EFFERENT NERVES OF THE TRANSPLANTED REINNERVATED KIDNEY*

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In previous investigations we showed that with anastomosis of the central end of the vagus to the peripheral ends of nerves from the transplanted kidney the afferent innervation of this organ is reestablished [6, 7]. In association with various types of stimulation to the interoceptors of the transplanted reinnervated kidney, reflex reactions are observed which are characteristic of the vagal center (coughing, vomiting, changes in the amplitude and rhythm of the respiratory movements). We had no facts available to show the restoration of efferent innervation under the conditions of the indicated anastomosis.

The central end of the vagus has been used many times by investigators for anastomosis with the peripheral ends of various nerves, thus obtaining the restoration of the organ's efferent innervation. The vagus is not only composed of preganglionic cholinergic fibers, but also afferent fibers and postganglionic fibers of the sympathetic system. The latter enter the trunk of the vagus from the superior cervical sympathetic ganglion and travel in a descending direction [4].

Innervation of the intact kidney consists principally of postganglionic sympathetic fibers, and thus it can hardly be doubted that the postganglionic sympathetic fibers entering into the composition of the vagus can regenerate in the postganglionic fibers of the transplanted kidney, since in this case we are dealing with regeneration of nerves belonging to the same system. On the other hand, despite the negative results of Langley and Anderson's experiments [10], a number of investigators have shown that preganglionic (cholinergic) fibers can regenerate in the postganglionic fibers of the sympathetic system (adrenergic) and reestablish functional connections.

Thus, the data in the literature clearly show that under the conditions of anastomosis between the n. vagus and the nn. renales there exists the necessary conditions for restoration of the efferent innervation of the transplanted kidney.

EXPERIMENTAL METHOD

In 4 experimental days we performed autotransplantation of the right kidney to the neck, joining the renal vessels to the carotid artery and jugular vein. During the operation the central end of the vagus was sutured to the peripheral ends of the nerves from the transplanted kidney. The discharging end of the ureter from the transplanted kidney was led out onto the skin of the chest, while the mouth of the ureter from the intact kidney was brough out onto the skin of the abdomen.

The experiments were begun no earlier than 4-6 months after transplantation of the kidney, when regeneration of the afferent fibers was already apparent. Usually within 1-2 months after the transplantation gentle massaging of the transplanted reinnervated kidney caused coughing. It could be expected that in the aforementioned interval (4-6 months) the regeneration of the efferent fibers would also occur.

To clarify the role of the efferent nerves in the function of the transplanted reinnervated kidney it was decided to study the changes in urinary output from this kidney during stimulation of the anastomosed vagus with an induction current.

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In order to exclude the generation of afferent impulses in this case, which could distort the results of the experiment, we transected the anastomosed vagus and stimulated its peripheral portion with the induction current. Thus, changes in urinary output from the transplanted kidney could only be a result of impingement of efferent impulses on the functional elements of the transplanted reinnervated kidney, via the anastomosed nerve.

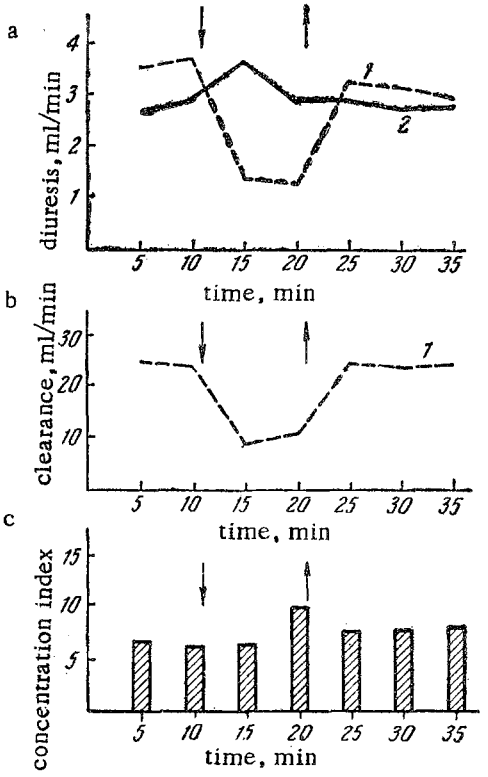

Fig. 1. Change in diuresis (a), clearance (b) and the concentration index (c) of endogenous creatinine in the transplanted kidney during stimulation of the peripheral portion of the anastomosed vagus by induction current. Experiment on the dog, Dezi, July 30, 1958. 1) Transplanted kidney; 2) intact kidney. Arrows indicate the beginning and end of stimulation.

