THE INNERVATION OF THE RENAL TUBULES*

V. F. Lysov

Department of Physiology (Head, Professor E. N. Pavlovskii), Kazan' Veterinary Institute
(Presented by Active Member AMN SSSR V. V. Parin)
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The problem of the existence of direct nervous reflex influences on the function of the renal tubules has not yet been finally solved. Much remains uncertain about the role of the vagus nerves in these reactions. Our previous researches [4, 5, 6] have shown that the weakening or abolition of the influences of the vagus nerves or of their main branches by means of novocaine, division or atropine causes a marked decrease in diuresis and an increase in the reabsorption of the glomerular filtrate in the tubules. Conversely, stimulation of the function of the vagus nerves leads to increased diuresis and a decrease in the tubular reabsorption of the glomerular filtrate. However, it cannot be concluded from these findings that the fibers of the vagus nerves have a direct influence on the renal tubules, for the decrease in diuresis may be the result of a change in the function of the afferent fibers of the vagus nerves, related to the activity of the hypophysis.

In the present study we attempted to discover whether afferent fibers for the kidneys were present in the vagus nerves.

EXPERIMENTAL METHOD

Acute experiments were carried out on 13 dogs under thiopental or combined morphine and thiopental anesthesia, and chronic experiments were performed on 9 dogs in which the ureters had previously been exteriorized to the skin of the abdominal wall. In order to find out if the vagus nerves contain afferent fibers for the kidneys, we studied the diuretic function of the kidneys during stimulation of the peripheral end of the divided vagus nerve induction current. To exclude any influence on other organs (especially the heart) during these experiments, the vagus nerve was divided in dogs Nos. 4 and 5 and in Zhuk in the neck after preliminary division of the cardiac branches; in Nos. 6 and 7 and Rys'—below the origin of the cardiac branches; and in Nos. 8, 9, and 10, Pestrushka and Vyalyi below the diaphragm. Special buried electrodes were fixed to the peripheral end of the nerve. In the acute experiments stimulation was carried out immediately after division of the nerve, and in the chronic experiments on the 2nd day and later until the effect had disappeared. In dogs Nos. 1, 2, 3, 11, Chernaya, and Schastlivyi, the vagus nerve was divided in the neck, and stimulation applied 2-5 days later, after degeneration of the cardiac and vascular fibers (control studies were made of the work of the heart and in the acute experiments the blood pressure was recorded). To exclude the indirect effect of stimulation of the vagus nerve via the adrenal hormones, preliminary denervation of one kidney was performed on dogs Nos. 7, 11, and Rys', and in the dog Chernaya the left kidney was transplanted into the neck. In dogs Nos. 3 and 6 the vagus nerve was stimulated before and after removal of the adrenals. To ensure that the effect was the result of excitation of the vagus nerve and not of the sympathetic accompanying it in a common trunk, in most experiments the sympathetic fibers were separated as far as possible and stimulated separately for control purposes. In dogs Nos. 12 and 13 and in V'yun the vagus nerve was preliminarily divided below the ganglion nodosum, and 2 weeks later in the neck; the effect of stimulation was investigated in the same order. For this purpose, in Pestrushka and Schastlivyi the vagus nerve was stimulated before and after a subcutaneous injection of 3 mg atropine.

To exclude afferent influences from the kidneys themselves during stimulation of the vagus nerve, in dogs Nos. 2 and 5 the splanchnic nerves and the intact vagus nerve were divided, and in Rys', Vyalyi, Chernaya, and Schastlivyi a suprapleural novocaine block of the splanchnic nerves or of the splanchnic and intact vagus nerve was carried out. In Belka and Raket the method of partial depancreatization was used, leading to a disturbance of the

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Effect of Stimulation of the Peripheral End of the Preliminary Divided Vagus Nerve* on Diuresis

