# SOME REFLEXES OF A TRANSPLANTED REINNERVATED KIDNEY

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We have shown previously [3] that the interoceptors of a transplanted reinnervated kidney may be stimulated by injecting solutions of potassium, sodium, calcium,or magnesium chloride into the renal pelvis, or alternatively by injecting sodium or potassium chloride solutions into the artery supplying the kidney in its transplanted position. In the experiments described above, the solutions were injected into the kidney itself; it was then not clear whether stimulation of the interoceptors could occur through the action of substances in concentrations which might be reached in the blood under conditions of high salt intake. It was decided to investigate whether or not such an effect could occur when the concentration of the substances mentioned in the blood was high, and when the kidneys were rapidly excreting the salts. The first observations were made by G. M. Shpuga [4]. A solution of 10-15 g of sodium chloride in 700-800 ml of water was introduced into the stomach of a dog with a transplanted reinnervated kidney. In addition to showing an increased diuresis, the animal coughed and made vomiting movements without actually bringing up the solution. The transplanted kidney was reinnervated from the central end of the vagus, and the results were explained as follows: The excretion of large amounts of sodium chloride results in stimulation of the interoceptors of the transplanted kidney, which in turn leads to the typical vagal response of coughing and vomiting. A similar experiment was carried out by V. N. Chernigovskii and his co-workers [1]. They observed expectorating and vomiting movements when the animal was given a fluid load of water and milk.

The object of the present investigation has been to study this reaction in dogs, and to determine the conditions under which it arises.

## METHODS

The experiments were carried out on two dogs—Zhulik (a male weighing 14.2 kg) and Daisy (a female weighing 24 kg); the right kidney was transplanted into the neck, and reinnervated by joining the central end of the vagus to the stump of the divided renal nerve. The orifice of the ureter of the intact kidney was brought out to the skin of the abdomen. At first we repeated G. M. Shpuga's experiment on a large number of dogs. However,no result was obtained from introducing salt solution into the stomach , i.e., there were neither coughing nor vomiting movements, and only in one dog was there a slight and very occasional indication of a cough. In considering this result it has occurred to us that the innervation may be established differently in each separate case, and the number of afferent fibers growing into the transplanted kidney might be different in different animals. Apparently, in our experiments the threshold of stimulation of the interoceptors of the transplanted reinnervated kidneys was too high to enable G. M. Shpuga's experiment to succeed. We therefore changed the method of introducing sodium chloride, in order to establish a higher concentration in the blood, and to cause it to be maximally excreted with the urine.

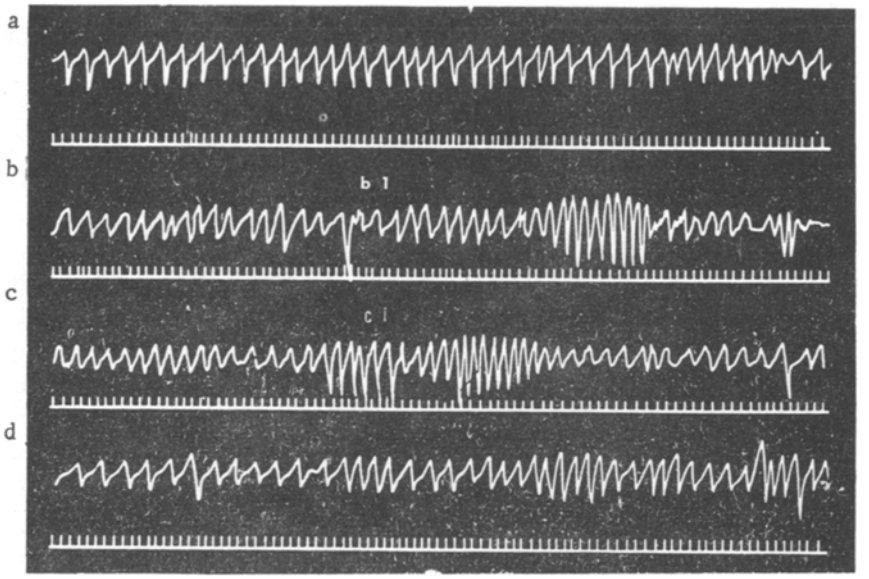


Fig. 1. Changes in respiration in the dog Zhulik following intravenous infusion of a 5% sodium chloride solution. Experiment of July 8, 1958. Duration of infusion 75 min. a) Control recording; b) 60 min after starting the infusion; c) 15 min, and d) 30 min after completing the infusion. b1) Cough; c1) cough.

