Changes of Electro-Shock Seizure Threshold in Alloxan Diabetic Rats

In previous experiments we found that the effectiveness of drugs inhibiting transmission process at the peripheral cholinergic synapses was altered by experimental diabetes. The ganglionic blocking effect of hexamethonium, TEAB, and D-tubocurarine was found to be significantly less expressed in depancreatized cats than in controls[1,2]. In normal animals, insulin exerted an opposite effect[3]. Furthermore, susceptibility to D-tubocurarine of the motor end-plates of alloxan diabetic rats was also shown to be decreased, whereas the effectivity of suxamethonium was prolonged[4]. These results were confirmed by QUEVAUVILLER and PODEVIN[5]. From the findings obtained the conclusion may be drawn that the altered pharmacological reactivity might be due to an increased excitability of the synaptic structures via a relative corticoid preponderance induced by insulin deficiency. In the present experiments, an attempt was made to elucidate whether or not the excitability of the central nervous system (CNS) of alloxan diabetic rats was also changed. Therefore, the electro-shock seizure threshold (EST) was determined.

Methods. Measurements were carried out on female rats of R-Amsterdam strain weighing 210–240 g with bitemporal electrodes according to WOODBURY and DAVENPORT[6] on every 2nd day for 4 weeks. A group of animals was injected with 40 mg/kg alloxan (Fluka) i.v. on the 14th day of the experiment. The other group received the same volume of isotonic saline.

The animals were divided into 3 groups: 1. Control (30 rats); 2. alloxan-treated non-diabetic (22 rats: blood sugar level under 200 mg/100 ml, only a temporary glycosuria without weight loss), and 3. alloxandiabetic group (26 rats: blood sugar level above 200 mg/100 ml, permanent glycosuria, weight loss of 20–40 g). Blood sugar was determined by the orthotoluidine reagent[7] at the end of the experiment.

Changes of EST in alloxan diabetic rats

Day of determination	EST in mA ± SD		
	Control group (30)	Alloxan-treated non-diabetic group (22)	Alloxan diabetic group (26)
1.	20.4 ± 1.2	20.5 ± 1.4	21.1 ± 1.4
3.	22.1 ± 1.3	22.6 ± 1.6	22.3 ± 1.5
5.	21.8 ± 1.5	22.9 ± 1.4	23.1 ± 1.3
7.	22.8 ± 1.4	22.8 ± 1.5	22.9 ± 1.5
9.	23.1 ± 1.5	23.3 ± 1.5	23.5 ± 1.3
11.	23.3 ± 1.4	23.1 ± 1.6	23.6 ± 1.4
13.	23.6 ± 1.3	23.3 ± 1.4	23.8 ± 1.4
Treatment	saline	alloxan	alloxan
15.	23.3 ± 1.5	23.6 ± 1.5	22.3 ± 1.7
17.	23.8 ± 1.4	22.4 ± 1.5	20.9 ± 1.5
19.	23.1 ± 1.5	22.1 ± 1.6	20.1 ± 1.5
21.	22.9 ± 1.2	22.6 ± 1.4	19.4 ± 1.3
23.	22.8 ± 1.3	22.1 ± 1.4	18.2 ± 1.4
25.	22.8 ± 1.4	21.9 ± 1.4	17.8 ± 1.2
27.	22.8 ± 1.3	22.1 ± 1.3	17.4 ± 1.2
Difference on the 27th day (%)	Control/alloxan-treated non-diabetic 3.1% $p > 0.2$		
	Control/alloxan-treated diabetic 23.7% $p < 0.001$		

SD = standard deviation; number of the experimental animals in parentheses.

Results and discussion. In all the 3 groups studied, after a transitory increase, the EST values were stabilized until the 14th day of the experiment. Either in the control or in the alloxan-treated nondiabetic groups, non considerable change occurred during the second 2 weeks, while in diabetic rats EST started to decrease 3 or 4 days after diabetes had been developed. This diminution was progressive and lasted till the end of the experiment. On the 27th day the average EST value in diabetic rats was found to be lower by 23.7% than that in controls (a statistically significant decrement; $p > 0.001$; see Table).

The decrease in EST during diabetes suggests that the excitability of the corresponding areas in the CNS is increased. Since alloxan treatment without inducing diabetes fails to alter EST, the phenomenon may be explained by a hormonal imbalance due to insulin deficiency. During diabetes, an endogeneous corticoid predominance develops. Natural glucocorticoids have been shown to increase excitability of the CNS[8]. Our data suggest that these hormonal changes lead to the decrease in EST during experimental diabetes. Consequently, an increased excitability is induced by diabetes not only at the peripheral cholinergic synapses, but in the CNS as well.

Summary. During a 4-week period, the electroshock seizure threshold (EST) of R Amsterdam rats was determined. When alloxan induced diabetes, the EST values significantly decreased, while in the alloxan-treated non-diabetic group they remained unchanged. The results suggest that diabetes induces increased excitability in the central nervous system.

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