EFFECT OF DEVELOPING INSULIN HYPOGLYCEMIA ON MONOSYNAPTIC SPINAL REFLEXES IN CATS

Yu. P. Pushkarev

UDC 612.349.8:612.833

Acute experiments on anesthetized and spinal cats showed that deepening insulin hypoglycemia causes inhibition of rhythmic monosynaptic EPSPs of motoneurons in the lumbar region of the spinal cord. In the initial period of hypoglycemia (a fall of the blood sugar to 50-60 mg%) the progressive decrease in the efficiency of trans-synaptic processes was not caused by pre- or postsynaptic inhibition or by depression and was due to exhaustion of the operative fraction of mediator. In deeper hypoglycemia the functions of the postsynaptic formation of the monosynaptic spinal reflex arc are disturbed.

KEY WORDS: spinal cord; monosynaptic potentials of motoneurons; insulin hypoglycemia.

Hypoglycemic states accompanying certain disturbances of the function of the internal organs, including the endocrine glands, as well as those accompanying adminstration of insulin, starvation, exhausting muscular work, and so on, give rise to definite changes in the activity of the nervous system. The few investigations of spinal cord functions which have been undertaken under conditions of deep insulin hypoglycemia have revealed a reduction in the amplitudes of motor reflexes [2, 6], a decrease in excitability of the spinal reflex arc [3, 10] and its time characteristics [6], and impairment of the summation power of segmental neuronal centers in relation to nociceptive impulses [9]. An increase in the intensity of interoceptive influences on the spinal motor apparatus, leading to greater competence of the skeletal muscles during the period of blood sugar deficit [5], has also been demonstrated. Clearly in this very widespread state of the internal milieu of the body only certain

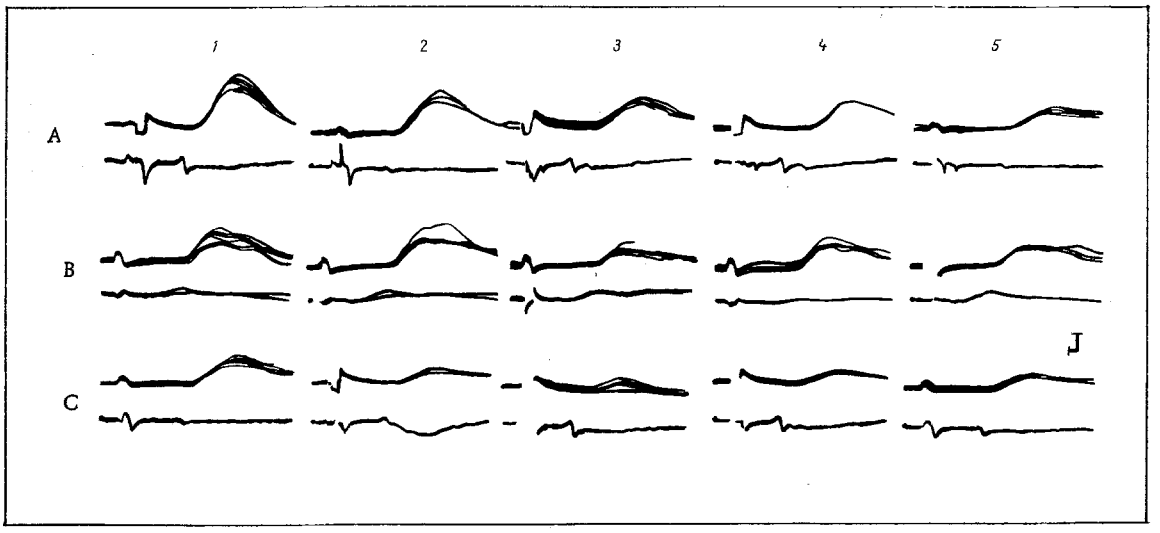

Fig. 1. EPSPs of gastrocnemius motoneurons during repetitive stimulation of corresponding nerve by long series of pulses at a frequency of 40 Hz. 1) 1st, 2) 10th, 3) 20th, 4) 40th, 5) 90th second. A) Blood sugar 150 mg%, B) 70 mg%, C) 30 mg%. Calibration: 0.5 msec, 5 mV.

Laboratory of Physiology of the Autonomic Nervous System, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 87, No. 4, pp. 305-308, April, 1979. Original article submitted May 12, 1978.