It was decided to introduce sodium fluoride solution intravenously. The method has been used by other authors to study renal function [5]. In our experiments, 50-70 ml of tap water was introduced into the stomach through a catheter, in order to produce a sufficient diuresis. After 45-60 min, continuous intravenous infusion of a 5% sodium chloride solution was begun. The solution was introduced into a vein of the hind,lower leg at 4-5 ml/min for 60-90 min (usually for 75 minutes). During this time, from 280 to 400 ml of the solution was injected. The amount and the rate caused no ill effects, and no case of poisoning or death occurred. We introduced on average 18.8 ml (from 14.1 to 24.6 ml) of solution per kg weight of the animal, whereas Selkurt and Post used on average 43 ml (from 30 to 54 ml) of the same solution intravenously per kg in a shorter time.

Before the beginning of the infusion and for 1-2 hr after it, breathing movements were recorded on a smoked drum using a pneumatic transmission system. During the whole of the experiment urine was collected at 15 min intervals, and its specific gravity was measured.

After the change in respiration following infusion of 5% sodium chloride solution had been determined, the vagus branch supplying the kidney was sectioned, and the experiment again repeated. In Daisy, three experiments were carried out before section of the vagus and three after, and in Zhulik—four before and two after.

## RESULTS

The experiments were begun 5-6 months after transplanting the kidney and simultaneously restoring its innervation. It was found that a light massage of the transplanted kidney caused coughing, which demonstrated that the afferent innervation had become established. The cough appeared on the 17th day after transplanting the kidney in Daisy and on the 28th day in Zhulik. By the 5-6th month, therefore, we could assume that the nerve fibers had completely regenerated.

Figure 1 shows the respiratory changes following intravenous infusion of sodium chloride. As a rule, during the first 15-20 min after the start of the infusion no changes were observed. After 30-60 min coughing started, either as a single cough, or more frequently as a series of coughing movements following closely on each other (coughing attack). In many experiments a cough occurred 15-45 min before the end of the intravenous infusion. During each experiment, the cough might occur once, though in some there were three to five coughing attacks. Out of the seven experiments on the two dogs, coughing occurred in six. In two,vomiting began 60 and 75 min after the infusion had been completed.

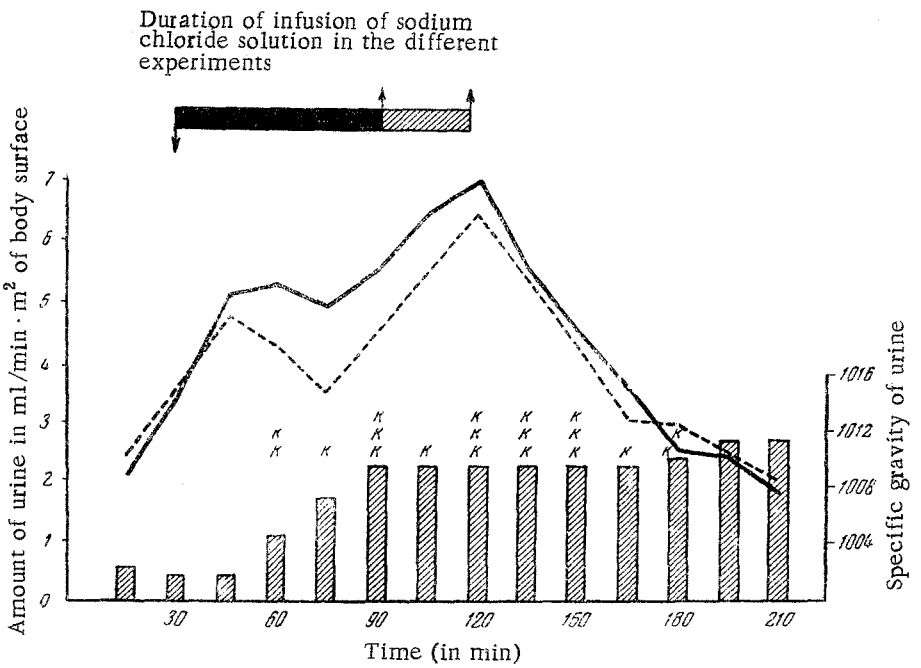


Fig. 2. Change in diuresis and the specific gravity of the urine from the reinnervated transplanted and from the unoperated kidney during intravenous infusion of a 5% sodium chloride solution (average figures for seven experiments on dogs Zhulik and Daisy).

