EFFECT OF CHANGES IN THE BLOOD GLUCOSE LEVEL ON THE STEADY POTENTIAL OF THE RABBIT EYE

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Carbohydrate metabolism plays an important role in function of the pigmented epithelium in the outer layers of the retina. Inhibition of glycolysis, by monoiodoacetate, for example, is known to lead to total disturbance of activity of the retina and degeneration of its outer layers, including the rods and cones [11, 12]. Phagocytosis of disks of outer segments of the photoreceptors in a culture of pigmented epithelial cells has also been shown to be definitely inhibited by glucose deficiency [8]. Glucose is supplied to the photoreceptors from the choroid through the pigmented epithelium, and disturbance of this transport is regarded as one possible factor causing diseases of the retina [3, 13].

One parameter of retinal function and of the state of the pigmented epithelium is the steady potential (SP) of the eye, which can be estimated indirectly from the electro-oculogram (EOG). The SP and its changes, induced by photic stimulation, reflect processes of interaction of the pigmented epithelium with the rods and cones and also, possibly, the choroid [2, 6, 9]. It has recently been shown that the light-induced rise of SP, which takes place 7-10 min after intensive illumination, as well as the dark drop, accompanying extinction of light, arise on the basement membrane of the pigmented epithelium [7].

In disturbances of carbohydrate metabolism developing in patients with diabetes, changes are observed in the EOG [4, 10]; low values are obtained, moreover, not only in the presence of a marked retinal lesion (retinopathy), but also in the absence of any visible changes in the fundus [1].

The aim of the investigation described below was to examine how an important factor in diabetes, namely the blood glucose concentration, affects the EOG in rabbits.

TABLE 1. Electro-Oculographic Parameters for Rabbits during Changes in Blood Glucose Concentration

Experimental conditions	Initial SP level, μV/deg	K_A, %
Control	17,0±1,4 (24)	156,0±2,2 (24)
Single injection of glucose	21,7±1,5* (14)	166,0±6,6 (14)
Single injection of insulin	12,4±1,5* (8)	113,0±2,1* (8)
Injection of insulin after administration of glucose	15,2±1,8 (5)	139,0±5,9* (5)
Long-term feeding with glucose: after end of feeding	13,6±1,4 (5)	129,0±5,6* (5)
4 months after end of feeding	15,7±1,0 (5)	150,0±3,1 (5)

Legend. Number of experiments given in parentheses. *P < 0.05 compared with control.

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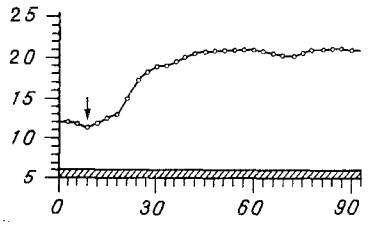

Fig. 1

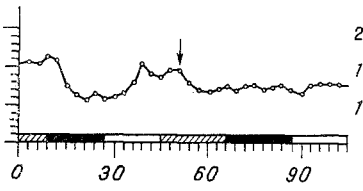

Fig. 2

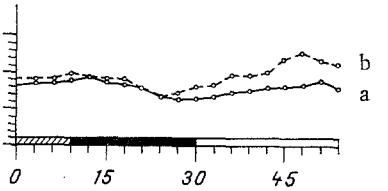

Fig. 3

Fig. 1. Changes in SP of the eye after injection of glucose into the blood stream. Abscissa, time (in min); ordinate, relative value of SP, estimated from EOG (in μV/deg). Shading denotes ordinary room lighting (50 lx). Arrow indicates beginning of glucose injection.

Fig. 2. Changes in SP during dark and light adaptation, before and after injection of insulin. Beginning injection K_A = 144, after injection K_A = 113%. Black band along abscissa denotes darkness, white band bright light (800 lx). Arrow indicates injection of insulin. Remainder of legend as to Fig. 1.

Fig. 3. Changes in SP during dark and light adaptation, after hyperglycemia. a) Immediately after end of glucose feeding (K_A = 125%), b) 4 months after end of feeding (K_A = 153%). Remainder of legend as to Figs. 1 and 2.

EXPERIMENTAL METHOD

Experiments were carried out on 48 grey rabbits. Changes in SP of the eye of the unanesthetized animal were recorded by a modified method [5]. Rotation of the eye required to record the EOG was produced forcibly by a ring sutured to the sclera under local anesthesia, by means of which the eyeball could be turned through 20° to either side (total angle of rotation 40°). Recording electrodes, consisting of injection needles, were inserted into the skin at the medial and lateral angles of the eye, and the reference electrode was fixed to the forehead. The EOG was recorded on an ÉÉGP4-02 electroencephalograph. It was recorded first with an intensity of illumination in the room of about 50 lx, then in darkness every 2 min for 30 min, and again in bright light (800 lx at the level of the pupil), also for 30 min. Changes in SP to light and in darkness were estimated as Arden's coefficient (K_A), namely the ratio of the height of the light-induced maximum to that of the dark-induced minimum, expressed as a percentage [2]. The absence of changes in SP corresponds to K_A = 100%.