No. or name of animal**	Experimental conditions	Kidney	Diuresis (ml/5 min)						
			before stimulation		after stimulation				
			1	2	3	4	5	6	7
1	Stimulation of right vagus nerve for 5 min 4 days after division in the neck	Right	3.1	3.3	6.4	4.4	2.2	3	3
		Left	2.6	2.8	6.9	4.2	2	2.3	2.9
2	Stimulation of right vagus nerve for 10 min 4 days after division in the neck. The left vagus and splanchnic nerves were divided below the diaphragm 30 min after stimulation.	Right	2.3	2.1	4	5.1	3.3	2.1	1.8
		Left	2.5	2.4	4.3	5.8	3.7	1.7	2.2
Pestrushka	Stimulation of left vagus nerve for 10 min 24 h after division below the diaphragm before and after subcutaneous injection of atropine	Right	9.4	10.1	16.2	18.3	4.7	9.5	8.2
		Left	8.4	8.8	17.5	19.6	6	7.9	7.3
		Right	2	1.8	2.1	2.3	1.7	2.2	1.9
		Left	2.2	2.1	2.3	2.4	2.2	2	2.1
6	Stimulation of right vagus nerve below origin of cardiac branches for 10 min 24 h after division and 1 h after adrenalectomy	Right	1.9	2.2	3.7	4.5	2.5	2.1	1.7
		Left	1.5	1.7	2.9	4	2.2	1.4	1.6
		Right	1.6	1.5	3.1	3.6	3	1.9	1.1
		Left	1.4	1.4	2.3	2.9	2	1.2	1.3
Schastlivyi	Stimulation of right vagus nerve for 5 min 4 days after division in the neck	Right	3	2.8	5.5	2.5	3.1	3.3	3.1
		Left	3.6	3.5	8.3	2.7	3.2	3.5	3.3
Raket	Stimulation of right vagus nerve for 10 min 3 days after division and partial depancreatization before and after injection of acetylcholine.	Right	6.8	6.6	6.8	6.5	6.9	7.1	6.5
		Left	8.5	8	8.6	8.7	8	8.4	7.7
		Right	5.5	4.9	6.2	6.8	4.1	4.5	3.9
		Left	7	7.3	8.7	9.2	6.4	6.8	6

* In all dogs except Pestrushka the right nerve was divided.

** The numbered dogs were used in the acute experiments.

acetylcholine formation in animals [3], and causing a substantial disturbance of the activity of the parasympathetic nervous system. Depancreatization by A. V. Kibyakov's method was carried out simultaneously with division of the vagus nerve in the neck. The effect of stimulation of the vagus nerve was investigated 3-4 days later and subsequently, before and 2 h after the intravenous injection of acetylcholine in a dose of 4 ml of a 1 : 100,000 solution.

Essential conditions for all the experiments were that the nerve should be in good condition and the heart working at near its normal rhythm (using absence of a pain reaction as criterion). The influence of the right and left vagus nerves was studied. Stimulation was by means of a current with a frequency of 1-2 imp/sec and with fast impulses (through the electromagnetic interrupter of a high-frequency generator). Stimulation continued for 3-15 min; with intervals if long periods of stimulation (more than 5 min) were used; 1 min of stimulation–1 min of interval, and so on. Stimulation was repeated several times in the course of the experiment with short (5 min) and long (50 min) intervals. The urine was collected during periods of 5-10 min. In some acute experiments when diuresis was relatively small, the volume of urine excreted was recorded by means of a drop counter on the drum of a kymograph. The effect of stimulation of the vagus nerve was studied in association with both the ordinary and water diuresis (introduction of 30 ml/kg body weight of water into the stomach). In the acute experiments, 150-200 ml of physiological saline was injected intravenously to stimulate diuresis.

The renal function was studied by the inulin and endogenous creatine methods.