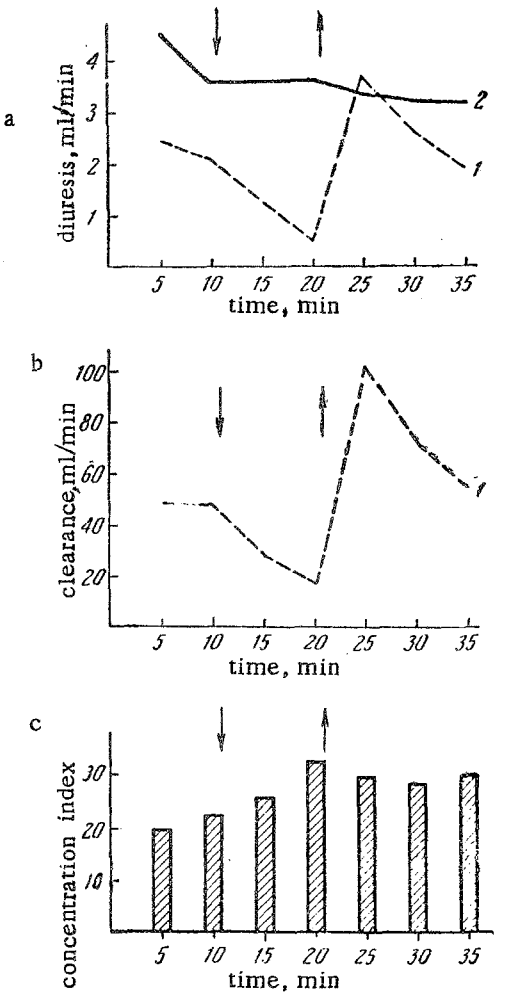

Fig. 2. Change in diuresis (a), clearance (b) and the contentration index (c) of inulin in the transplanted reinnervated kidney during stimulation of the peripheral portion of the anastomosed vagus by induction current. Experiment on the dog, Avve, April 22, 1959. Symbols the same as in Fig. 1.

The right anastomosed vagus was transected under local anaesthesia, as far as possible cranially. Its peripheral portion was taken in a ligature and conducted under the skin of the dog's neck; skin sutures were applied. On the 2nd day following the transection we removed 2-3 of the skin sutures, the vagus was aseptically drawn out to the surface, and we stimulated the nerve with silver electrodes, using induction current from a sliding coil. In some of the experiments we employed stimulation with a current frequency of 5 imp/sec. In others, stimulation was performed with frequent impulses (through an electromagnetic contact breaker on the sliding coil). In all the experiments the stimulation was continued for 10 minutes intermittently: 1 minute of stimulation – 1 minute of rest, and so on. The urine was collected separately from the two kidneys at five-minute intervals. We stimulated the nerve in the setting of a water diuresis, caused by the introduction of water into the dog's stomach (50 ml per kg of body weight). The functioning of the kidney was studied by the method of endogenous creatinine, and also by the inulin method.

EXPERIMENTAL RESULTS

In all 4 of the experimental dogs stimulation of the peripheral end of the anastomosed vagus caused inhibition of the urinary output from the transplanted reinnervated kidney, while the diuresis from the intact kidney remained unchanged (Fig. 1, a and Fig. 2, a). Inhibition of the urinary output already began in the first five-minute interval following initiation of the nerve stimulation; in the second five-minute interval the decrease in urinary output became even greater. After termination of the stimulation the urinary output returned to the original level in the very next five-minute interval.

Urinary output from the intact kidney did not change during stimulation of the anastomosed vagus; thus, we concluded that the reduction in urinary output from the transplanted reinnervated kidney was a result of the flow of efferent impulses along the anastomosed vagus to the functional elements of the transplanted kidney. The character of the reaction, i.e., the rapid onset of diuresis inhibition and the quick return to the original level upon termination of the stimulation all support this conclusion.

Inhibition of the urinary output was observed most clearly in the course of the first 2-3 days after transection of the vagus; then stimulation of the anastomosed vagus yielded a progressively weaker effect, and usually, by the 4th-8th day, stimulation no longer caused a change in urinary output. This can be explained by a degeneration of the nerve fibers following transection of the vagus. In the dog Dezi, stimulation of the vagus caused the most sharply defined effect, which only disappeared on the 8th day; the least clear effect was observed in the dog Zhulik.

Despite the varying rate of the impulses and the different distance of the coils in the apparatus, employed for the stimulation of the vagus in the separate experiments, we observed only the one effect—inhibition of the urinary output.

It was of interest to study the change in the filtration-reabsorption function of the kidneys under the influence of stimulation to the anastomosed vagus.

