blood pressure or renal blood flow. It was seen upon stimulation in most areas of the posterior

column from D₁ to D₁₂ segments and almost all areas except the lateral column and the posterolateral border of the anterior column from D₁₃ to L₃ segments.

Fig. 1 G-type response: A fall in blood pressure and a decrease in renal blood flow. It was observed at all 6 points and these points were scattered from D₁ to L₃ segments. At all these points both a fall of blood pressure and a decline of renal blood flow took place 2 to 4 sec. after the onset of stimulation.

In this study, changes in blood pressure and renal blood flow often continued even after the cessation of electrical stimulation (Fig. 1 H). Occasionally biphasic (Fig. 1 I) or triphasic changes (Fig. 1 J) in blood pressure and renal blood flow were observed during or after stimulation.

The changes of blood pressure and renal blood flow observed in this experiment are summarized in Table II and the stimulated points are mapped out in Fig. 2.

Table II. Results of Changes in Blood Pressure and in Renal Blood Flow (Experiment I)

D ₁ —D ₄				
RBF \ BP	Pressor response > 10%	No change	Depressor response < -10%	Total
Decrease < -10%	2	0	2	4
No change	5	8	0	13
Increase > 10%	8	0	0	8
Total	15	8	2	25
D ₅ —D ₁₂				
RBF \ BP	Pressor response > 10%	No change	Depressor response < -10%	Total
Decrease < -10%	24	6	2	32
No change	3	23	0	26
Increase > 10%	7	0	0	7
Total	34	29	2	65
D ₁₃ —L ₃				
RBF \ BP	Pressor response > 10%	No change	Depressor response < -10%	Total
Decrease < -10%	1	4	2	7
No change	0	20	1	21
Increase > 10%	3	0	0	3
Total	4	24	3	31

Experiment 2.

To avoid possible influences of the upper centrum such as the hypothalamus and medulla oblongata, complete transection of the spinal cord was

Fig. 2. Diagrammatic drawings showing the arrangement of stimulated points in the spinal cord in Exp. 1. Blood pressure responses are represented on the left side, and changes in renal blood flow on the right side. Stimulation parameters: 100 cps, 1 msec., 10 volts, and 10 sec.

Table III. Number of Stimulation Points and Experiments in the Spinal Cord (Experiment 2)

Segment of Spinal Cord	No. of Points	No. of Exper.	Segment of Spinal Cord	No. of Points	No. of Exper.
D ₅	2	5	D ₁₁	7	23
D ₆	1	2	D ₁₂	5	15
D ₇	5	14	D ₁₃	8	20
D ₈	9	26	L ₁	6	13
D ₉	13	37	L ₂	6	13
D ₁₀	11	29	L ₃	1	3
			Total	74	200

carried out before stimulation. In this experiment, stimulations were given 200 times at 74 points in the spinal cord from D₅ to L₃ in 16 dogs (Table III). Dogs usually fell into a severe shock immediately after the transection of the cervical cord, and therefore the stimulating experiment of the spinal cord from D₁ to D₄ segments could not be performed. Upon stimulation in the spinal cord from D₅ to L₃ segments after the transection, it was usually observed that the magnitude of changes in both blood pressure and renal blood flow was de-

creased compared with that of Exp. 1. Consequently, in Exp. 2 changes in both above 5% of control level were regarded as significant. The distributions of responses in this experiment is shown in Table IV.

Table IV. Results of Changes in Blood Pressure and in Renal Blood Flow (Experiment 2)

D ₅ —D ₁₂					
RBF	BP	Pressor response >5%	No change	Depressor response < -5%	Total
Decrease < -5%		13	5	3	21
No change		0	26	0	26
Increase >5%		5	1	0	6
Total		18	32	3	53

D ₁₃ —L ₃					
RBF	BP	Pressor response >5%	No change	Depressor response < -5%	Total
Decrease < -5%		2	2	0	4
No change		0	17	0	17
Increase >5%		0	0	0	0
Total		2	19	0	21

Fig. 1 A-type response was observed at 11 points and Fig. 1 B-type response at 4 points. These points were seen upon stimulation in nearly the same regions as in Exp. 1, especially in the lateral column and lateral border of the anterior column from D₉ to D₁₂ segments. Fig. 1 C-type response was never observed in this experiment. Four points of all 5 points of Fig. 1 D-type response were seen upon stimulation in the lateral column and anterior column from D₅ to D₈ segments. In these responses, renal vascular resistances were never decreased. Fig. 1 E-type response was seen at all 7 points and these points lay in the same areas as in Exp. 1, that is, at the lateral column and surface of the transitional zone between the anterior and posterior column from D₅ to L₃ segments. Fig. 1 F-type response was observed in quite the same areas as in Exp. 1. Fig. 1 G-type response was encountered at only 3 points and was seen upon stimulation in the transitional zone between the anterior and posterior column from D₅ to D₁₂.

In this experiment, the response in which changes in both blood pressure and renal blood flow continued even after the cessation of stimulation was sometimes observed but biphasic (like Fig. 1 I) and triphasic responses (like Fig. 1 J) were not observed. In Fig. 3, the stimulated points in Exp. 2 are mapped out.

Fig. 3. Diagrammatic drawings showing the arrangement of the stimulated points in the spinal cord in Exp. 2. Blood pressure responses are represented on the left side, and changes in renal blood flow on the right side. Stimulation parameters are the same as in Exp. 1.