To obtain a considerable but brief increase in the blood sugar concentration, 20 ml of a 40% solution of glucose was injected into the rabbit's auricular vein in the course of 1 h by means of a special automatic device ensuring a uniform rate of injection. The blood sugar level was lowered by an injection of insulin in a dose of 4 U/kg. The initial EOG was recorded for 30-60 min after the injection, followed by changes in the EOG during dark and light adaptation. The blood sugar was determined by the orthotoluidine method before and after recording of the EOG.

Prolonged-hyperglycemia was induced by feeding the rabbits daily with glucose (6 g/kg) for 4 months. Both before and after the end of glucose feeding, a standard set of measurements of the EOG (initial value, in darkness and in light) was taken, and the blood sugar was determined. After 4 months of normal feeding of the animals the blood sugar was again determined and the EOG investigated.

After the end of the investigations histological sections of the animals' eyes were stained with hematoxylin and eosin, by Van Gieson's method, and for elastin.

EXPERIMENTAL RESULTS

Control data were obtained on 24 animals. The relative value of the initial SP was 17.00 ± 1.45 μV/deg and K_A = 156.0 ± 2.2%, a little below the average values of this ratio in man. The curve showing changes in SP of the rabbit's eye during dark and light adaptation was generally similar with that obtained in man (with some differences of detail). The blood sugar concentration, as shown by the results of tests on 27 animals, was 103.0 ± 2.0

mg %. As a result of injection of 20 ml of 40% glucose solution in the course of 1 h the blood sugar rose to 338.0 ± 36.9 mg %. SP under these circumstances rose appreciably during the first 30-40 min (Table 1, Fig. 1) and thereafter did not change significantly. K_A also rose a little, although on average its increase was not statistically significant.

Injection of insulin lowered the blood sugar concentration to 45.0 ± 7.3 mg %, and was accompanied by a considerable reduction in SP and K_A (Table 1, Fig. 2). EOG disturbances were observed in the phases of the dark fall and light rise of SP. Meanwhile injection of insulin after administration of glucose (in the same concentrations as in the previous experiments) did not induce any significant hypoglycemia (91.0 ± 4.9 mg %). Under these conditions the changes in SP and K_A were correspondingly smaller (Table 1).

The prolonged supply of large doses of glucose cause the blood sugar to rise to 154.0 ± 14.4 µg %. The EOG, recorded after the end of feeding, revealed a significant fall in K_A compared with the control. The value of SP also was depressed somewhat. The EOG disturbances were more marked in the phase of the light rise of SP (Fig. 3). Later, the rabbits were kept for 4 months under ordinary conditions on a normal diet. The blood sugar during this period fell to 118.0 ± 12.9 mg %. Recording the EOG again showed an increase in both SP and K_A, the mean values of which were virtually indistinguishable from normal (Table 1, Fig. 3). Restoration of K_A took place mainly on account of a great light rise of SP.

During the first ophthalmoscopic examination, in the course of the experiment, and 4 months after the end of glucose feeding no visible changes were found in the fundus of the eye. Histological investigations revealed no pathological changes in the retina, iris, and blood vessels.

An increase in the glucose concentration in the rabbits' blood thus caused a rapid and considerable rise of SP. This rise evidently reflects intensification of carbohydrate metabolism in the pigmented epithelium and rods and cones in response to the supply of the principal energy-yielding material. Meanwhile lowering the blood sugar level by injection of insulin led to a sharp decrease in the EOG parameters. These changes were probably due to the hypoglycemia and not to the influence of the insulin itself, because compensation of the insulin-induced hypoglycemia by injection of an excess of glucose into the blood stream led to a much smaller reduction of the parameters.

During a prolonged increase in the blood sugar concentration a reduction of SP and K_A was observed. These observations indicate that an excess glucose concentration over a long period of time inhibits the function of the pigmented epithelium. After the end of glucose feeding the parameters were restored to normal, evidence that the changes were functional in character. This conclusion is confirmed by the results of the ophthalmoscopic and histological investigations. The possibility cannot be ruled out that a longer period of hyperglycemia might have led to the appearance of organic changes in the retina and in the vascular system of the eye.

The results of the electro-oculographic investigations demonstrated the effect of hypo- and hyperglycemia on SP of the rabbit eye. A fall in the blood glucose level, even for a short time, and prolonged elevation of its level lead to depression of function of the pigmented epithelium.

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