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EFFECT OF THYROTOXICOSIS ON SKELETAL MUSCLE PROPRIOCEPTOR ACTIVITY

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The effect of prolonged administration of thyroid hormones on the discharges from muscle spindles of the cat soleus was investigated. In animals with thyrotoxicosis the response of the primary spindle endings to a constantly acting and to a sudden rapid stretching increased considerably in both the dynamic and the static phase. The discharge frequency of the secondary endings remained substantially unchanged. It is postulated that the observed changes in activity of the primary endings are connected with disturbances of metabolism in the muscle and also with its atrophy.

KEY WORDS: thyroid hormones; muscle receptors; motor disturbances.

Among the most characteristic symptoms of thyrotoxicosis are motor disturbances, expressed as muscular weakness, rapid fatigue, tremor of the limbs and trunk, etc. [6, 7].

In the analysis of these motor disturbances the study of the state of receptor function of the muscles is particularly important, for afferent impulses from the muscles and joints play an important role in the process of movement control.

It was therefore decided to study the function of muscle spindles in experimental thyrotoxicosis.

EXPERIMENTAL METHOD

Discharges from receptors of the soleus muscle were studied in normal cats and in cats receiving thyroid extract with the diet in accordance with a special scheme [3]. By the end of the second week of the experiment the animals showed tachycardia, a loss of weight of 10-15%, and an increase in the serum protein-bound iodine concentration from 4-5 to 18-20 μg %. Under urethane-chloralose anesthesia (500 and 50 μg/kg respectively) both limbs of the animals were denervated except the muscle branch to the soleus muscle on the test side. After laminectomy the anterior and posterior roots were divided from L_5 to S_1 inclusive. Throughout the experiment the temperature of the body and of the operation wound, which was flooded with mineral oil, was maintained

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TABLE 1. Changes in Discharge Frequency of Primary Ending of Muscle Spindles during Constant Stretching (weight of 100 g) and Sudden Additional Stretching at Different Speeds in Control and Hyperthyroid Animals (M ± m)

Group of animals	Spontaneous activity, spikes/sec	Speed of stretching, mm/sec	Dynamic phase, spikes/sec	Period of static phase (in sec)			Phase of relaxation, spikes/sec
				1st	2nd	3rd	
Control	17±1,5	20	67±1,5	26±1,3	28±1,8	28±1,6	9,0±1,9
		40	113±1,7	38±1,3	36±1,1	32±2,1	8±0,7
Thyrotoxicosis	28±0,88	20	104±3,69	44±1,8	41±1,54	40±1,43	8±1,5
		40	150±4,96	40±1,45	36±1,28	34±1,1	8±1,48

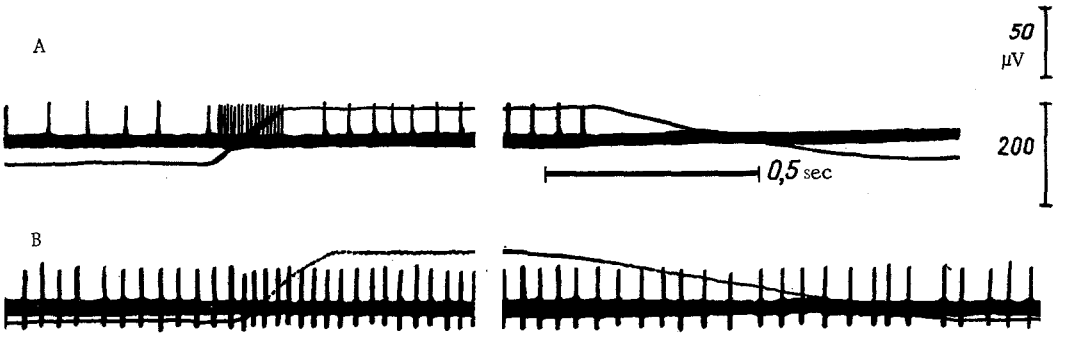

Fig. 1. Discharges of primary (A) and secondary (B) endings of muscle spindle during stretching of soleus muscle. Top beam records discharges of spindles before and after stretching muscle, at beginning of static phase and during period of relaxation; bottom beam records mechanogram of stretching; time marker, in sec. Gap in top and bottom records measures 2 sec. Calibration: top beam 50 μV, bottom beam 200 g.

at 36-38°C. Constant stimulation of the muscle receptors was produced by stretching the muscle with a weight of 100 g. Afferent fibers arising from the test spindles were identified after splitting the posterior root into separate bundles by the discovery of regular spike activity in them. The muscle receptors were identified from their response to muscle contraction. Cessation of afferent activity against the background of muscular contraction showed that the ending belonged to a muscle spindle. Afferent endings were subdivided into primary or secondary on the basis of the velocity of conduction of excitation. Fibers conducting excitation with a velocity of 70 m/sec or higher were classed as primary endings, those conducting more slowly as secondary [1, 2, 13]. In the course of the experiments the muscle was further stretched by a special instrument by means of which it could be stretched through 3, 6, 9, and 12 mm at speeds of 20 and 40 mm/sec and kept in the stretched state for 3 sec [1]. Contraction and stretching of the muscle were recorded by the UTS-VT-12 strain gauge. The action potential of the muscle fiber and the record of mechanical contraction were photographed from the screen of a dual-beam oscilloscope.

The experimental data were obtained from 20 primary and 6 secondary endings of muscle spindles from muscles of normal cats and 20 primary and 4 secondary endings from muscles of animals receiving thyroid extract.