 0007-4888/79/8704-0304$07.50

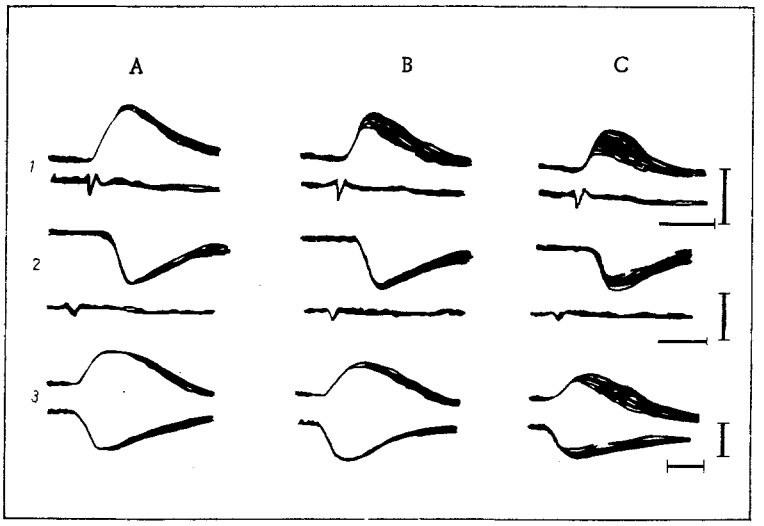

Fig. 2. Spinal cord potentials during deepening insulin hypoglycemia. A) Blood sugar 150 mg%, B) 70 mg%, C) 30 mg%. 1) Monosynaptic EPSPs of gastrocnemius motoneuron during stimulation of corresponding nerve by series of pulses at 40 Hz for 10 sec. 2) IPSP of recurrent inhibition during antidromic stimulation of ventral root L7 at 40 Hz. 3) Dorsal root potentials (above) and dorsal cord potentials (below) during stimulation of nerve to semitendinosus at a frequency of 40 Hz. Calibration: 10 msec (1), 4 msec (2), 20 msec (3); 5 mV (1, 2) and 0.3 mV (3).

integral characteristics of the functions of the monosynaptic reflex arc have been studied, with no attempt at concrete analysis of the complex neuronal apparatus of the spinal cord at the segmental level.

The object of this investigation was to study the effect of deepening insulin hypoglycemia on the various component elements of the spinal reflex arc.

EXPERIMENTAL METHOD

In acute experiments on five high-spinal (transection of the spinal cord immediately below the medulla during the operation), eight low-spinal (transection of the cord at level L1-L2 in the course of the experiment), and also on four cats with an intact brain, anesthetized with a mixture of pentobarbital and chloralose (15 and 30 mg/kg, intraperitoneally), hypoglycemia was induced by intravenous injection of insulin in a dose of 5-10 units/kg body weight. The blood sugar was determined by the method of Somogyi and Nelson. During stimulation of afferent fibers of various muscular nerves to the hind limb monosynaptic discharges of the divided L7 ventral root and excitatory postsynaptic potentials (EPSPs) of identified motoneurons of the same segment of the spinal cord were recorded. Intracellular potentials were derived by means of glass microelectrodes, filled with potassium citrate, with a resistance of 10-20 MΩ, and led through a cathode follower and dc amplifier and recorded on photographic film from the screen of a dual-beam cathode-ray oscilloscope. Characteristics of the functions of the spinal neurons were determined by the usual methods, which are described along with other technical details in the previous publication [1].

EXPERIMENTAL RESULTS

Injection of insulin into the blood stream caused a gradual (in the course of 4-8 h) decrease in the blood sugar from the postoperative hyperglycemic level (about 300 mg%) to 30 mg% or below. When a hypoglycemic state was reached progressive inhibition of the mono- and polysynaptic discharges of the ventral root was observed, with a decrease in amplitude of the corresponding EPSPs evoked by activation of both flexor and extensor nerve fibers (Fig. 1). Rhythmic potentials underwent particularly marked depression during prolonged

afferent stimulation. In all cases there was particularly clear inhibition of monosynaptic potentials arising in response to stimulation of afferent fibers at just above the threshold intensity (1.2-1.5 T) during deep hypoglycemia, when the blood sugar level had fallen below 60 or even 50 mg%. Intravenous injection of 5-10 mg of 40% glucose solution restored the amplitude of the reflex responses only partially.