Similar experiments were carried out on both dogs after section of the vagus supplying the transplanted kidney. Infusion of the same amount of sodium chloride at the same rate as before caused no coughing or vomiting in any of the five experiments.

In neither set of experiments was there any definite change in respiration. In Zhulik there was no change either before or after section of the vagus. In Daisy, in both experiments there was a slight increase in rate in response to the intravenous infusion of sodium chloride. Evidently the increase in respiration rate observed in certain experiments does not depend on the presence of or absence of a vagal innervation of the kidney, but is probably due to the resorptive effect of sodium chloride.

The experiments show therefore that injecting large amounts of sodium chloride into the blood stimulates the interoceptors of a transplanted reinnervated kidney, so that the typical vagal response of coughing and vomiting occurs. The correctness of this interpretation is confirmed firstly by the control experiments in which the vagus supplying the transplanted kidney was sectioned, and secondly, by experiments carried out previously [3] in which sodium chloride solution injected into the artery supplying the transplanted kidney was shown to induce a coughing attack.

In our experiments, at the same time that the respiratory movements were recorded we also measured diuresis and the specific gravity of the urine from both kidneys, and it was interesting to compare the two figures. Figure 2 shows the average results of seven experiments carried out on both dogs before vagal section. In order to compare the experiments on the two dogs, the diuresis has been referred to 1 $m^2$ of body surface, and the average results of seven experiments given. The specific gravity of the urine was the same in all samples for both the reinnnervated transplanted and the intact kidney, so that the results for both kidneys are given together.

After introducing water into the stomach, diuresis was noticeably increased. In the control part of the experiment, before the intravenous infusion of sodium chloride solution, the kidneys excreted about the same amounts of urine of a very low specific gravity (1.001-1.003). After the sodium chloride infusion had begun, diuresis was somewhat reduced, and then again increased. Despite the increase, the specific gravity rose to 1.010-1.014, showing that large amounts of sodium chloride were being excreted with the urine. During osmotic diuresis induced by the injection of sodium chloride, the reinnervated transplanted kidney excreted less urine than did the other, whereas for the water diuresis both kidneys produced about the same amount of urine. The difference

was not due to any incompleteness of the innervation, because the same difference remained after vagal section. It appeared that as far as osmotic diuresis was concerned, the transplanted kidney was less efficient than the intact one.

Figure 2 also shows the relationship of the time of appearance of the cough to the amount of urine excreted and its specific gravity. The coughing attacks occurred when the volume of urine was large and its specific gravity high, i.e.,when maximal amounts of sodium chloride were excreted. At the end of the experiment, when the diuresis had considerably abated, despite the continued increase in specific gravity of the urine there was no cough.

As Sel'kurt and Post [5] showed, when large amounts of 5% sodium chloride are injected into the blood stream, there is a rapid increase in the excretion of sodium with the urine. Sodium excretion increases as a result of a marked increase in filtration, which is caused by a reduction in the oncotic pressure of the plasma, an increased blood volume, and some increase in blood pressure. The increased sodium concentration and more rapid filtration causes a considerable increase in the amount of filtered sodium; consequently the reabsorption of of sodium is somewhat increased and the amount per 100 ml of filtrate may be actually somewhat reduced. All these factors facilitate the rapid excretion of sodium with the urine. Under a sodium load the kidneys do more work in concentrating the urine against a high osmotic gradient [2].

It is difficult to say which of the factors are concerned in the reflex responses. Our experiments appear to demonstrate only that when large amounts of sodium chloride are excreted with the urine, the interoceptors of a reinnervated transplanted kidney are stimulated, so that a typical "vagus" response, as shown by a coughing attack, is induced.

## SUMMARY

In dogs, one kidney was transplanted into the neck and reinnervated by Shpuga's method; the central end of the sectioned vagosympathetic nerve was joined to the peripheral end of renal nerves, and the change in respiration due to different stimuli was studied. A reflex change occurred when the kidney was stimulated mechanically or by induced current, or when the renal pelvis was dilated by fluid under pressure or irrigated by sodium, potassium, calcium, or magnesium chloride solutions. By this method it was possible to experiment on the kidney interoceptors in chronic preparations.

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* Original Russian pagination. See C.B. translation.