CHANGES IN SPINAL REFLEXES IN THYROTOXICOSIS

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The latent period and duration of the monosynaptic response are reduced in cats with experimental thyrotoxicosis and its thresholds are lowered. The cycle of excitability of the motoneuron pool is shortened. The carrying capacity of the spinal reflex apparatus is increased at high (from 10 to 50/sec) frequencies of stimulation. Posttetanic potentiation of monosynaptic responses is weakened considerably as regards both the intensity and duration of the effect.

Disturbances of motor activity in thyrotoxicosis are usually attributed to the direct action of an excess of thyroid hormones on the muscle tissue [10-12] or are regarded as the result of morphological changes in the central nervous system [1, 6, 13, 14]. However, a factor of no less importance in thyrotoxicosis could be functional changes in the segmental apparatus of the spinal cord. Previous investigations revealed differences in the conduction of excitation along the spinal reflex arc in animals with experimental thyrotoxicosis [2]. The object of the present investigation was to continue the analysis of the effect of thyroid hormones on the spinal reflex apparatus.

EXPERIMENTAL METHOD

Experiments were carried out on 56 adult cats anesthetized with urethane and chloralose (400 and 35 mg/kg respectively). Nerve branches running to both heads of the gastrocnemius muscle were dissected in one limb. After laminectomy, the ventral roots from L6 to S1 were divided intradurally and placed on platinum electrodes for monophasic recording of their action potentials. The peripheral nerves were stimulated with square pulses 0.3 msec in duration. Frequencies from 1 to 100/sec were used for repetitive stimulation. Tetanic stimulation was applied at a frequency of 300/sec for 20 sec. The duration of the recovery cycle of the motoneuron pool was estimated from the decrease in amplitude of the testing monosynaptic response when investigated at various time intervals (from 1 to 1000 msec) after application of the conditioning stimulus (the method of paired stimuli).

All indices were studied in animals of the control and experimental groups, the latter receiving thyroid. Thyrotoxicosis was induced by feeding the animals with dry thyroid extract, mixed with the food, in doses increasing from 0.4 to 8 g daily for 20-22 days. The animals developed tachycardia, they lost 10-20% of their body weight, and their concentration of protein-bound iodine in the plasma rose from 4-5 to 18-22 μg%.

EXPERIMENTAL RESULTS

In the animals of the control group, the monosynaptic reflexes evoked by stimulation of supramaximal strength for fibers of the first group developed after a latent period of 3.7 ± 0.07 msec ($M \pm m$) and the duration of the spike potential was 3.2 ± 0.02 msec. In the animals receiving thyroid, the latent period and the duration of the monosynaptic spike were both shortened (to 2.9 ± 0.01 msec, $P < 0.01$ and 2.8 ± 0.1 msec,

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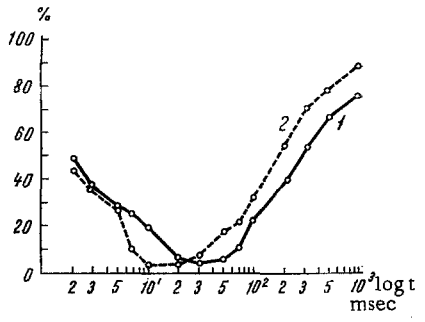

Fig. 1

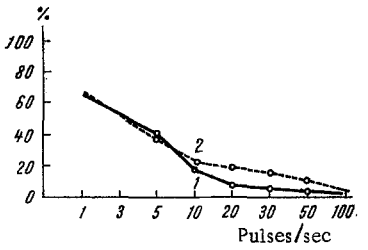

Fig. 2

Fig. 1. Cumulative curve of course of recovery cycle of motoneuron pool in control animals (1) and animals with experimental thyrotoxicosis (2). Changes in amplitude of monosynaptic reflexes evoked by stimulation of nerve to gastrocnemius muscle under the influence of conditioning volleys in the same fibers during supermaximal stimulation. Abscissa, time between conditioning and testing stimuli (in msec; logarithmic scale); ordinate, amplitude of monosynaptic responses to testing stimulation of nerve to gastrocnemius muscle (in % of control value).

Fig. 2. Reproducibility of monosynaptic responses during repetitive stimulation in control animals (1) and animals with thyrotoxicosis (2). Abscissa, frequency of stimulation of nerve to gastrocnemius muscle (pulses/sec); ordinate, averaged amplitude of first 10 discharges (in % of control value of monosynaptic response).

$P < 0.01$; respectively). The difference between the values in the control and experimental groups was significant. The only exceptions were three cats which received thyroid for more than four weeks and in which locomotor activity was severely disturbed (ataxia and discoordination of movement) and wasting was severe (weight loss more than 50%). The latent period in these animals was longer (3.5-4 msec) than in the other experimental animals. It can be postulated that this was due to growth structural changes in the gray matter of the spinal cord (deformation of remaining synapses, death of motoneurons), as described by several workers in the severe form of thyrotoxicosis in animals, and also at postmortem in patients with hyperthyroidism [1, 13, 17]. All the experimental cats showed a lowering of the threshold strength of stimulation (from 134 ± 4.5 to 104 ± 1.8 mV; $P < 0.001$).