The data on the changes in filtration for endogenous creatinine are presented in Fig. 1b, and for inulin, in Fig. 2b. The absolute figures for filtration of creatinine were lower than those determined by the inulin method, but the changes were comparable in both methods.

Stimulation of the anastomosed vagus caused a reduction in filtration even in the first five-minute interval after the initiation of the stimulation. In the second five-minute interval the filtration rate in some of the trials remained at the same level as in the first five-minute interval (see Fig. 1b), while in other trials the reduction in filtration became even greater (see Fig. 2b). Immediately upon termination of the stimulation the filtration rose to, sometimes even exceeded, the initial level (see Fig. 2b).

The change in the concentration index for endogenous creatinine is presented in Fig. 1c, and for inulin, in Fig. 2c, in response to stimulation of the anastomosed vagus. In both experiments the concentration index of the indicated substances increased markedly, which testifies to an intensification of the filtrate reabsorption in the renal tubules.

In all the experiments that we performed the maximum increase in reabsorption was only observed in the second five-minute interval after initiation of vagal stimulation, and in the experiment on the dog, Peri, the maximum increase in reabsorption occurred only after termination of vagal stimulation. In the first five-minute interval the concentration indices for the indicated substances either remained unchanged (see Fig. 1c) or increased insignificantly (see Fig. 2c). Analyzing the changes in diuresis, filtration, and water reabsorption under the influence of stimulation of the anastomosed vagus, it can be noted that while in the first five-minute interval after initiation of vagal stimulation the diuresis primarily alters by means of a decrease in filtration, in the second five-minute interval importance in the mechanism of the observed oliguria is already shifted to the intensification in reabsorption in the tubules.

It must be noted that the experiment on the dog, Dezi, (see Fig. 1) was performed on the 2nd day after transection of the vagus, and the experiment on the dog, Avve, (see Fig. 2) was done on the 3rd day after transection i.e., both experiments were carried out with the most preserved vagus, the latter not yet having undergone degeneration. In other experiments, at later periods after the transection, we observed a comparable picture of changes in diuresis in response to stimulation of the nerve, but the diuresis was lessened by a reduction in filtration, and reabsorption remained almost unelevated. At still later intervals, when stimulation of the nerve no longer caused

changes in the diuresis, filtration and reabsorption also remained unchanged. There was a definite relationship between the changes in filtration and reabsorption: the more filtration was reduced, the greater the reabsorption of water. With a small decrease in filtration the reabsorption did not increase.

The experiments performed unquestionably show that the efferent fibers entering into the composition of the vagus grew into the parenchyma of the transplanted reinnervated kidney and are capable of influencing both the functioning of the renal vascular apparatus (glomerular filtration) and the functioning of the tubules (water reabsorption).

It is interesting to compare the results obtained with the data of investigators who studied the effect on urinary output of stimulating the efferent nerves of the intact kidney. Thus, for example, Study and Shipley [11] showed that stimulation of the efferent nerves of the kidney under strict experimental conditions causes a lowering of the filtration rate as determined by inulin, and of the renal blood flow as determined by diodrast. Lowering of the filtration to the zero point was observed by A. G. Ginetsinskii and co-workers [2] with stimulation of the efferent renal nerves under long-term experimental conditions. In our experiments stimulation of the anastomosed vagus also led to reduction in filtration. In addition, an increase in water reabsorption in the renal tubules was observed in our experiments under the influence of stimulation of the efferent fibers in the anastomosed vagus. Comparable results were obtained by A. G. Ginetsinskii and co-workers [2], stimulating the efferent nerves of the intact kidney.

Thus, despite the fact that the transplanted kidney acquired new efferent innervation, normally not characteristic for the organ, the effect of stimulating the anastomosed vagus was the same as with stimulation of the efferent nerves of the intact kidney. In other words, in our experiments we obtained support for the fact that has been established a number of times by many investigators: the function of a nerve is determined by its ending. No matter which nerves approach the nerve endings as a result of anastomosis, they always adopt those terminal synaptic forms which are characteristic for the given tissue [1, 3, 5, 12].

The filtration mechanism plays a decisive role in altering the diuresis during stimulation of the efferent nerves to the transplanted reinnervated kidney. The reabsorption mechanism is often involved later than the filtration process, and causes an even greater inhibition of the diuresis.

SUMMARY

A dog's kidney was transplanted to the neck and the central end of the vagus was joined to the peripheral end of the nerves of this kidney. In 4-6 months, stimulation of the peripheral end of the anastomosed nerve by an induction current reduced diuresis in the transplanted kidney without producing any effect on the function of the intact kidney. Diminished diuresis was due to a drop of filtration and partially to intensified reabsorption.

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