# FATIGUE IN THE RECEPTORS OF THE KIDNEYS

## (RESULTS OF AN ELECTROPHYSIOLOGICAL INVESTIGATION)

Yu. L. Pines

UDC 612.467.3.014.32

In a previous investigation [4] the nature of the depression of the activity of the renal receptors arising during the first 1-5 sec of their transient and intensive stimulation (the phenomenon of adaptation) was studied.

The object of the present investigation was to continue the electrophysiological analysis of the activity of the renal receptors and to study their activity in the conditions of prolonged stimulation, for a period of tens of minutes.

## EXPERIMENTAL METHOD

Experiments were carried out on 26 cats anesthetized with hexobarbital (70 mg/kg body weight intravenously). An oscillographic method was used to detect and record the bioelectrical activity from the unseparated nerves in the renal plexus. The biopotentials were recorded from the peripheral ends of the divided nerve. The renal receptors were stimulated by stopping the flow of blood from the kidney by clamping the renal vein; in this way the kidney tissues became considerably stretched, as shown by the increase in the volume of the kidney recorded by oncography. Stimuli of long duration (about 30-40 min, loading) and of short duration (about 5 sec, testing) were used.

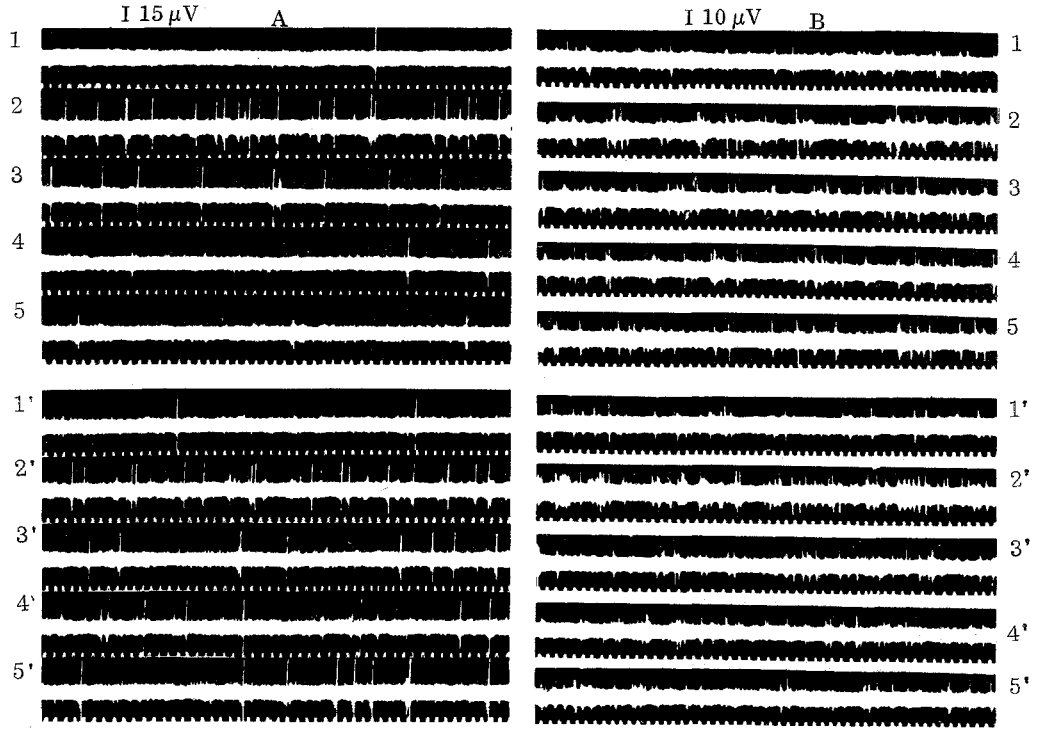


Fig. 1. Disturbance of function of the renal receptors during their prolonged stimulation before and against the background of the action of calcium chloride or potassium chloride. A, B, 1) Spontaneous impulses in renal nerves; A, B, 2-5) impulses 5 sec, and 3, 10, and 15 min respectively after clamping the renal vein; A, 1'-5' the same after injection of 20-25 ml 1.1% $CaCl_2$ solution; B, 1'-5') the same after injection of 20-25 ml 1.1% KCl solution. Time marker 0.02 sec.

Laboratory of General Physiology, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad (Presented by Academician V. M. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 62, No. 12, pp. 16-21, December, 1966. Original article submitted April 11, 1965.

