CERTAIN REFLEXES OF THE REINNERVATED TRANSPLANTED KIDNEY

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The reflex influences of the kidney, pelvis and ureter upon the functions of various organs and systems have been investigated by many authors.

N. P. Simanovsky [5], observed reflex alterations in blood pressure and cardiac rhythm when the pelvis and ureter were stimulated. V. V. Zakusov [2] studied reflex influences of the kidney vessel interoceptors using the perfusion method and came to the conclusion that only high concentrations of nicotine and aconite could alter reflexly the blood pressure and respiration. V. N. Chernigovsky [7] gave decisive proof in favor of the existence of kidney interoceptors when he showed that such substances as acetylcholine, carbonic acid and similar substances produced reflex alterations in blood pressure and respiration when they were present in concentrations approaching their usual physiological levels.

V. N. Chernigovsky, as well as O. S. Merkulova [3] and I. P. Nikitina [4], performed acute studies only. Relatively little has been done concerning the role of interoceptors of the kidney in the intact organism.

G. M. Shpuga [8] proposed a method for restoring the innervation of the intact kidney after it had been transplanted, the procedure being to anastomose the central end of the vagus-sympathetic trunk in the neck to the peripheral ends of the kidney nerves. This method has been used to study the role of efferent nerves in urinary formation [9] and also permits an approach to an investigation of reflexes arising from the kidney interoceptors under the conditions of a chronic experiment.

EXPERIMENTAL METHODS

In five dogs an autotransplantation of a kidney was performed, it being moved to the neck region. The right kidney was transplanted to the cervical region, the right carotid artery being anastomosed to the renal artery and the right jugular vein being joined to the renal vein. After the circulation in the transplanted kidney had been restored, the central end of the right vagal sympathetic trunk was joined to the peripheral end of the kidney nerves. The nerves were sewn end to end, a fine caproned thread being used for the one or two ties. In this manner, conditions were set up permitting the vagus to grow into the transplanted kidney parenchyma. The kidney thus became reinnervated, the nerves lost during the transplantation becoming replaced. It should be observed that the new innervation is materially different from that possessed by the intact kidney.

EXPERIMENTAL RESULTS

Following one or two months after the transplantation, in the experimental dogs the following phenomenon developed: light massage of the transplanted kidney evoked coughing; a similar effect was produced when the transplanted kidney was tapped lightly with the handle of a scalpel.

In the first experimental series we studied respiratory changes produced by mechanical irritation of the transplanted, reinnervated kidney as well as the changes produced by stimulating the kidney parenchyma by means of an induction current. In the first 2-3 months after the transplantation, mechanical irritation of the kidney produced the following stages of respiratory alterations. First, mechanical stimulation of the kidney increased the depth of respiration, this being followed by individual cough impulses and, finally, there would be a fit of coughing. After 3-4 months following the operation the coughing attack would be succeeded by a retching movement which would not, however, lead to any production of vomitus.

