THE MECHANISM OF INSULIN ACTION

COMMUNICATION V. EFFECT OF INSULIN ON BLOOD GLUCOSE CONTENT IN DOGS DURING ELECTROSLEEP

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One of the present authors presented experimental data concerning the role of the cerebral cortex in the mechanism of insulin action in communications published previously [3-7]. The influence of insulin on the blood sugar level and development of the hypoglycemic syndrome was studied during inhibition of the higher regulatory centers by narcotics as well as upon surgical removal of the cerebral cortex and direct application of the hormone to nerve centers. In connection with this work it was thought interesting to study the development of the insulin syndrome during inhibition of the cerebral cortex induced by weak, rhythmic electric impulses, i.e., during electrosleep. This is particularly important because electrosleep approaches natural sleep in its physiologic characteristics [2].

There are references in the literature indicating that electrosleep does not exert any appreciable effect on carbohydrate metabolism and that the blood sugar content does not leave the limits of physiologic fluctuations [1, 2].

The present work is concerned with the study of the glycemic curve under conditions of electrosleep on the one hand, and elucidation of the effect of electrosleep on the development of the insulin syndrome during hyperinsulinism on the other hand.

EXPERIMENTAL METHODS

Dogs were used in the experiments following 16-18 hours of fasting. A preliminary determination of the blood sugar curve was made under normal conditions and after administration of insulin, samples being taken over a period of 3-6 hours. The blood glucose content was then studied during electrosleep and after administration of insulin (from 1-2 to 5-10 units per 1 kg body weight) against the background of electrosleep.

Electrosleep was induced by means of an apparatus constructed in the laboratory by Iu. N. Kasatkin. As can be seen from the diagram (see Fig.; stage I) the generator of square-wave pulses mounted on tube 6N8 (L_1) is on the lines of an asymmetric multivibrator with positive shift which increases stability of the multivibrator performance. Regulation of the frequency of the multivibrator is achieved by changes in the magnitude of the resistance R_3. Impulses from the multivibrator (from the left half of the 6N8 tube) pass through the condenser C_3 to the grid of tube $6L_6$ (L_2). Impulse amplifier (stage II) is mounted on tube $6L_6$ (L_2) whose anode circuit includes resistance R_7 which is the anode load. The whole circuit is supplied by a rectifier (stage III) assembled on the two-half period system on tube 5Ts4S (L_5) whose output is balanced by two tubes 5G-4S (L_3 and L_4). Balanced voltage is equal to 300 v. This construction permits smooth regulation of frequency within the range of 50-200 cps with constant duration of 0.3 milliseconds and a duty ratio of 1 : 10. The object is put in parallel with the anode load in series with the milliammeter graduated to 10 ma. The apparatus described, based on the multivibrator, is simple to construct and reliable in performance.

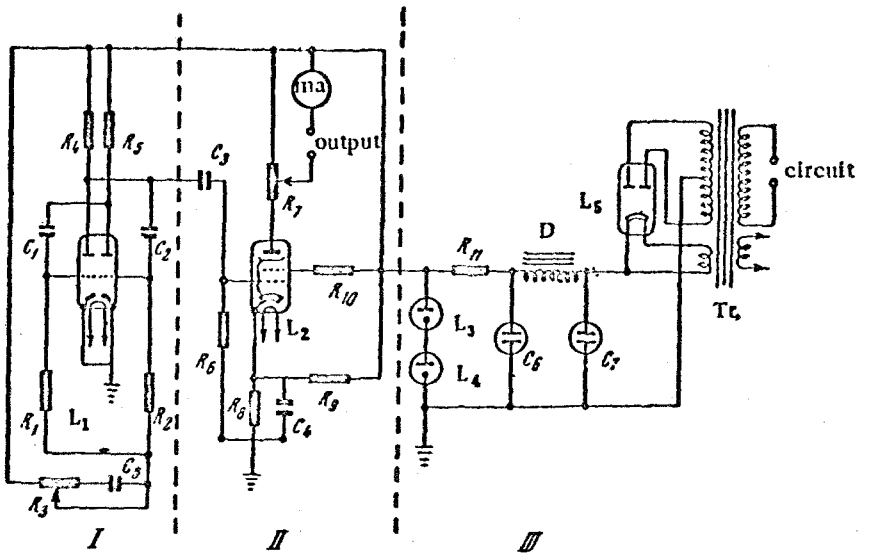

Diagram of apparatus used for inducing electrosleep. L_1-L_5) tubes; R_1-R_{11}) resistances; C_1-C_7) condensers; ma) milliammeter; Tr) transformer; D) inductor; I-III) stages.