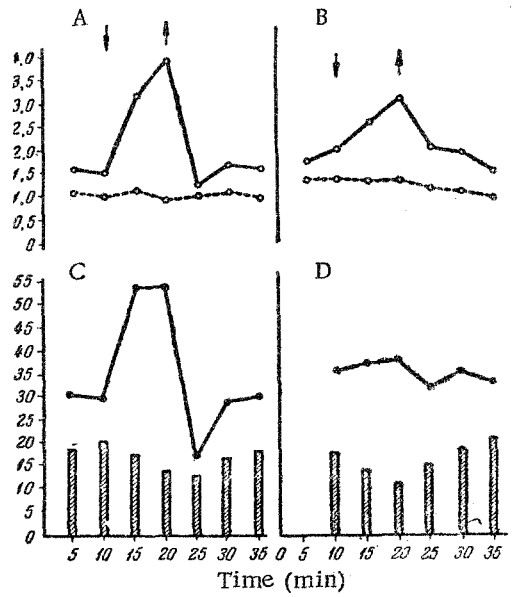
In order to ascertain the effect of stimulation of the vagus nerve on the phosphatase activity in the kidneys, histochemical methods were used (in four dogs 1 h after division of the vagus nerves and immediately after stimulation their diuresis could not be counted). Alkaline phosphatase was detected by Gomori's method as modified by Biesele [7].

EXPERIMENTAL RESULTS

Stimulation of the peripheral end of the divided vagus nerve in dogs caused an increased diuresis from both kidneys (see table), as a rule more marked on the same side. An exception was given by dogs in which the vagus nerve was divided in the neck and stimulated a comparatively long time afterwards, after degeneration of the cardiac and vascular fibers: the reaction of the kidney on the same side was usually lower in this case than on the opposite side. It is evident that at this time structural changes [1] were taking place in the kidney on the side of division of the nerve, and that diuresis was significantly reduced [4, 5, 6].

Stimulation of diuresis began during the first 5-min interval after stimulation of the nerve; with resumption of stimulation of the nerve the diuresis increased still further during the second 5-min interval. After stimulation had been discontinued, the diuresis returned comparatively quickly (in 10-20 min) to its initial level. Stimulation of the vagus nerve was repeated several (up to 5) times at intervals of 5 min or longer, and an increased diuresis always resulted. No direct relationship was observed between the degree of increase of diuresis and the time elapsing after division (within the first 5 days). The effect subsequently decreased, and disappeared on the 8th-9th day. In some dogs the increase in diuresis was more marked during the first days after division, in others later (on the 4th-5th day). The degree of increase of diuresis was also independent of the site of stimulation of the vagus nerve.

In the experiments in which the kidney was transplanted into the neck (Chernaya) or one kidney was denervated (Rys'), during stimulation of the vagus nerve the diuresis from the intact kidney increased while that from the grafted and denervated kidneys was unchanged. Adrenalectomy likewise had no appreciable influence on the effect of stimulation of the vagus nerve. Stimulation of the sympathetic nerve, separated from the vagus, and of the whole peripheral end of the vago-sympathetic trunk after preliminary division of the vagus nerve below the ganglion nodosum, and also stimulation after injection of atropine caused no significant change in diuresis. Hence, we concluded that the increased diuresis from the kidneys during stimulation of the vagus nerve was the result of the passage of efferent impulses along the vagus nerve directly to the functioning elements of the kidneys. We consider that this conclusion is confirmed by the results of the experiments in which the vagus nerves were stimulated in dogs after partial pancreatectomy and administration of acetylcholine. Stimulation of the vagus nerve on the 3rd-4th day after removal of the pancreas caused no visible change in the diuresis; similar stimulation of the vagus nerve 2 h after injection of acetylcholine. led to an increase in diuresis.



Effect of stimulation of the peripheral end of the vagus nerve, preliminarily divided in the neck, on diuresis (A), filtration and the concentration index (B); the same after novocaine block of the splanchnic nerves (C and D). Experiment on the dog Chernaya with the left kidney transplanted into the neck 3 days after division of the left vagus nerve. The value of the inulin concentration index is shown by the columns. a) Left transplanted kidney (reaction absent); b) right kidney. The arrows mark the beginning and end of stimulation.