DISCUSSION

It has been known that the kidneys of man are richly supplied with autonomic nerves extending from the 4th dorsal to the 4th lumbar segments.²¹⁾ On the other hand, Bradford²²⁾ reported that the renal vasoconstrictor of the dog arose from the 6th dorsal to the 2nd lumbar nerves. In 1929, Nitta⁹⁾ showed that in the case of the dog, the sympathetic nerve cells in the spinal cord from D₁ to L₃ segments are mainly located in the lateral column and surface of the transitional zone between the anterior and the posterior column. In the present study, Fig. 1 A- and Fig. 1 B-type responses were obtained upon stimulation in about the same regions that had been regarded as sympathetic areas from D₅ to D₁₂ segments. Usually renal vascular resistance in these responses was remarkably increased, indicating a vigorous vasoconstriction of the kidney. The transient increase in renal blood flow during the initial phase of stimulation that was seen in Fig. 1 B-type response could be explained by considering that the vasoconstriction of the kidney would be preceded by that of the rest of the abdomen.

In Fig. 1 C-type responses that were seen upon stimulation in the upper dorsal segments in Exp. 1, dominant systemic peripheral vasoconstriction took place simultaneously with minor renal vasoconstriction inferred by the slight increase of renal vascular resistance, so renal blood flow might be little influenced. The reason Fig. 1 C-type response was never seen in Exp. 2 could

be the fact that the stimulating experiment in the upper dorsal segments ($D_1 \sim D_4$) was not performed owing to spinal shock.

Many points of Fig. 1 D-type response mainly lay in the upper dorsal segments, and the increase in both blood pressure and renal blood flow was accompanied with little or no change in renal vascular resistance, suggesting that renal vasoconstriction never occurred. Increase of renal blood flow of this type would seem to be partly attributable to a change in prerenal circulation such as an increase in cardiac output. According to Ellenberger et al.,¹⁹⁾ autonomic nerve fibers extending from the 6th cervical to the 4th dorsal nerves are associated with the stellate ganglion. Furthermore, Randall et al.²³⁾ reported that electrical stimulation of the stellate ganglion and associated nerve pathway elicited the cardio-augmentor response. These facts may support our presumption. This matter should be investigated further in the future.

In Fig. 1 E-type response, decrease in renal blood flow was usually less than that of Fig. 1 A- or Fig. 1 B-type response and the degree of increase in renal vascular resistance was intermediate between Fig. 1 A- or Fig. 1 B-type response and Fig. 1 C-type response. This response suggested the existence of a nerve center which affects mainly the renal vessels in the lateral column and surface of the transitional zone between the anterior and the posterior column of middle dorsal, lower dorsal and lumbar segments.

In the present study, upon stimulation in most regions of the posterior column from D_1 to L_3 segments there occurred little or no change in both blood pressure and renal blood flow, suggesting that these areas do not affect the renal circulation.

In Fig. 1 G-type response, the decrease in renal blood flow was accompanied by a hypotensive response without bradycardia, so that this response was not similar to the response that had been observed on efferent stimulation of the divided vagal nerve, but to the response that had been often observed on afferent stimulation of the divided femoral or sciatic nerve in a previous experiment.¹⁾

In experiments of diencephalic⁴⁾ and bulbar stimulation,⁵⁾ it has been emphasized that renal hemodynamics are altered by not only neural factors but also humoral ones. At some points of Fig. 1 A-, B- and C-type responses in the present study, it was also observed that the pressor response or decrease of renal blood flow persisted for a considerable time after the removal of stimulation, suggesting the participation of humoral factors as well as neural ones.

It has been supposed that the autonomic center in the spinal cord might be influenced by the upper centrum such as the medulla oblongata, hypothalamus and cerebral cortex, and to this date many reports concerning the

descending¹¹⁾⁻¹⁵⁾ and ascending pathways¹⁶⁾⁻¹⁸⁾ mediating the autonomic functions have been published, though no definite conclusion has been reached. In the present study, the biphasic or triphasic response (Fig. 1 I and J) observed in Exp. 1 was thought to be induced by these influences, so complete transection of the spinal cord was carried out in Exp. 2. In consequence of this procedure, these responses were never seen, suggesting that the biphasic or triphasic response was induced by a certain complicated mechanism mediated by the upper centrum.

SUMMARY

(1) An increase in renal blood flow accompanied by the pressor response was often seen upon stimulation in the lateral column and lateral border of the anterior column of the upper dorsal segments. Renal vascular resistance in this response was usually little or only slightly increased. This change might occur due in part to an increase in cardiac output.

(2) Stimulation of the lateral column, lateral border of the anterior column and surface of the transitional zone between the anterior and the posterior column from D₅ to D₁₂ segments resulted in an increase in blood pressure and a decrease in renal blood flow. The latter was attributed to renal vasoconstriction.

(3) Upon stimulation in the spinal cord from D₁₃ to L₃ segments, there usually occurred little change in both blood pressure and renal blood flow, but in some cases a decrease only in renal blood flow was observed. The existence of nerves affecting mainly the renal blood vessels was suggested.

(4) Upon stimulation in the posterior column from D₁ to L₃ segments, no changes were usually observed in blood pressure and renal blood flow.

(5) In case of the complete transection of the spinal cord, the results of stimulation of the spinal cord from D₅ to L₃ segments were almost similar to those without transection, although the changes in both blood pressure and renal blood flow were usually decreased. In addition, biphasic and triphasic responses observed in the latter experiment were never seen in the former.

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