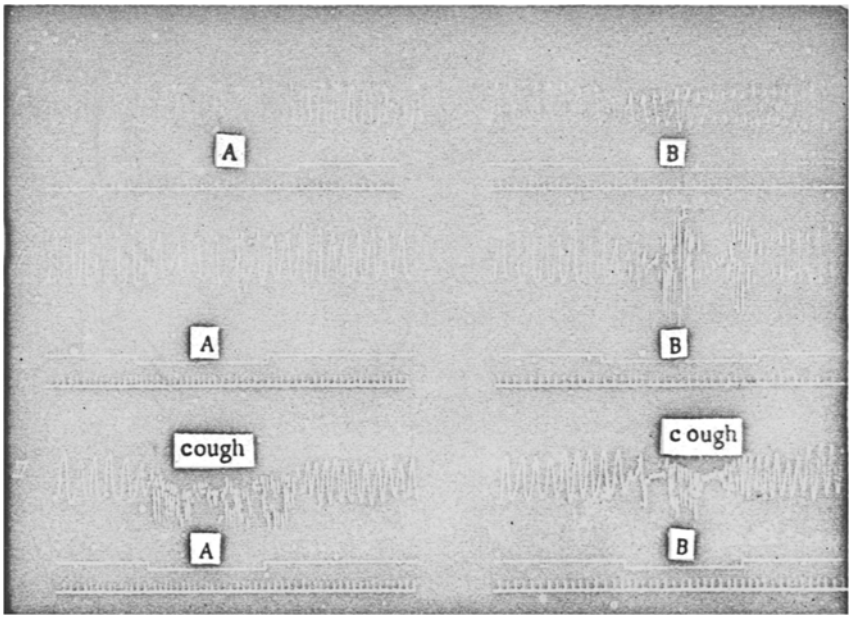

Fig. 1. Respiratory changes induced by kneading (A) and tapping (B) the reinnervated kidney of the dog Bulb. I) After 39 days; II) after 48 days; III) 53 days after transplantation of the kidney and restoration of the innervation.
Significance of tracings (from above): respiration, stimulation, time record (2 seconds).

The cough, arising from tapping the kidney, appeared sooner after the operation of transplantation than did the cough due to massage (Fig. 1).

Control experiments in which the skin and muscles around the kidney were stimulated proved that there would be coughing only when the kidney itself and not the surrounding tissues were stimulated. These experiments indicate that it was the vagus that reinnervated the kidney.

The cough reflex which we observed when we stimulated the transplanted kidney which had become reinnervated by the vagus nerve is readily understood when the experiments of P. K. Anokhin and A. Ivanova [1] are studied.

The parenchyma of the reinnervated transplanted kidney was stimulated by means of an induction current. The parenchyma of the transplanted reinnervated kidney was pierced by needle electrodes introduced through the overlying skin and connected to the secondary coil of the induction apparatus. When the intensity of the stimulus was increased, the following events were observed. Cough appeared first, this being followed with increasing current strengths by typical retching and raising of vomitus (Fig. 2).

Comparing the results of this experiment with the data of other workers [2], we can affirm that induction current stimulation of the parenchyma of the transplanted, reinnervated kidney produces more clearly evident reflex response than does stimulation of the intact kidney.

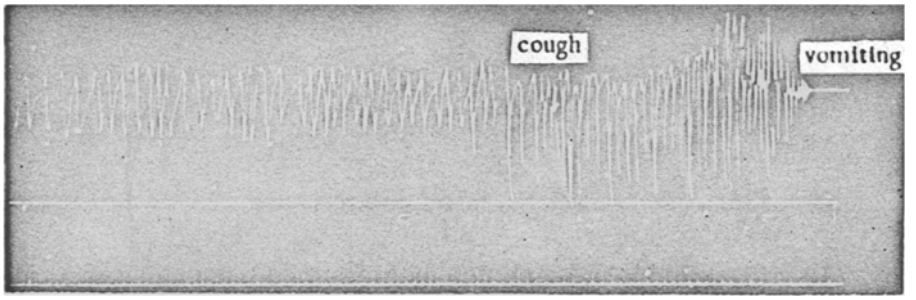

Fig. 2. Respiratory changes induced by stimulating with induction current (obtained from transformer apparatus, voltage in first coil being 4 V with a frequency of 60 stimuli per minute) the parenchyma of the transplanted reinnervated kidney. Significance of tracings as in Fig. 1. The figures in centimeters the distance of the coils in the sled apparatus.

Thus, the first series of experiments indicates that mechanical and electrical stimulation of the parenchyma of the transplanted, reinnervated kidney causes irritation of its interoceptors which manifests itself by corresponding reflex reactions.

In the second series of experiments we explored the reflexes in the transplanted, reinnervated kidney when its pelvis and ureter were stimulated mechanically and chemically.

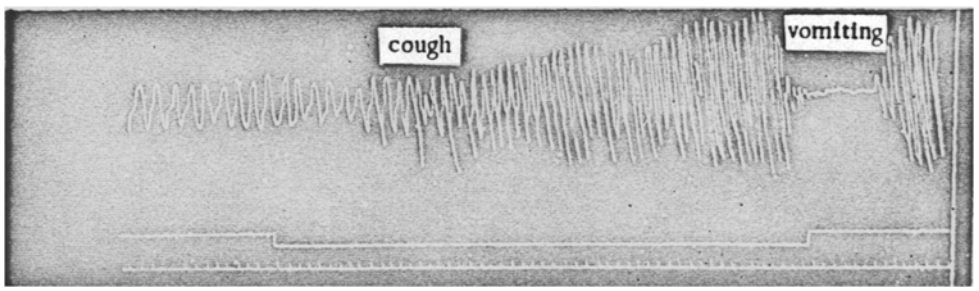

Fig. 3. Respiratory changes when the pelvis of the transplanted, reinnervated kidney was distended by the pressure of the contained fluid.
Significance of tracings the same as in Fig. 1.