Beofre switching on the apparatus, the electrodes (2.5 × 4.5 cm) were attached in the following way: the positive electrode was placed on the occiput, the negative on the frontal bone, its lower edge between the orbits. After establishing a certain frequency (100-150 impulses/sec) the current strength was gradually raised to 7-12 ma. In some sessions the current strength was raised rapidly to 20 ma with subsequent reduction to 5-10 ma. Later, experimental conditions were selected individually for each dog. In most experiments, sleep of sufficient depth ensued after 8-10 minutes following switching on of the current.

Blood for analysis was taken from the ear. Blood glucose content was determined by the Hagedron-Jensen method.

EXPERIMENTAL RESULTS

Experimental results proved to be consistent and therefore only part of the material is presented in Tables 1 and 2. Table 1 shows that the blood glucose level during 3 hours of electrosleep does not pass the limits of physiologic fluctuations.

TABLE 1

Fluctuations in Blood Glucose Level Under Normal Conditions and During Electrosleep

No. of experiment	Date of experiment	Experimental conditions	Blood glucose content in mg %					
			initial level	from start of experiment (in min.)				
				15	30	60	120	180
1	4/12 1957	Normal	87	86	83	90	92	89
	4/13 1957	Electrosleep	93	98	96	101	91	98
	4/18 1957		82	86	86	89	97	91
3	4/24 1957	Normal	93	87	94	89	87	91
	4/25 1957	Electrosleep	102	94	92	97	100	105

The influence of insulin on blood glucose level during electrosleep is illustrated by data in Table 2 which show that marked hypoglycemia developed when insulin was administered to animals during electrosleep.

It must be noted that convulsive seizures occurred in normal animals under ordinary conditions within 2-3 hours from the time of administration of large doses of insulin, whereas during electrosleep administration of the same dose of insulin was not accompanied by convulsions although the blood glucose level dropped to 30-40 mg%. However, 1-2 hours after cessation of electrosleep (5-6 hours after administration of large doses of insulin) there was a gradual onset of the main manifestations of hyperinsulinism – salivation, dyspnea, immobility. In isolated cases these manifestations were joined by convulsions. We did not succeed in observing enhancement and prolongation of the hypoglycemic action of insulin against the background of electrosleep as indicated by N. I. Akishina.

TABLE 2

Influence of Insulin on Blood Glucose Level During Electrosleep

Date of experiment	Date of experiment	Dog's weight in kg	Experimental conditions	No. of units of insulin admin.	Blood glucose content in mg%					
					before insulin administration	after insulin administration (in minutes)				
						15	30	60	120	180
1	4/21/57	8.1	Control (without sleep)	8	101	91	56	53	51	51
	4/23	8.0	Electrosleep	8	99	87	65	62	57	51
	5/9	8.3	Control (without sleep)	40	102	89	55	50	45	39
	5/10/57	8.2	Electrosleep	40	98	91	57	60	47	47
3	5/8	11.8	Control (without sleep)	110	103	99	100	63	47	36
	5/7	11.8	Electrosleep	110	107	102	99	76	59	45
	5/4	10.5	Control (without sleep)	55	88	71	43	37	30	—
6	5/6/57	10.4	Electrosleep	55	92	84	54	39	34	32

The results of these investigations demonstrate that electrosleep does not affect the hypoglycemic action of insulin. During electrosleep the insulin-induced hypoglycemia is not accompanied by the characteristic manifestations of hyperinsulinism.

SUMMARY

Variations in the concentration of blood glucose are not above or below the level of the physiological changes during electrosleep induced by weak rhythmical electric impulses. Electrosleep has no effect on the hypoglycemic action of insulin. However, when massive doses of insulin are introduced the characteristic symptoms of hyperinsulinism do not appear. A new design for a more stable apparatus for inducing electrosleep is presented.

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