THE EFFECT OF INSULIN HYPOGLYCEMIA ON FROG SPINAL REFLEXES

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At the present time a great deal of work is being done on the effect of hypoglycemia on the different parts of the nervous system. However as has been pointed out by E. Gel'gorn [1] very little information is available concerning the spinal cord. He quotes only one paper [5] in which it is reported that the tendon reflexes disappeared during insulin coma. Also, I. I. Gurevich [2] has shown that in the frog, spinal reflexes are reduced when hypoglycemia is induced by removing the viscera and maintaining the animal in a thermostat.

The object of the present investigation has been to determine the effect of insulin hypoglycemia on spinal cord reflexes in a warmblooded animal.

METHODS

Cats were anesthetized with ether, and the spinal cord cut below the medulla. Heat was applied to maintain body temperature, and respiration sustained artifically. Recordings were made from a pair of antagonist muscles, the semitendinosus and the rectus femoris is response to stimulation of the central end of the peroneal nerve. A wide range of stimulus voltages was applied by a neon lamp stimulator at a frequency of 80 cps. Blood for analysis was removed from the femoral or carotid artery; sugar was estimated using Hagedorn-Hensen's method. Insulin and glucose were injected into the femoral or jugular vein.

When the preparation had been made, after an interval of half an hour, the threshold excitation of the peroneal nerve was determined at 15 min intervals. Every 60 min a record was made of the contraction of the muscle in response to a submaximal stimulus equal to 3-5 times the rheobase applied to the nerve, blood was withdrawn and the blood sugar measured. When there was a change in the reflex response, the measurements were made more frequently.

By continuously draining the wound with strips of gauze placed above and below the electrodes so as not to touch the nerve, and by fixing the electrodes firmly to a stand we were able to prevent fluid reaching the electrodes and to preserve the nerve undamaged. In control experiments on ten animals which were kept for 6-10 hours after making the preparation, both the threshold of reflex stimulation and the amplitude of contraction of the semitendinosus muscle in response to a submaximal stimulus showed no appreciable change (Fig. 1).

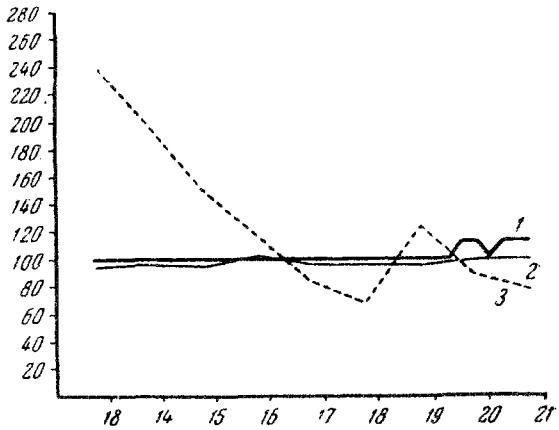

Fig. 1. Control experiment. The abscissa represents time of day in hours; ordinate: 1) Threshold stimulation of peroneal nerve, as percentage of original value; 2) amplitude of contraction of semitendinosus muscle in response to a submaximal stimulation of peroneal nerve, as percentage of original value; 3) blood sugar level (in mg%).

RESULTS

In cats, 60-90 min after sectioning the spinal cord the blood sugar was 200-350 mg%, and it fell during the experiment reaching finally the value of 100 mg%. As can be seen from Fig. 1 the fall was smooth, it did not fall to a hypoglycemic level, and did not affect the threshold of excitation nor the contraction of submaximal stimulation. After the excitatory threshold had remained constant for 45-60 min, five or ten units per kg of insulin were injected intravenously.

In 35 of the 40 animals (87%), 3-6 hours after the insulin injection there was an increase in excitatory threshold and a reduced contraction of the muscle to submaximal stimulation (Fig. 2). The figure shows that as the blood sugar level falls there is a reduction in the contraction of the semitendinosus. The reflex was restored by injecting 4-10 ml of a 40% glucose solution. The recovery was maintained for 2-30 min in all the experiments except two, although it was not always complete.

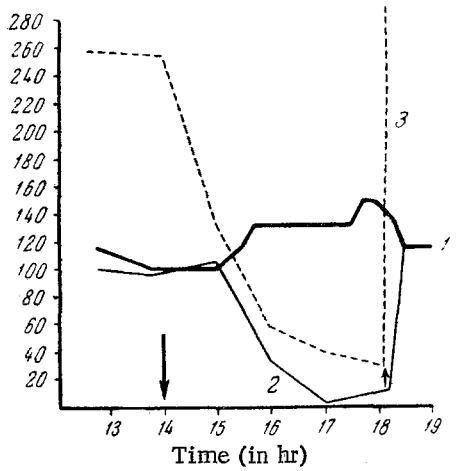

Fig. 2. Changes in the threshold of excitation and amplitude of contraction in response to a submaximal stimulus, after injecting insulin and glucose. Arrows indicate moment of injecting insulin (↓) and glucose (↑). Indications as in Fig. 1.

No case was observed of inhibition of the antagonist muscle caused by hypoglycemia.