To stimulate mechanically the pelvis and ureter we employed the following method. With the aid of a fine ureteral catheter we introduced into the pelvis a solution of physiological saline. A soft intestinal clamp was placed at the ureteral orifice stopping outflow of fluid from the pelvis and ureter.

Distension of the pelvis and ureter under a pressure of 80-100 mm mercury produced in the first experiment coughing and vomiting (Fig. 3) but, when the pelvis was distended the second, third, and fourth times, cough also was produced but vomiting could be induced only with considerably higher, more prolonged

periods of distension and, in further experiments, could not be induced at all. Still later, succeeding experiments could not evoke coughing at all, the distension of the pelvis and ureter causing typical movement reactions on the part of the animal accompanied by increase in amplitude and rate of the respiratory movements, i.e., an illness type of reaction.

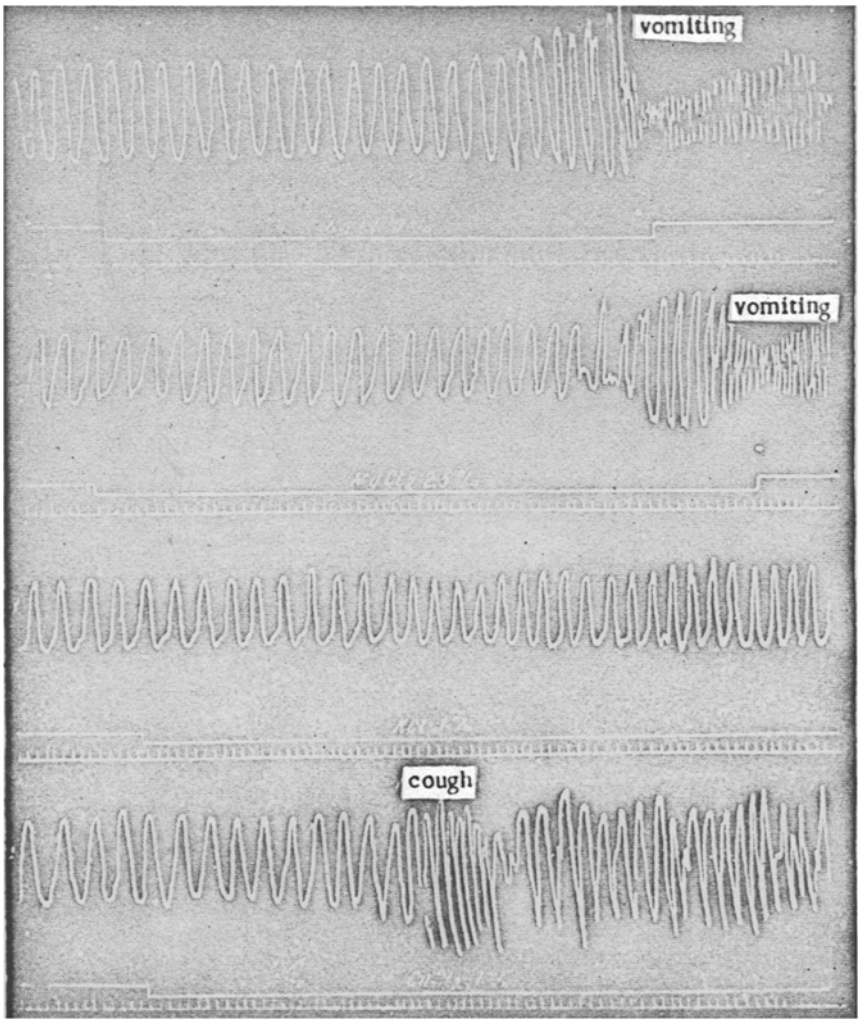

Fig. 4. Changes in respiration induced by irrigation of the pelvis of a transplanted, reinnervated kidney with chlorides of sodium, magnesium, potassium and calcium. Significance of tracings the same as in Fig. 1.

