OSCILLATORY EVOKED POTENTIALS IN THE RABBIT VISUAL SYSTEM IN EXPERIMENTAL RETINAL PATHOLOGY INDUCED BY MONOIODOACETATE ADMINISTRATION

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Dystrophy induced by intravenous injection of monoiodoacetic acid (MIAA) is often used as an experimental model of retinal pathology. It has been shown [11-15] that this pathological state is very similar to retinitis pigmentosa in man or in animals with hereditary degeneration of the retina. The similarity is manifested not only in the clinical picture, but also in the character of the morphological changes in the retina and even in the pathogenetic molecular mechanisms.

The present investigation had two aims: to discover any particular features of disturbance of formation of the electroretinogram (ERG) and evoked potentials (EP) in the superior colliculus (SC) and visual cortex (VC) in experimentally induced retinal pathology of varied degrees of severity, and to analyze the nature of the unequal changes and their possible relationship to the phenomenon of "compensation."

EXPERIMENTAL METHOD

Experiments were carried out on waking gray chinchilla rabbits under chronic conditions. The ERG was recorded by means of a contact lens with steel electrode mounted in it. The lens was filled with physiological saline. A 0.5% solution of amethocaine and a 1% solution of atropine were instilled into the eye. The reference electrode was fixed in the nasal bones. The investigations were conducted under dark adaptation conditions. Nichrome electrodes, inserted to coordinates of a stereotaxic atlas [16], and connected to a UPB2-03 ac amplifier, were used to record EP in VC and SC. EP signals were photographed from the screen of a dual-beam S1-18 cathode-ray oscilloscope. Photic stimulation to evoked electrical responses of the retina and brain structures of the visual system was carried out by means of the FFS flash photic stimulator (Medicor, Hungary). EP of the brain structures and retina were recorded under oscillatory conditions (frequency range of the amplifiers 333-2000 Hz). These conditions enabled all complex components of evoked potentials both of the retina and of the central structures of the visual system to be discovered [2], and it was hoped that this would provide additional opportunities for judging the character of their disturbances. Since the photopic system of the retina is directly involved in the genesis of oscillatory EP, it seemed advantageous to use them for the adequate detection of changes in the functional state of the visual cortex after the creation of retinal pathology, for the macular region and the surrounding region of cones are predominantly represented in it. Experimental retinal dystrophy was produced by the method in [11-15], by intravenous injection of a 4% solution of MIAA. Depending on the planned severity of retinal damage, the dose of MIAA was varied between 18 and 25 mg/kg body weight. In some cases 2 or 3 injections were given. The degree of retinal involvement was monitored by data of electrophysiological, ophthalmoscopic, and morphological investigations [1]. Structures of SC were injured by electrocoagulation through implanted electrodes, by means of an "Élektrotom" high-frequency diathermy apparatus. The degree of injury was monitored electrographically (by disappearance of EP and depression of spontaneous activity), and also anatomically (in total serial brain sections). SC was stimulated by local application of a 2% solution of strychnine through implanted chemical electrodes, and also by anodal polarization (5-10 μA for 10 min).

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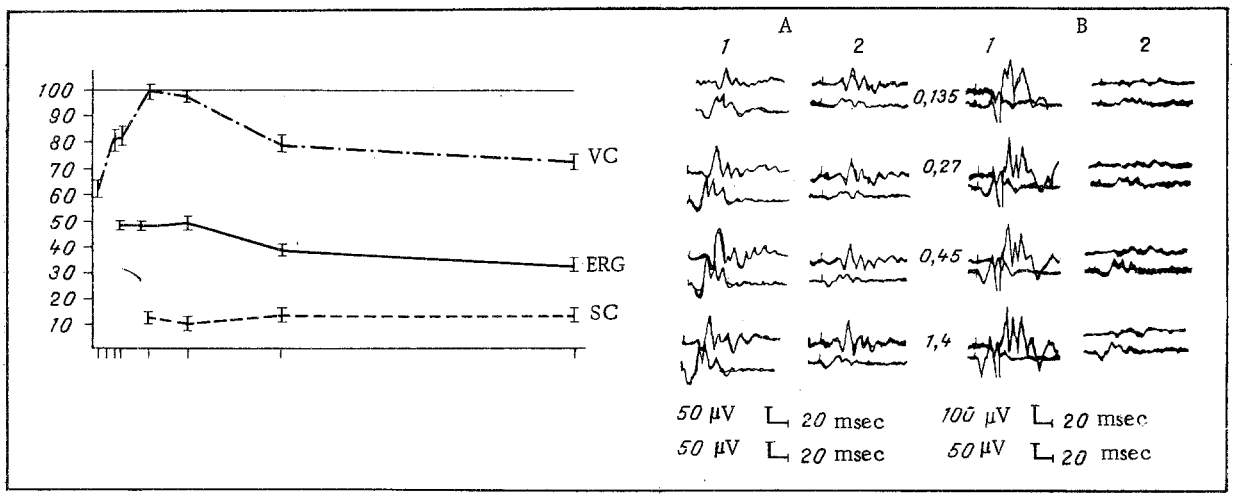

