MEDICAL SCIENCES

CHANGES IN THE MODULATORY EFFECT OF SPINAL CORD INTERNEURONS ON THE CENTRAL LINK OF THE SOMATIC REFLEX ARC IN THE LONG TERM OF ANDROGEN DEFICIENCY

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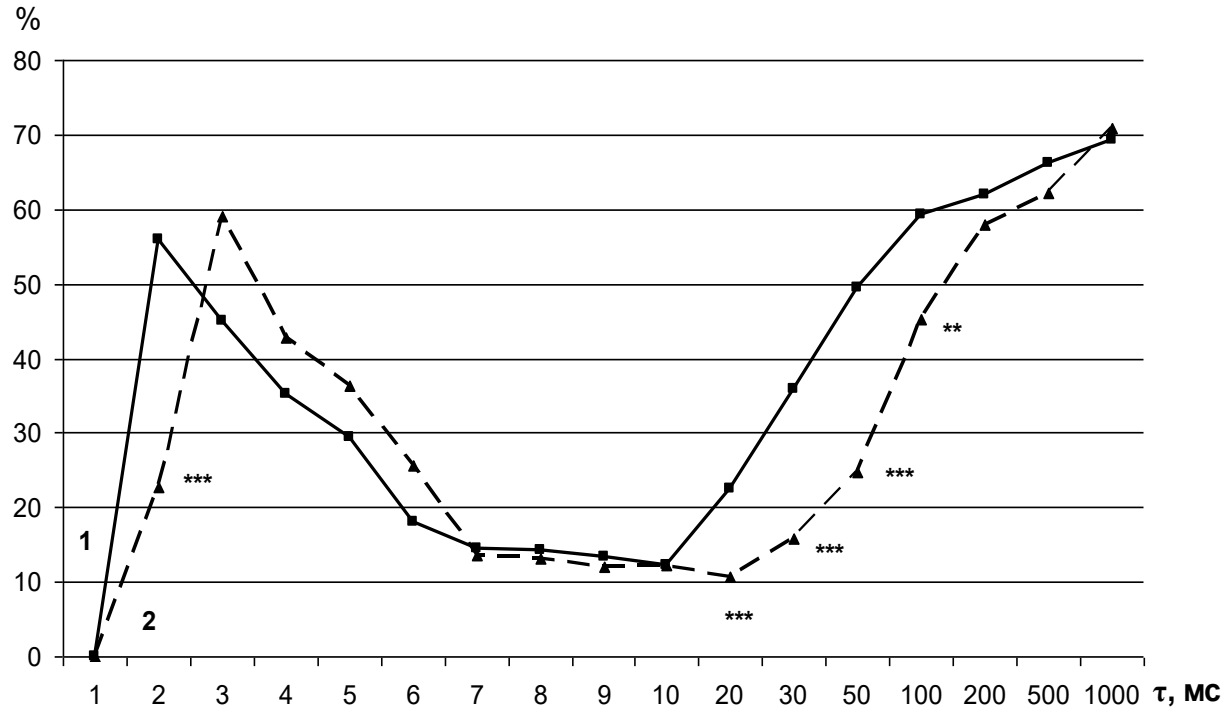
Intraduction. One of the methods of prostate hyperplasia and prostate cancer treating is to reduce the effect of androgens on tumor cells. However, due to the absence of the modulating effect of testosterone, there are disorders in the functioning of other systems, in particular, the nervous system. Considering the prevalence of anti-androgen hormone therapy, the study of changes in the bioelectrical activity of the motoneuron pool of the spinal cord in connection with interneuron groups, as a component of the functional unit of the motor system, is relevant.

Aim. The aim was to study the peculiarities of the influence of interneuron chains on the activity of motoneurons of the anterior horns of the spinal cord in the remote periods of androgen deficiency, which arose acutely.