These experiments seem to indicate that continued pelvic irritation in the transplanted, reinnervated kidney changes the vagal responses – cough and vomiting – by a reaction of illness. The disappearance of this "vagal" response to systematic stimulation of the pelvis and ureter may be due to a "transformation" [1] of the center or, possibly, an adaptation of the pelvic interoceptors to continuing irritation.

In further experiments we decided to observe whether there would be a response on the part of the pelvic interoceptors of the transplanted reinnervated kidney to chemical stimuli.

The pelvis of the transplanted, reinnervated kidney was irrigated through the ureteral catheter with various fluids which were permitted to flow out freely. Control experiments on the transplanted, reinnervated kidney using normal saline showed that respiration was unaffected.

The greatest respiratory alterations were observed when the pelvis was irrigated with various salt solutions. Sodium chloride in 5-10% solutions induced vomiting; smaller concentrations did not materially affect respiration. Vomiting was also induced by a 2.5% solution of magnesium chloride. When the pelvis was irrigated by potassium chloride solutions as weak as 1%, the amplitude and frequency of the respirations was increased. It is interesting that potassium chloride in concentrations as high as 5-10% produced neither cough nor vomiting. Beginning with 1% concentrations, irrigation of the pelvis with calcium chloride produced definite increase in the amplitude and frequency of the respiratory movements. In Fig. 4 is seen the effect of a 1% solution.

When the pelvis was irrigated with solutions of ammonia and glucose, even in concentrations as strong as 10%, respirations were unaffected, the same being true of solutions of acetylcholine and adrenalin (1: 10,000).

It is evident from these experiments that the interoceptors of the pelvis are most sensitive to saline solutions, as some of these evoke effects in concentrations as weak as 1%. However, these results do not mean that the pelvic interoceptors play an important role in normal physiological surroundings as relatively high concentrations of the salts are required to stimulate them.

Comparison of experiments performed in irrigating the pelvis of the transplanted, reinnervated kidney with those made on the intact kidney leads to the conclusion that this is a valid method for examining those interoceptor reflexes which cannot be studied under normal conditions.

This method of reinnervating the transplanted kidney permits a study of interoceptor influences existing in the vessel stream under chronic experimental conditions. Our experiments are only preliminary. Into the artery going to the reinnervated transplanted kidney a 2% solution of sodium chloride injection would induce coughing, while a 0.5% solution of potassium chloride would result in increased frequency of respirations. Control experiments injecting similar solutions into the jugular vein did not alter respirations. This must mean that the injection into the artery leading to the transplanted, reinnervated kidney stimulated the interoceptors of the vessel bed in the kidney. It is probable that this reinnervation will permit kidney perfusions in chronic experiments.

DISCUSSION OF RESULTS

The experiments described above indicate the presence of reflex mechanisms when the parenchyma of the transplanted, reinnervated kidney is stimulated mechanically or electrically, and when the pelvis is stimulated mechanically or chemically. These effects are more evident than when the intact kidney is stimulated in a parallel manner.

This lesser reflex response on the part of the intact kidney may be due to the fact that the stimulus spreads diffusely through the entire nervous system [7, 3, 4, 6]. As these authors have shown, under specific conditions reflexes from kidney interoceptors affect blood pressure, respiration, the skeletal musculature and lymphatic circulation.

The impulses arising during stimulation of the transplanted, reinnervated kidney interoceptors enter the vagus nerve by way of its afferent pathways and flow to the respiratory, coughing and vomiting centers. In the experimental animals we observed a very sensitive response of the respiratory center to the most varied stimuli to the interoceptors of the transplanted, reinnervated kidney. It may well be that other systems are also affected. It is only the simplicity and proven sensitivity of the respiratory system that made us confine our studies to just this indicator.

It must be true that the respiratory, cough and vomiting centers respond in their specific manner when the interoceptors of the transplanted, reinnervated kidney are stimulated; while this limits somewhat the investigative procedures, it does permit a clarification as to just which stimuli and to what degree will affect the interoceptors of the transplanted, reinnervated kidney.

SUMMARY

The right kidney was transplanted in 5 dogs, being moved to the cervical region. The vagus was anastomosed to the nerve trunk leading to this kidney. The afferents grew in from the kidney so that mechanical and chemical, as well as electrical stimulation of the kidney parenchyma or the kidney pelvis would lead to respiratory alterations or affect the vomiting and cough centers.

Results, so far, are preliminary in nature and further studies will be undertaken.

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