## EXPERIMENTAL RESULTS AND DISCUSSION

In the initial experimental conditions the background impulsation in the renal nerves consisted of single oscillations with a duration of 1-2 msec, and an amplitude of 15-20 μv, out of step with the pulse rhythm. When the vein was clamped for a long time the volume of the kidney rose to a maximum after 2-5 min and remained at this level as long as the vein was clamped. Despite the continuing stimulation, the frequency of the afferent impulses, after a sharp initial increase, gradually became slower and, in some experiments, after 20-40 min reached a stable minimum (Fig. 1A, B, 1-5). The amplitude of the potentials in these circumstances was lowered by 33-50%.

To analyze the nature of the observed phenomena, the effect of a hyperpolarizing agent ($CaCl_2$) and of a depolarizing agent (KCl) on the receptors was used. Intravenous injection of 20-25 ml of isotonic (1.1%) $CaCl_2$ solution into the general circulation in 50% of cases did not alter the flow of impulses, while in 50% of cases, it weakened the impulses in the renal nerves or delayed the arrival at a stable minimum of activity during stimulation as described above (Fig. 1A, $1^1$-$5^1$). The amplitude of the potentials in these circumstances sometimes increased. Injection of 20-25 ml of isotonic (1.1%) KCl solution in 50% of cases had no effect, while in the other 50%, it caused a more rapid diminution of the flow of impulses (Fig. 1B, $1^1$-$5^1$). The flow of impulses was modified although no visible differences were found in the reaction of the volume of the kidney to clamping the renal vein before and after the injection of KCl or $CaCl_2$. Impulses were recorded when the transient changes in the general blood pressure resulting from the administration of calcium or potassium had disappeared and the pressure was reestablished at a value close to the initial level.

Similar results were observed previously in the muscle receptors of the frog during prolonged stretching of the muscles [11]: replacement of the Ringer's solution bathing the muscle by KCl solution led to a decrease in the intensity of receptor activity, quickly progressing to complete inexcitability; conversely, an increase in the concentration of $CaCl_2$ in the solution delayed the development of inexcitability. Similar results have also been obtained in experiments on the spinal cord [2].

The dynamics of the depression of the function of the renal receptors during their prolonged stimulation was studied by the application of test stimuli of short duration after preliminary loading stimuli of varied duration. The scheme of the experiment was as follows. A test stimulus 5 sec in duration was applied, producing the initial reaction of the receptors, and 20-30 sec later, a loading stimulus with a duration of 1 min was applied; 20-30 sec after this had ended the test stimulus was again applied, followed 20-30 sec later by the loading stimulus again, this time with a duration of 3 min. In this way the duration of the loading stimulus was increased to 5, 10, 20, 25, and 30 min, and each time the reaction of the receptors to the test stimulus was examined 20-30 sec after its end (Fig. 2, scheme of experiment). The first test stimulus caused an intensive, sharply increasing reaction of intensification of receptor activity (the frequency in the first seconds was 200-250 impulses/sec), followed by a slowing of the frequency of the afferent impulses, i.e., by adaptation (Fig. 2A). Immediately after the loading stimuli of increasing duration, initially less intensive reactions without adaptation (frequency 75-150 impulses/sec) developed in response to the test stimuli, but later the reactions followed after an increasingly longer delay, and with each successive stimulus their intensity diminished (Fig. 2B-F). After the prolonged stimuli (25-30 min) a paradoxical reaction of the renal receptors was observed: the frequency of the impulses in response to the test stimulus did not exceed, but became weaker and was less intensive than the background frequency before application of the stimuli (Fig. 2G-H).

Such reactions of the receptors with the development of a paradoxical reaction were not the only type of reaction to the loading stimuli. In some experiments, for instance, the reactions of the receptors to the test stimuli decreased along with a decrease in the initial flow of impulses in the intervals between stimuli.

The different reactions of the receptors to test clampings of the vein took place in association with reactions of the kidney volume which were approximately equal in magnitude and, what is particularly important, equal in their gradient of increase (Fig. 2, kymograms).

After the prolonged stimulation had ended, the initial background activity, and in particular, the initial reactions of the receptors to stimulation of short duration, were restored in many cases slowly and gradually (Fig. 3). This phenomenon was illustrated by an experiment in which test stimuli of equal strength were applied at different intervals of time after the prolonged loading stimulus had been discontinued.