Let us examine the possible causes of inhibition of monosynaptic processes in the spinal cord during insulin hypoglycemia. Among the causes of inhibition of monosynaptic motoneuron potentials could be a disturbance of the functions of the neurons themselves. However, in the initial period of hypoglycemia, against the background of marked depression of the homonymous rhythmic EPSPs, there was no change in the heteronymous responses. Antidromic passage of action potentials into motoneurons took place just as easily as when the blood sugar level was normal. Changes in the mean level of the motoneuron membrane potential likewise could not be found. Only during deep hypoglycemia (with a fall of blood sugar below 50 mg%), was a decrease in the intensity of the IPSP of both di- and polysynaptic origin observed, as well as of the IPSP connected with the mechanism of recurrent inhibition. During this same period of hypoglycemia evidence of a decrease in the intensity of presynaptic inhibition could be observed (Fig. 2). Other potential postsynaptic mechanisms of inhibition of reflex responses, namely desensitization and accommodation, do not operate at the frequencies of stimulation used [1].

Neither pre- nor postsynaptic inhibition nor any other postsynaptic depression of the motoneurons was thus the mechanism responsible for the progressive fall in effectiveness of rhythmic transsynaptic processes in the monosynaptic spinal reflex arc in the presence of mild insulin hypoglycemia. The rapid fall in the intensity of posttetanic potentiation of EPSPs of the motoneurons, the increased exhaustion of the persistent shifts of polarization created by high-frequency series of stimulation, and various other features are all evidence of a deficiency of the excitatory action of the primary afferent endings. It has been suggested that insulin hypoglycemia, creating a deficiency of carbohydrates in neuronal structures, causes a decrease in the synthesis of high-energy compounds and of mediator principally in the presynaptic endings, which are characterized by intensive metabolism. Under these conditions prolonged stimulation causes exhaustion of the operative pool of mediator. So far as deeper hypoglycemia is concerned, in this case there is a disturbance of the functions of not only the presynaptic, but also postsynaptic formations. The great resistance of the latter is possibly explained by their high polysaccharide reserves [3, 4, 8, 11, 13].

Hypoglycemia in the present experiments thus produced a monophasic inhibitory effect on monosynaptic spinal reflexes. Even in the period of hypoglycemic convulsions, which in cats with a transected spinal cord were observed infrequently and were of mild degree, there was no appreciable change in the amplitude of the corresponding EPSPs. The cause of these convulsions is evidently strengthening of visceral influences on motoneurons [5]. On the whole, the pattern of inhibition of segmental monosynaptic responses observed in the present experiments is in full agreement with the functional and biochemical disturbances in nerve tissues described by various workers during the development of insulin hypoglycemia [11-13].

LITERATURE CITED

1. V. D. Avelev and Yu. P. Pushkarev, Fiziol. Zh. SSSR, No. 9, 1369 (1974).
2. N. A. Emel'yanova, Byull. Éksp. Biol. Med., No. 4, 9 (1960).
3. I. N. Kantorovich, Fiziol. Zh. SSSR, No. 6, 697 (1954).
4. N. S. Kositsyn, Microstructure of Dendrites and Axodendritic Connections in the Central Nervous System [in Russian], Moscow (1976).
5. O. S. Merkulova, Interoceptors and Skeletal Musculature [in Russian], Moscow—Leningrad (1959).
6. Yu. P. Pushkarev, Byull. Éksp. Biol. Med., No. 7, 12 (1963).
7. Yu. P. Pushkarev, Dokl. Akad. Nauk SSSR, 155, 238 (1964).
8. A. L. Shabadash, Problems in Histochemical Investigation of Glycogen in the Normal Nervous System [in Russian], Moscow (1949).
9. A. I. Shapovalov, Farmakol. Toksikol., No. 6, 24 (1955).
10. A. I. Shapovalov, in: New Data on the Pharmacology of the Reticular Formation and Synaptic Transmission [in Russian], Leningrad (1958), p. 181.
11. H. E. Himwich, Brain Metabolism and Cerebral Disorders, Baltimore (1951).
12. B. Ljunggren, Effects of Oxygen and Substrate Depletion on Brain Energy Metabolism, Lund (1974).
13. J. K. Tews, S. H. Carter, and W. E. Stone, J. Neurochem., 12, 679 (1965).