Materials and methods. Hypoandrogenemia was modeled by bilateral orchidectomy on male Wistar rats aged 5-6 months and weighing 180-260 g. Evoked potentials of motoneuron and interneuron pools within one segment were studied by recording (with bipolar electrodes) monosynaptic discharges of the ventral root (MDVR) and the potential of the dorsal surface of the spinal cord (PDS SC) in the focus of maximum activity (unipolar electrode), respectively. Stimulating electrodes were located on the dorsal root of L5. We used rectangular paired stimuli with an

application interval from 1 to 1000 ms.

Results and discussion. During the analysis of the second MDVR amplitude recovery dynamics when applying paired stimuli with different time intervals, it was found that in intact rats, at an interval between stimuli of 2-100 ms, there was a suppression of the evoced response amplitude to the test stimulus with a maximum at an interstimulus interval of 10 ms (12.31±1, 73% of the value of the evoced response amplitude to the conditioning stimulus) followed by its gradual recovery. In the experimental group, suppression began at an interval of 3 ms and reached a maximum at 20 ms (10.79±1.09% compared to the amplitude of the first evoked responce). In addition, inhibition in the interval from 3 to 7 ms was less pronounced, and the recovery of the amplitude of the response to the test stimulus was slower. Starting from 1000 ms inclusive, both graphs coincided (Fig. 1)



1 – control; 2 – animals with experimental hypoandrogenemia.

Fig. 1. The recovery of the amplitude of MDVR in response to the test stimulus.

Probability level ** – $p<0.01$; *** – $p<0.001$

relative to the corresponding values of the control group

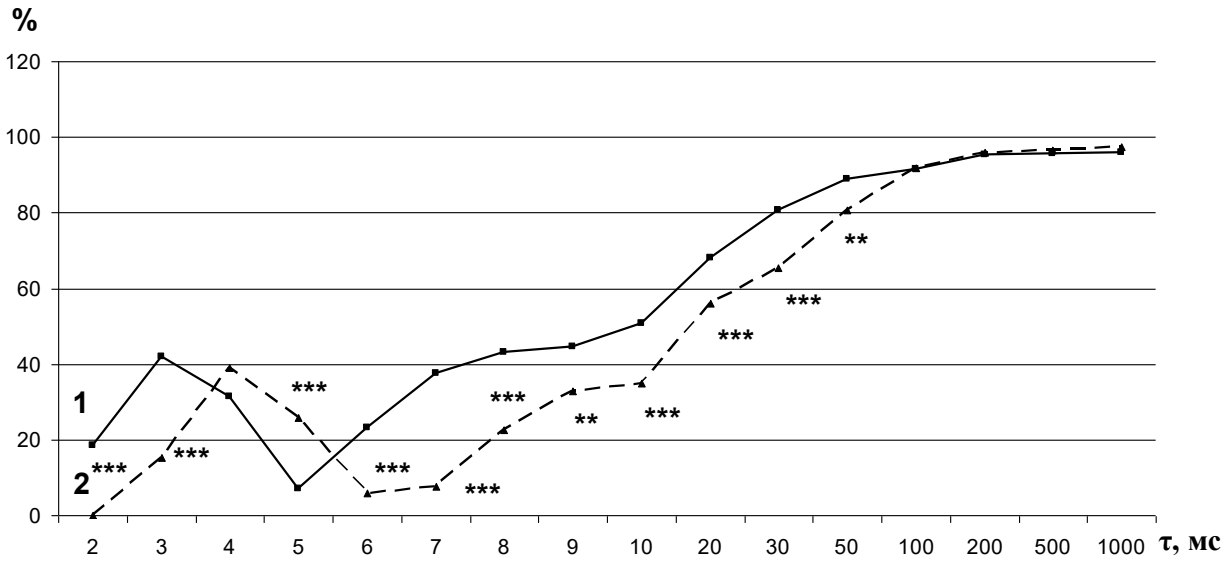
The amplitude of afferent spike of PDS SC increased by 98.33±5.88%, N1 component by 51.08±2.86%, N2 component by 49.64±2.40%, N3 component by 207.41±4.82% ($p< 0.001$). The amplitude of the P-wave showed a tendency to increase by 19.61±4.92% relative to the same indicator of the control group ($p>0.05$).