Fig. 1. Effect of retinal dystrophy of conventional average severity on formation of ERG and EP in VC and SC. Graph on left: abscissa, brightness of stimuli — short vertical lines from left to right indicate 0.016, 0.023, 0.045, 0.068, 0.135, 0.27, 0.45 and 1.4 J, respectively; ordinate, amplitude of first two components of responses of retina, SC, and VC (in percentages of amplitude of responses in control, before creation of the lesion). Traces from oscilloscope screen shown on right. A) responses of VC (top trace) and ERG (bottom trace) before (1) and after (2) creation of retinal dystrophy; considerably weaker inhibition of EP in VC than of ERG (under conditions of retinal pathology); B) responses of SC (top trace) and ERG (bottom trace) before (1) and after (2) creation of retinal dystrophy: EP in SC are depressed by a greater degree than ERG. Intensity of stimuli, from top to bottom: 0.135, 0.27, 0.45, and 1.4 J. Oscillatory potentials recorded, frequency range of amplifiers 333-2000 Hz.

EXPERIMENTAL RESULTS

By varying the dose of MIAA, the number of repeated injections of it, and the times between them, retinal lesions which differed in depth and severity could be obtained: from mild to absolute, and accompanied by total loss of visual function and, correspondingly, by total absence of the ERG.

Comparative studies of ERG and EP formation in VC and SC to photic stimuli of varied intensity (on normal rabbits and on rabbits with experimental retinal dystrophy) showed that under pathological conditions, besides inhibition of ERG formation, the principal components of EP also were inhibited at the same time in VC and SC. The degree of their inhibition depended on the severity of the dystrophic changes in the retina, but it differed for VC and SC. It was shown, for instance, that the primary response (PR) of EP in VC was inhibited in every case of pathology (whether expressed in absolute terms or in percentages of the original control data) to a much lesser degree than the ERG. This was clearly exhibited over the whole range of brightnesses of the photic stimuli studied (0.016-1.4 J) and in different degrees of retinal pathology, including severe. Whereas in conventionally weak pathology the amplitude of the ERG, depending on intensity of the photic stimuli, was lowered by 25-36%, the total amplitude of the primary responses of EP in VC was depressed by only 10-17%, and in conventionally moderate pathology it was depressed by 45-60% and by 25-35%, respectively, and in conventionally severe pathology by 75-85% and 55-67%, respectively. The typical picture of ERG and EP formation in VC to photic stimuli of varied intensity, before and after creation of a retinal lesion of conventionally average severity, is shown in Fig. 1, II, A, which demonstrate that, despite very marked depression of ERG formation, less significant inhibition of the primary response of EP in VC was observed.

The results show that definite resistance of VC to disturbance of retinal function exists, but it has a definite range, and with intensification of the pathological process in the retina, it gradually diminishes.

A different picture was observed when changes in evoked activity in SC were analyzed (Fig. 1: II, B). Whatever the degree of retinal pathology, EP in SC were depressed more than EP in VC and more than the ERG. In this case, for instance, depending on the intensity of photic stimuli, depression of the overall amplitude of the ERG was 52-64% of the original control