As the receptor activity was restored, the reactions of the volume of the kidney to test clampings of the vein were almost equal in magnitude and in gradient of increase.

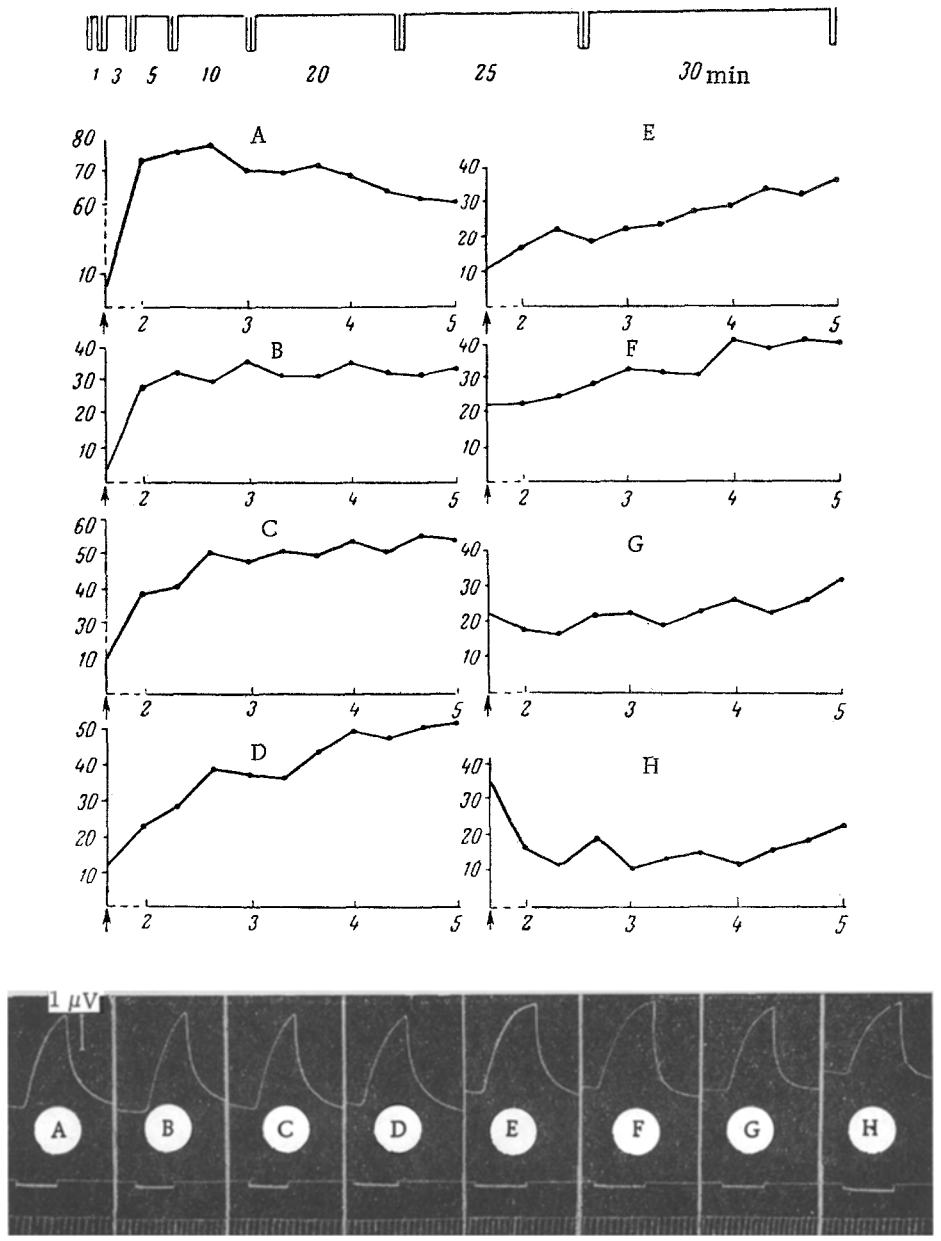


Fig. 2. Dynamics of development of disturbances of the function of the renal receptors. Scheme of experiments: test stimuli of short duration (⊥) and loading stimuli of varying duration (⎍). Vertical axes of graph—frequency of impulses (impulses/0.3 sec); horizontal axes—time (in sec), the arrow points to the time of clamping the renal vein; A—initial reaction of receptors to test stimulus; B-H—the same, 30 sec after loading stimuli of duration of 1, 3, 5, 10, 20, 25, and 30 min respectively. The kymograms (from top to bottom) represent: oncogram of the kidney, marker of clamping the renal vein; time marker (5 sec); A—initial reaction of the volume of the kidney to clamping the vein; B-H—the same 30 sec after loading clamping of the vein for a duration of 1, 3, 5, 10, 20, 25, and 30 min respectively.

