THE EFFECT OF INSULIN HYPOGLYCEMIA ON THE STRENGTH-DURATION CURVE OF THE SPINAL REFLEX ARC IN THE CAT

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The level of the blood sugar is an essential element of the internal milieu of the organism. There is now considerable experimental and clinical evidence indicating that during the development of hypoglycemia following administration of insulin, functional changes take place in the nervous system: the electrical activity of the brain is depressed [9, 10, 11], the conditioned and unconditioned reflexes are depressed [2, 6, 10], the potentials of the ascending reticular formation of the brain stem are decreased, and the excitability of the motor zone of the cerebral cortex is lowered [1].

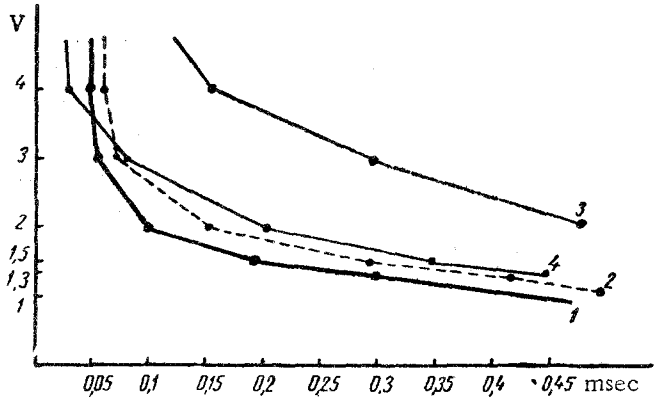
Findings relating to the functional state of the autonomic nervous system in hypoglycemia are more controversial [3, 4, 13-15]. We know of only a few published investigations of the functional state of the spinal cord in insulin hypoglycemia. These are primarily the observations of clinicians, who have found that during hypoglycemia the spinal reflexes are initially intensified, with the appearance of pathological reflexes (Babinski reflex), and this is followed by the development of total areflexia. I. N. Kantorovich [8] showed that the excitability of the spinal cord of cats is lowered in hypoglycemia, but that before convulsions develop there are periods of increased excitability and generalization of reactions. A. I. Shapovalov [12] states that insulin lowers the summation of subthreshold nociceptive impulses and the motor reflex to temperature stimulation of the skin in rabbits. Sometimes this decrease is preceded by a short phase of increased excitability.

For a number of years work has been proceeding in Professor E. N. Speranskaya's laboratory to study the effect of hyper- and hypoglycemia on the functional state of various divisions of the nervous system and, in particular, the effect of hypoglycemia on the functional state of the spinal cord has been investigated by N. A. Emel'yanov [7], who observed a decrease in the magnitude of the motor reflexes in this state.

The object of the present research was to study the changes in the strength – duration **curve** of the spinal reflex arc as an index of the functional state of the spinal cord during the development of insulin hypoglycemia.

EXPERIMENTAL METHOD

The spinal cord was divided below the medulla in an acute experiment under deep ether anesthesia in order to abolish the subordinating influences of the brain on the cord. In the course of the experiment, both during the control period and after injection of insulin parallel determinations were made of the blood sugar level (by the Hagedorn-Jensen method), the reflex contraction of the semitendinosus muscle during stimulation of the central end of the peroneal nerve, and also the strength-duration curve of the same reflex reaction by means of a type ISE-01 stimulator. In order to plot the strength-duration curve, 6 points were found: during stimulation with strengths of 1.0, 1.3, 1.5, 2.0, 3.0, and 4.0 rheobase respectively. The intervals between individual stimuli were not less than 15 sec, so that all traces of the preceding stimulus had disappeared. Hypoglycemia was produced by injection of insulin into the femoral vein in a dose of 10 units/kg body weight.



Changes in the strength-duration curves (mean results of 30 experiments) during the development of insulin hypoglycemia. Along the axis of abscissas – duration of impulses of stimulating current (in millisec); along the axis of ordinates – strength of stimulating current (in rheobases); 1) control (blood sugar 200 mg %); 2) first period of hypoglycemia (blood sugar 80 mg %); 3) second period of hypoglycemia (blood sugar 40 mg %); 4) 5 min after injection of glucose (blood sugar 180 mg %). In the first period of hypoglycemia (1-2 h) the strength-duration curve is shifted upward and to the left; in the second period (5-8 h) it moves away from the axes of coordinates. After injection of glucose the curve returns to normal.

EXPERIMENTAL RESULTS

Thirty experiments with hypoglycemia and 7 control experiments were carried out. Immediately after section of the spinal cord the blood sugar concentration was 200-250 mg %. In the control experiments (without injection of insulin) it fell in the course of 6-8 h to 100-120 mg %. The amplitude of reflex contraction of the semitendinosus muscle changed during the experiment by not more than 8% of its initial value. The threshold level of stimulation from the stimulator (single and rhythmic impulses) changed during the control experiment by not more than 8% of its initial value. In the course of the experiment the time indices of stimulation increased only very slightly, evenly, and uniformly, so that the strength-duration curve underwent only quantitative but not qualitative changes. The most labile value was the threshold duration of stimulation at 1.0 and 1.3 rheobase.

In the experiments with hypoglycemia, parallel to the increase in the threshold of stimulation and the decrease in the amplitude of reflex contraction of the muscle, the time indices of stimulation showed regular changes (Fig. 1).

In the first period, from 1 to 2 h after injection of insulin, when the blood sugar level fell approximately to 70-65 mg %, the indices became less stable and the vertical limb of the hyperbolic curve came nearer to the ordinate, thus demonstrating increased physiological lability. During the same period, against a background of a general fall in excitability, shown by movement of the horizontal limb away from the axis of abscissas, this limb moved temporarily towards the axis of abscissas. During the second period of development of hypoglycemia, when the blood sugar level fell to 40 mg % or below, the increase (tenfold) in the rheobase was accompanied by a marked increase in the duration of stimulation at all points of the strength-duration curve. The curve is shifted upward and to the right, indicating a lowering of the excitability and lability of the reflex arc; the shift of the first part of the curve is expecially marked. The shifts in the strength-duration curve for the motor nerve were much less well defined, giving further evidence in favor of the hypothesis that the changes in the strength-duration curve reflect the functional state of the spinal centers.

Injection of glucose rapidly restored the reflex excitability and returned the strength-duration curve to its initial level, or sometimes actually below that level.

Statistical analysis of the results by the Student-Fisher method was applied to the experiments with hypoglycemia by dividing them into periods: 1) before injection of insulin (control period); 2) 2 h after injection of insulin; 3) 5 h after injection; 4) after injection of glucose – and to the control experiments which were also divided into corresponding time intervals. The differences between the time indices of excitability in the control series were not statistically significant ($P > 0.1$), whereas in the experiments with hypoglycemia statistically significant shifts were observed ($0.02 < P < 0.5$). Comparison of the mean indices of the experiments with hypoglycemia and the control experiments also revealed statistically significant changes in the time indices during the development of hypoglycemia ($P < 0.05$).

The changes in the threshold of excitability and in the time indices of stimulation were similar to the picture of parabiosis observed in other experimental conditions. Similar changes in the strength-duration curve were observed, in particular, by Hoagland [15] during disturbances of the adrenal cortical function, by N. V. Golikov [5] in strychnine poisoning and during the action of certain ions, and also by other writers.

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