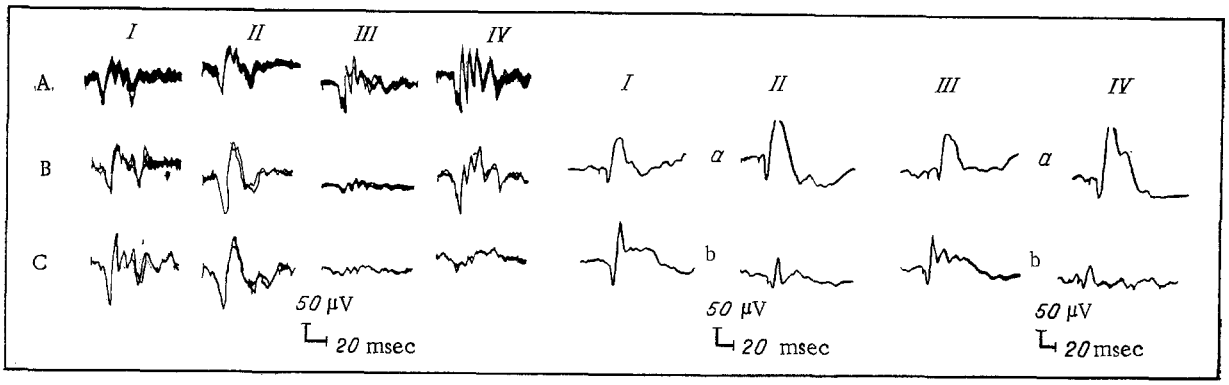

Fig. 2

Fig. 3

Fig. 2. Effect of coagulation injury of SC on EP formation in VC. I, II) EP in right and left VC, respectively; III, IV) EP in right and left SC, respectively. A) Control, B) after injury to right SC, C) after additional injury to left SC. Injury to left SC leads to an increase in amplitude of EP in left VC, whereas injury to left SC leads to an increase in amplitude of EP in right VC.

Fig. 3. Effect of stimulation of SC by strychnine and by anodal polarization on EP formation in SC itself and also in contralateral VC. a) EP of right SC, b) EP of left VC. I, III) control, II) after application of strychnine to SC, IV) after anodal polarization of SC.

level, whereas the overall amplitude of the first two components of EP in SC was depressed by 85-90%. Depression of the amplitude of the corresponding components of EP in VC in this same case was by 25-37% of the original level.

Comparative data on changes in formation of the ERG and of primary responses of EP in VC and SC in the presence of retinal pathology of conventional average degree are given in Fig. 1:I.

It can be concluded from analysis of the results that the greater severity of the disturbance of function of SC was probably due to the following circumstances. According to existing information [7, 9], SC differs from VC in having its main input solely from the rod system, whereas, according to data in the literature [15], in retinal dystrophy induced by injection of MIAA, it is this same rod system that is affected first and foremost. This explains the more marked depression of EP in SC than in VC, and even in the retina, where both rod and cone systems participate in the genesis of evoked responses.

The question arises: why should EP in VC be very resistant (naturally, within a certain range of pathology) to disturbances of retinal function and why should it be depressed by a much lesser degree than the ERG?

It is natural to suggest that a lesion affecting mainly (although by no means exclusively) the rod system of the retina is reflected only a little in EP formation in VC, since its contribution to the genesis of this EP is not decisive. Evidently this factor cannot be ruled out to that extent, although we used a technique of recording oscillatory EP, the main contribution to whose genesis is also that of the cone system of the retina. However, acknowledging the multichannel nature of conduction of information into VC and the role of the retinocolliculocortical channel (RCCC) in this process [4, 5] raises the question of a possible role of changes in relations between the retinogeniculocortical channel (RGCC) and RCCC in the conduction of information at the VC level in retinal pathology. If it is assumed that under normal conditions RCCC exists in opposite relations to the main RGCC, greater functional depression of SC, caused by the more marked limitation of excitation arriving in SC from the retina could facilitate the formation of excitation reaching VC along the main RGCC. This hypothesis was tested in two series of experiments. In series I the state of EP in the right and left VC was studied before and after injury to the right and left SC by electrocoagulation. It was found that injury to the right SC facilitates the formation of EP in the left VC; it had virtually no effect, however, on the response of the right VC. Meanwhile, additional injury to the left SC led to an increase in amplitude of EP in the right VC also (Fig. 2).

In the experiments of series II the effect of local stimulation of SC by strychnine and by anodal polarization on EP formation in VC was studied. The experiments showed that stimulation of the right SC by strychnine leads to an increase in amplitude of EP in SC itself and,

at the same time, to a significant fall in amplitude of EP in the left VC. Anodal polarization of SC had a similar effect (Fig. 3).

Consequently, injury to SC facilitates EP formation in the contralateral VC, whereas excitation of SC by strychnine or by anodal polarization considerably inhibits the formation of these same responses. This suggests that under normal circumstances RCCC for the conduction of visual information inhibits the contralateral RGCC. Consequently, one possible cause of the comparative resistance of VC to a disturbance of retinal function due to experimental dystrophy (induced by injection of MIAA) may be its release, to a greater or lesser degree, from the inhibitory influence of the colliculocortical input. It must be remembered that interaction between these channels can take place not only at the cortical level, but also in the lateral geniculate body (LGB). There is morphological evidence [6, 8] of the presence of input from SC in its dorsal nucleus and also electrophysiological evidence of the inhibitory effect of pulsed stimulation of SC on the formation of LGB responses to flashes [3, 10].

Changes in the character of relations between the different channels conducting visual information may therefore be one factor in the compensatory shifts in the visual system and they must be taken into account when pathological states in that system are analyzed.

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