The changes in latency, duration, and threshold strength of stimulation of the monosynaptic reflex in animals with thyrotoxicosis thus indicated facilitation of conduction in the monosynaptic reflex arc.

Functional ability to generate each successive response of the motoneuron pool is determined by the duration of the recovery cycle. Using the last method of paired stimuli for testing, it was shown that after administration of thyroid the period of prolonged functional depression of the second test response is shortened if the interval between stimuli is 20 msec or more (Fig. 1).

Depression in this method of testing is known to be the result of prolonged after-hyperpolarization of the postsynaptic membrane, associated with postspike changes on the soma of the motoneuron and with Renshaw reciprocal inhibition [8, 9]. On the other hand, during supramaximal stimulation other mechanisms of post- and presynaptic inhibition may also be implicated. In hyperthyroidism, there is evidently a weakening of one or more of these processes, thus facilitating the depolarizing effect of the EPSP in this time interval.

When the interval between stimuli was between 5 and 20 msec the amplitude of the testing response in the experimental animals was lower than in the controls. Evidently under these conditions the deepening of postspike hyperpolarization was the main reason for the decrease in excitability of the motoneuron, for special experiments showed that under these conditions there are no grounds for suggesting strengthening of reciprocal inhibition [3]. At the same time, in these time intervals it is difficult to expect any definite manifestation of other inhibitory influences.

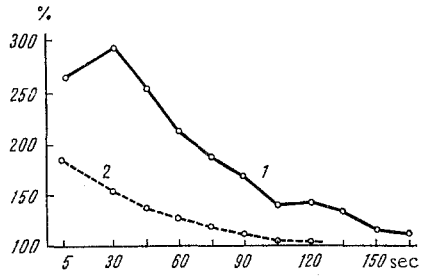

Fig. 3. Development of posttetanic potentiation over a period of time in control animals (1) and in animals with thyrotoxicosis (2). Abscissa, time after discontinuing tetanic stimulation (in sec); ordinate, amplitude of monosynaptic response (in percent of control value).

According to Eccles [8], deepening of after-hyperpolarization develops as the membrane potential decreases. The results of the present experiments can evidently provide indirect evidence of a decrease in the membrane potential of the motoneuron during hyperthyroidism, more especially as this has been demonstrated experimentally, including in work undertaken in the author's laboratory [4], in relation to other excitable structures.

To determine the characteristics of the functional state of the spinal reflex apparatus, it was important to investigate the carrying capacity of the effective output system in the same way as that used by Kryzhanovskii and D'yakonova [5] to study this parameter in rats with an experimental tetanus.

Repetitive stimulation of the nerve to the gastrocnemius muscle by stimuli of supramaximal strength evoked a series of responses in the control animals, which diminished in amplitude at a comparatively low frequency, starting from 5-10/sec. In animals receiving thyroid, the reproducibility of the monosynaptic responses was increased within the range of frequencies from 10 to 50/sec (Fig. 2).

Subthreshold depolarization of the motoneuron is known to increase the frequency of discharges reproducible by the cell very sharply [7]. In experimental tetanus there is an increase in the carrying capacity of the efferent channel in the presence of additional postsynaptic activation of the motoneuron [5]. In the present experiments a marked increase in the polysynaptic components of the reflex responses in the animals with thyrotoxicosis was observed even when single volleys were used. It can accordingly be postulated that activation of the system of interneurons during thyrotoxicosis facilitates the genesis of action potentials during repetitive stimulation.

In thyrotoxicosis conduction of both single and repetitive volleys in the spinal reflex apparatus is thus facilitated. The reason for these changes must be sought in a disturbance of the processes responsible not only for postsynaptic, but also for presynaptic regulation of the efferent channel.

To determine the state of the presynaptic apparatus in the control and experimental animals, the course of posttetanic potentiation was studied; an important factor in the development of posttetanic potentiation is an increase in the output of mediator in the postactivation period [9, 11]. Comparison of results obtained in the control and experimental animals showed that in thyrotoxicosis there is marked weakening of this phenomenon as regards both intensity and duration (Fig. 3). These results are evidence of difficulty in the mobilization of mediator in the postactivation period, probably in connection with a decrease in the control of mediator in the presynaptic endings.

Analysis of the functional state of the various components of the monosynaptic reflex arc during experimental thyrotoxicosis suggests that changes taking place in the spinal cord reflex apparatus are due in all probability to changes in the state of the postynaptic membrane and to a disturbance of processes in the presynaptic endings of afferent fibers.

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