EXPERIMENTAL RESULTS AND DISCUSSION

The frequency of afferent impulses from a muscle spindle is determined by local processes, which are closely connected with the parameters of the mechanical stimulus. The response to sudden stretching of the muscle consists of two phases: an initial, dynamic phase, corresponding to the moment of stretching, and a later, static phase, due to the stretched phase of the muscle [1, 2, 8, 9, 12].

In the present experiments a regular spike discharge, the frequency of which depended on the degree of stretching of the muscle, was recorded in the isolated fiber of the posterior-root bundle in response to constant stretching of the muscle. For instance, in the control animals during stretching of the soleus muscle by a weight of 100 g, the activity of the primary endings had a frequency of 17 ± 1.5 spikes/sec and of the secondary 19 ± 1.5 spikes/sec. Typical responses of the primary and secondary endings of the soleus muscle of the

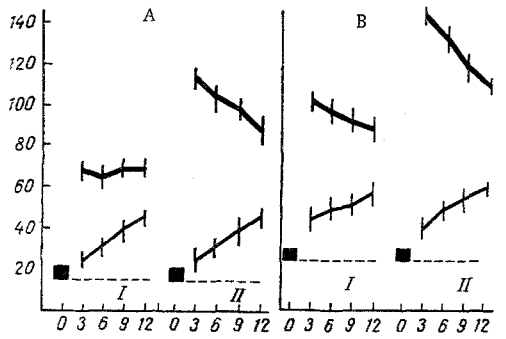

Fig. 2. Changes in discharge frequency of primary endings of muscle spindles in control (A) and hyperthyroid (B) cats depending on amplitude and speed of stretching of soleus muscle. Abscissa, amplitude of stretching (mm); ordinate, discharge frequency (spikes/sec). Speed of stretching: I) 20 mm/sec, II) 40 mm/sec. In all graphs: Top curve shows discharge frequency in dynamic phase, middle curve (thinner) 1st sec of static phase; bottom broken line frequency of original spontaneous activity.

normal cat to sudden stretching are given in Fig. 1. At the moment of stretching the discharge frequency in the primary ending rose sharply. After a short pause, discharges reappeared in the static phase. In some investigations, the faster the muscle was stretched, the longer the period of the pause [8, 11]. The response of the secondary ending was characterized by a weak reaction to stretching in the dynamic phase and absence of the pause in the static phase.

In the animals with thyrotoxicosis the response of the primary endings both to constant stretching and to sudden additional stretching was considerably increased (Table 1). In the dynamic phase the discharge frequency of the primary endings of the cats with thyrotoxicosis was on average 1.5 times higher than the control for all values of stretching. The discharge frequency of the secondary endings in both groups of animals did not differ significantly whether during constant or during sudden stretching ($P > 0.1$). Differences in the response of the primary endings of normal and hyperthyroid animals to stretching the soleus muscle at different speeds and by different amounts are illustrated by the graphs in Fig. 2. Clearly the intensity of the response of the primary endings in the cats receiving thyroid extract was sharply increased. The spontaneous discharge frequency was appreciably higher and the dynamic component was strengthened relative to the spontaneous activity. The excess of the dynamic component over the frequency of the static component was almost the same in the control and experimental animals. The shape of the curves reflecting changes in the response to stretching also was about the same. This indicates that the relationship between the discharge frequency of the static component of the response and the length of the muscle and also between the dynamic component of the response and the speed of stretching is still linear in animals with thyrotoxicosis.

Since the discharges from single functional elements were investigated, the increase in the response could have arisen as a result of lowering of the threshold of sensitivity to the stimulus used. There are indications of very similar changes in receptor discharges in a denervated muscle, not only to mechanical stimulation, but also to administration of drugs [2, 12, 17].

Division of the anterior roots in the present experiments ruled out any possible influence of the γ loop, and consequently the changes observed could be connected with processes taking place in the muscle tissue itself. Investigations have shown that in thyrotoxicosis the deficiency of high-energy phosphorus compounds disturbs the work of the ionic pump, which plays an important role in maintaining the level of excitability, with the result that depolarization processes on the membranes of excitable structures are intensified [4, 5, 15]. Receptor discharges are known to be connected with depolarization of sensory endings, leading to the development of a receptor or generator potential [14, 16]. Very probably an increase in the depolarization of sensory endings, can lead to strengthening of receptor discharges.

However, features distinguished above could also have been attributable to mechanical factors, if the atrophy of muscle tissue that develops in thyrotoxicosis is borne in mind. According to recent morphological investigations [10] the elastic structures of the muscle spindle are connected by cross bridges with the perimysium of the extrafusal muscle fibers. The number of bridges in the central part of the spindle, where the primary endings are situated, is several times greater than in the polar part. During atrophy of the extrafusal

fibers the primary endings will be deformed to a greater degree than the secondary, with the result that the discharge will be intensified. This explanation may account for the differences in the response of the primary and secondary endings in the animals receiving thyroid.

Changes in the sensitivity of primary endings of the intrafusal fibers may evidently be one cause of the motor disturbances arising in thyrotoxicosis.

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AGE DIFFERENCES IN THE ACID – BASE BALANCE AND BLOOD CLOTTING SYSTEM DURING STARVATION

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The state of the acid–base balance and of the blood clotting system during starvation was studied in young (5-6 months) and old (24-26 months) male rats. The times of maximal changes in the two systems were found to coincide, but in the young animals the acidotic crisis and hypercoagulation developed earlier and were more severe. The old animals were more resistant to starvation and died later than the young rats.

KEY WORDS: starvation; age; acid–base balance; blood clotting.

Some workers have regarded starvation as a therapeutic factor in certain diseases and also as a condition favoring the prolongation of life [1, 3, 4, 8]. This latter view is particularly interesting in the light of data

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