One of the factors responsible for depression of receptor function was the intensity of stimulation. If the level of the general blood pressure was lowered by bleeding, the increase in the volume of the kidney in response to clamping the vein was diminished and delayed, i.e., the strength of stimulation of the receptors was reduced. In cases when the blood pressure was lowered to 30-45 mm Hg, it was found that the strength of the afferent impulses was not lowered throughout the experiment (clamping the vein for 25-30 min).

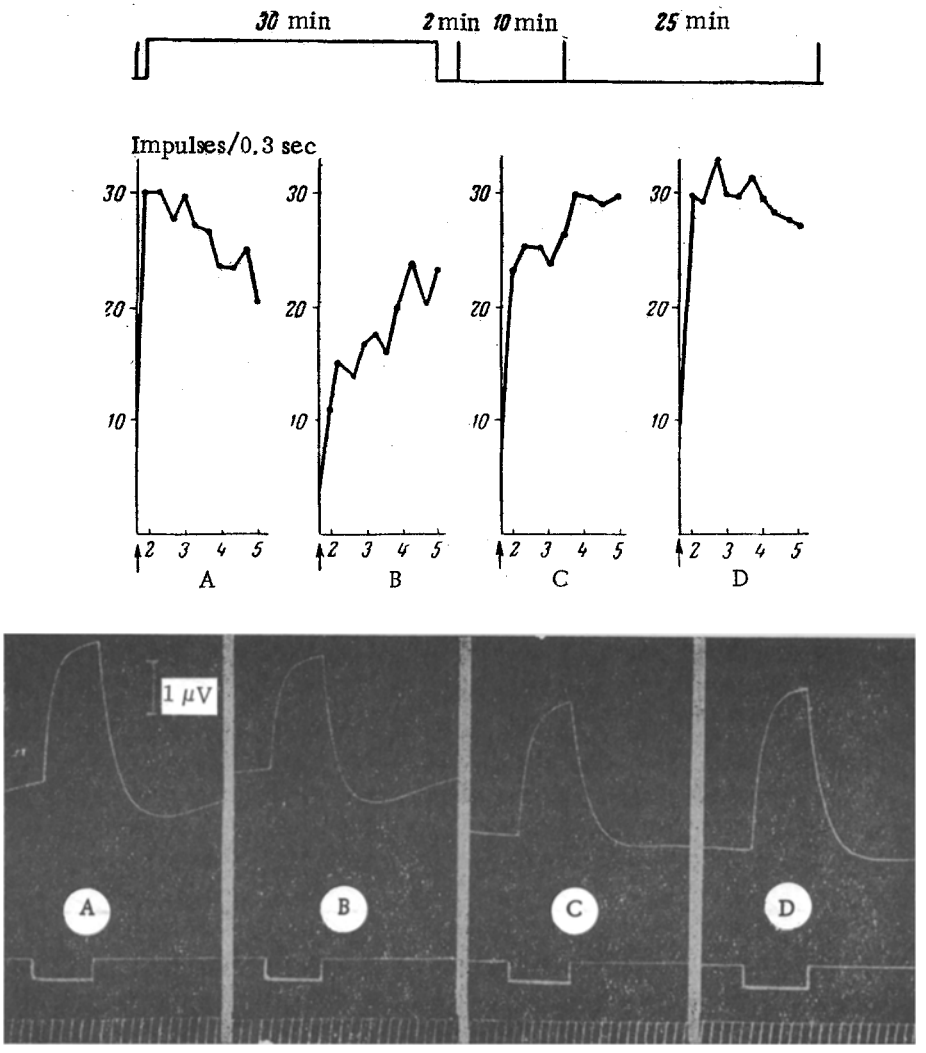


Fig. 8. Restoration of activity of the renal receptors after prolonged stimulation. A—Initial reaction of receptors to test stimulation; B-D—2, 12, and 37 min after removing the loading stimulus with a duration of 30 min. Kymograms: A—Initial reaction of volume of the kidney to clamping the vein; B-D—2, 12, and 37 min respectively after loading clamping of the vein for a duration of 30 min. Rest of legend as in Fig. 2.