It is important to note that in hypoglycemia the threshold stimulus changes less than the response to submaximal stimulation. Figure 2 shows that as the blood sugar level falls, the contraction to the submaximal stimulation falls almost 50 times, whereas the threshold value increases by only 50%, i.e., the condition resembles the equalizing phase of parabiosis.

The blood sugar level at which there was a considerable reduction in the reflex activity varied in different animals. In most experiments, the reduction occurred when the level fell below 50 mg%, and sometimes not until it had fallen to 25-30 mg%; however, in others the relfexes were reduced at a blood sugar level of 100 mg%. It is evident that the effect is not only caused by the actual blood sugar level but also by its rate of fall.

To find whether hypoglycemia affects chiefly the nervous system, the neuromyal junction, or muscular excitability, we arranged a set of experiments on 11 animals in which stimultaneous recordings were made of the reflex contraction of the semitendinosus muscle of one side, and the contraction in response to direct stimulation of the motor nerve, on the other.

Figure 3 shows the traces obtained in such an experiment, and it can be seen that as the blood sugar level falls, the reflex contraction is reduced, and that when glucose is injected, the contraction returns to its original value. There was no change in the response obtained to stimulation of the motor nerve. A similar effect was observed in seven other experiments. In the remaining three animals, the response to stimulation of the motor nerve was also reduced, but only at blood sugar levels below that which affected the reflex contraction, and the response returned more rapidly to normal after the glucose injection.

In most cases the threshold of excitation of the motor nerve increased during the experiment, but this increase cannot be attributed either to the reduction in blood sugar level or to its increase after the glucose injection, but was evidently a consequence of dividing the nerve. There was no reduction in the excitability of the muscle.

We may suppose therefore that the reflex changes are the result of altered conditions in the spinal cord itself.

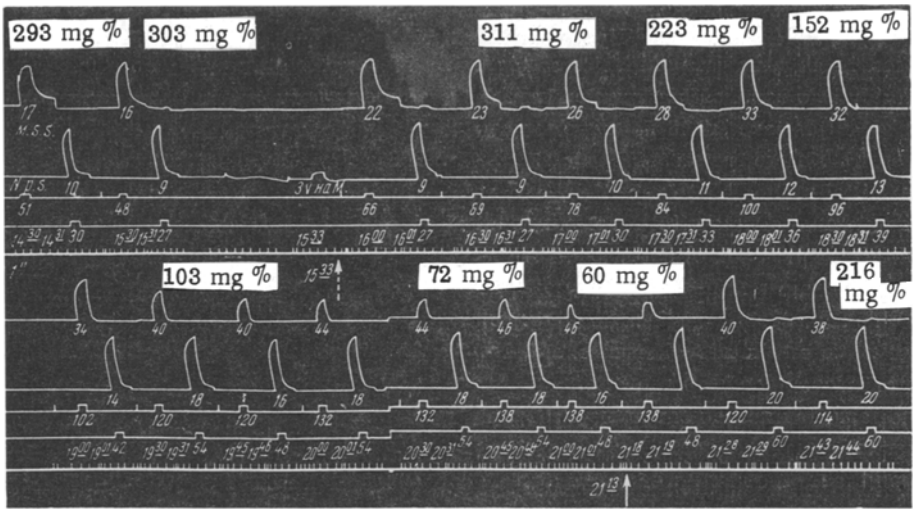

Fig. 3. Contraction of the semitendinosus muscle during hypoglycemia in response to stimulation of an afferent or a motor nerve. Curves, from above downwards: Blood sugar level in mg% (figures); contraction of left semitendinosus muscle; figures below curve represent threshold stimulus value; contraction of right semitendinosus muscle; stimulus marker of left peroneal nerve (afferent); stimulus marker of right semitendinosus nerve (efferent); time of day in hours and min; time marker (one second). The lower part of the curve is a continuation of the upper part.

Even during hypoglycemic convulsions, we found no increase in reflex excitability. Evidently the spasms are not caused in this way, but possibly result from an increased effect of proprioceptor influence on skeletal muscle [3,4].

Gell'gorn [1] has decided on the basis of published results that hypoglycemia may be a biphasic effect on the autonomic system, but only depresses the somatic nervous system, i.e., it acts monophasically.

In our experiments, we too have been able to observe only a depression effect. However, the phasic nature of the reaction is a very well established phenomenon, and it would certainly be premature to deny its existence in somatic nervous reactions. Under the conditions obtaining in our experiments, cat spinal reflexes were reduced by insulin hypoglycemia. The depression increased with greater degrees of hypoglycemia, but returned to normal after the glucose had been injected. We did not observe any reduction in the inhibition of the antagonist to be caused by hypoglycemia. Neuromyal transmission was either unaffected, or affected very much less than was the reflex response. There was no change in muscle excitability. Evidently the observed changes in the reflexes were due to alterations in the spinal centers.

SUMMARY

Experiments on spinal cats in insulin hypoglycemia showed that spinal cord reflexes were depressed. They were restored by intravenous glucose injections. There was no phase of increased excitability nor was there any inhibition of the action of the antagonist muscle. The changes in the reflexes evidently originate in the central part of the arc, because myoneural transmission was not affected and muscle excitability remained unchanged.

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