The results showing the change in filtration and in the concentration index are given in the figure. Stimulation of the vagus nerve caused an increase in the filtration during the first 5-min interval. If the stimulation was continued, the filtration remained at the same level during the second 5-min interval as during the first, or showed a further increase. Immediately stimulation ceased, the filtration fell below its initial level; its restoration began during the next 5-min interval.

The concentration index of both creatine and inulin was considerably reduced after stimulation of the vagus nerve, indicating a decrease in the reabsorption of filtrate in the renal tubules. The decrease in reabsorption was observed during the first 5-min interval after the beginning of stimulation of the vagus nerve, but reached its maximum only during the second or third 5-min interval (even if stimulation lasted only 5 min), and on cessation of the stimulation the reabsorption returned to normal in the course of 1-15 min.

We stated above that some of the chronic experiments involved stimulation of the vagus nerves after degeneration of their vascular fibers. Here too, however, the reabsorption was decreased and filtration increased. A chain

reaction was evidently set in motion in these conditions, due to the change in the state of the kidney elements, and leading ultimately to an increase in the blood supply to the kidney, and hence to an increase in filtration.

Stimulation of the vagus nerve after novocaine block of the splanchnic nerves (see figure, C, B, D) caused an increase in diuresis and a decrease in reabsorption, but left the filtration almost unaffected. At later intervals after the block, when the function of the nerves had been restored, stimulation of the vagus nerves also led to changes in the filtration.

There is no agreement in the literature regarding the effect of stimulation of the vagus nerve on the diuretic function of the kidneys. Some writers [10] consider that stimulation of the vagus nerve leads to a delay in the secretion of urine, while others [8], on the other hand, consider that secretion is increased. Certain writers [9] deny that the vagus nerve has any direct influence on the renal function.

In our experiment stimulation of the peripheral end or the previously divided vagus nerve led to an increase in diuresis. The time difference between the onset of the changes in filtration and reabsorption under these circumstances, and also the fact that during stimulation of the vagus nerve after blocking the splanchnic nerves only the reabsorption was altered, suggest that the increase in diuresis during stimulation of the vagus nerves is the result of the transmission of efferent impulses along these nerves, not only to the renal vessels, but also directly to the functioning elements of the renal tubules. Investigation of the alkaline phosphatase activity in the renal tubules showed that it was decreased during stimulation of the vagus nerves. This was additional evidence of the passage of impulses along the vagus nerves to the renal tubules.

SUMMARY

Investigations were conducted on 13 dogs in experimental conditions under thiopental or morphine-thiopental anesthesia, and on 9 dogs in chronic experimental conditions with the ureters exteriorized on the abdominal wall. As shown, stimulation of the peripheral end of the previously divided vagus (on the neck, below the point of origination of the cardiac branches, under the diaphragm) increased the amount of glomerular filtrate, and reduced water reabsorption by the convoluted tubules with a rise of diuresis. Stimulation effect could be removed by atropinization. Denervation of one kidney eliminated the stimulation effect on this kidney. Disturbance of the acetylcholine-forming process by partial depancreatization by Kibyakov's method also removed the stimulation effect. The effect was partially restored by acetylcholine administration for the purpose of compensation. Stimulation of the vagus nerve in the animals with divided splanchnic nerve and intact vagus mainly reduced the reabsorptive function and increased diuresis. Alkaline phosphatase activity diminished in the kidneys as a result of vagus stimulation. No significant effect was exerted in the function by stimulation of the sympathetic nerve which follows the vagus course. The effect produced by vagus stimulation was not eliminated by adrenalectomy. Therefore the action exerted by the vagus upon the renal tubules is considered to be direct.

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