Another factor weakening the activity of the receptors in these experimental conditions could have been the influence of ischemic factors (the accumulation of breakdown products as a result of oxygen deficiency), accelerating and aggravating the disturbance of receptor function. It has previously been shown, for instance, that the development of ischemia in the kidney caused by clamping the renal artery leads after various time intervals—from 10 to 30 min depending, evidently, on the initial functional state of the receptors—to weakening of the flow of impulses observed in the renal nerve [3]. This effect develops as a rule after an initial increase in the frequency of the impulses.

Analysis of the depression of the flow of impulses in the renal nerves observed during intensive and prolonged (20-40 min) stimulation of the receptors showed that calcium ions prevent the development of this effect, whereas potassium ions accelerate it. Because of the well-known hyperpolarization action of calcium ions and the depolarizing action of potassium ions, it may be postulated that the weakening of the function of the renal receptors during prolonged stimulation may be a process of depression of the excitability of the receptors, based evidently on the deep depolarization of the receptor membrane. Depression of receptor activity of this type as a result of prolonged and intensive stimulation has been interpreted by some authors as fatigue [9-11]. Depression of the activity of the renal receptors identified when test stimuli were applied after prolonged loading stimuli cannot be explained by a decrease in the strength of the test stimuli, and it also must be regarded as fatigue of the receptors.

Processes of a different character, lying at the basis of the depression of the function of the renal receptors in response to stimuli of short duration, were demonstrated in a previous investigation [4]. In those conditions the depression of receptor activity during the first seconds after their excitation (the phenomenon of adaptation) on the contrary was accelerated by an agent lowering excitability (calcium) and retarded by an agent increasing excitability (potassium). It was therefore, concluded that adaptation of the receptors is based on a process of lowering of the excitability of the receptors as a result of the hypopolarization of the nerve membranes.

Both adaptation and fatigue of the receptors are therefore associated with a decrease of their excitability, but these two phenomena are based on opposite processes.

Another sign distinguishing fatigue of the receptors from adaptation is the duration of development of the changes in the receptor activity. Whereas during fatigue, the processes of depression and restoration of receptor function occupy tens of minutes, in adaptation they occupy only a few seconds.

In the conditions of the present experiment, as also in the case of fatigue of the muscle receptors investigated by Bronk [10] and Matthews [11], the possibility that at least two factors may exert an influence must be borne in mind: the prolonged activity of the receptors and the ischemic disturbance of the metabolic processes.

## LITERATURE CITED


1. I. S. Beritov (Beritashvili), General Physiology of the Muscular and Nervous System [in Russian], 1, Moscow-Leningrad (1947), p. 392; 2, p. 217.
2. T. M. Mamonets, Effect of Potassium and Calcium Ions on the Reflex Activity of the Spinal Cord. Candidate Dissertation, Kiev (1955).
3. Yu. L. Pines, in the book: Problems in the Physiology and Pathology of the Nervous System [in Russian], Moscow-Leningrad (1959), p. 395.
4. Yu. L. Pines, Fiziol. Zh. SSSR, No. 9, 1116 (1965).
5. V. V Rozenblatt, The Problem of Fatigue [in Russian], Moscow (1961).
6. É. I. Slivko, Effect of Stimulation of the Proprioceptors of Muscles on Processes of Fatigue and Recovery in the Nervous Centers of the Spinal Cord. Author's abstract of Dissertation, Kiev (1961).
7. S. A. Tanin, Effect of Stimulation of the Interoceptors of the Internal Organ on the Course of Fatigue and Recovery in the Spinal Cord. Author's abstract of Candidate Dissertation, Kiev (1955).
8. G. V. Fol'bort, in the book: Processes of Fatigue and Recovery in the Activity of the Organism [in Russian], Kiev (1958), p. 3.
9. V. A. Cherkes, The Study of the Processes of Fatigue and Recovery of the Functional Capacity of the Nervous Centers of the Spinal Cord. Author's abstract of Candidate Dissertation, Kiev (1949).
10. D. Bronk, J. Physiol. (London), 67 (1929), p. 270.
11. H. Matthews, J. Physiol. London, 71 (1931), p. 64.