The duration of the N3 component increased to 193.96±2.42%; the duration of the P-wave decreased to 73.72±3.2% of the control value with a high level of reliability ($p<0.001$).

When studying changes in presynaptic inhibition in the structures of the posterior horn of the SC using the method of stimulation with paired stimuli, we evaluated the restoration of the amplitude of the N1 component in response to the second (testing) stimulus as a percentage of the amplitude of the N1 component in response to the first (conditioning) stimulus with a gradual increase interval between stimulation pulses.

In animals of the control group, at intervals from 0 to 3 ms, an increase in the N1 component amplitude of the second PDS was observed, and from 3 to 5 ms, a decrease in the ones amplitude. Starting from the interval of 6 ms, the growth of the amplitude of the N1 component of the response to the test stimulus had an almost linear character, slowing down slightly in the interval of 200 - 1000 ms. In animals with a hypoandrogenic state, the N1 component of the second response was recorded for the first time at an interstimulus interval of 3 ms, and inhibition of its amplitude growth was observed at intervals from 4 to 7 ms. The rate of further growth of the amplitude of the N1 component also lagged behind the values of the control group, matching only at an interval of more than 100 ms (Fig. 2).

It is interesting that the range of interstimulus intervals in which a pronounced inhibition of the response evoked by the non-testing stimulus was observed was almost the same for both interneuron and motoneuron pools (Fig. 1, Fig. 2), and in terms of duration and location on the time axis of the diagram, it coincided with the duration and location of the P-wave of the SC PDS.



1 – control animals;

2 – animals with experimental hypoandrogenemia.

Fig. 2. Recovery of the N1 component of the SC PDS in response to the test stimulus.

Probability level ** – $p<0.01$, *** – $p<0.001$

in relation to the values of the control group

Suppression of the N1 component of the second PDS in the experimental group during double stimulation of the dorsal root with intervals of 5-100 ms may indicate the activation of presynaptic inhibition of interneurons of the IV plate of the SC gray matter [1], including from the gelatinous substance, the neurons of which are mostly involved in the formation of P -waves [2, 3, 4]. This is supported by the correspondence of the interval from the 5th to the 78th ms of the duration of the positive component of the first evoked response, the amplitude of which in the experimental group showed a tendency to increase by 19% compared to the control animals.

A significant delay in the recovery of the second evoked potential amplitude of the motoneuron pool when it is indirectly stimulated by paired pulses under conditions of androgen deficiency can be explained by a decrease in the activity of Na+/K+-ATPase, and, as a result, a delay in the recovery of the normal transmembrane gradient of ions after membrane excitation [5, 6].

Another reason for the decrease in the amplitude of the second MDVR can be post-activation depression associated with depletion of neurotransmitter reserves in presynaptic terminals and desensitization of postsynaptic membranes [7, 8].

An additional justification for the above may be the fact that the selective ERα antagonist presynaptically facilitates excitatory synaptic transmission to neurons of the gelatinous substance, therefore, under conditions of androgen deficiency, which can lead to a decrease in estrogen production by aromatization of testosterone in the posterior horns of the SC, presynaptic inhibition of its primary afferents may be increased by inhibitory neurons [9].

Conclusions. Under conditions of long-term androgen deficiency, the activity of the interneuron pool increases, primarily due to disinhibition of segmental and non-segmental interneurons, and some increase in the activity of neurons of the gelatinous substance, which can affect the central link of the somatic reflex arc in the form of a decrease in the excitability of motoneurons and deterioration of temporal characteristics, namely a decrease in lability at an excitation frequency of 10 to 50 Hz due to the deepening of the post-activation depression.

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