in part by Grant No. EY01171 from the National Institutes of Health and a grant-in-aid from Fight for Sight, Inc., New York, N. Y. Submitted for publication April 8, 1974.

Key words: outer segments, cyclic AMP, cyclic GMP, phosphodiesterase, cyclase, protein kinase, adaptation.

REFERENCES


The electroretinogram of children deprived of pattern vision. U. YINON AND E. AUERBACH.

The electroretinogram (ERG) was studied with flash stimulation in 16 children who, at young ages, suffered from monocular and binocular visual deprivation. No significant difference was found between the b-wave amplitudes of normal and of deprived eyes (0.4 > p > 0.2). The slight increase in the retinal response (b-wave) seen after cataract removal is due to changes in the optical properties of the eye and not as a result of neural changes in the retina. No direct relationship was found between changes in the level of visual acuity and the level of responsiveness expressed by the amplitude and the latency of the ERG. In addition, wave-form complexity was the same in the normal and in the visually deprived eyes. That the visual acuity level was sharply decreased in all subjects, despite the abovementioned findings in the ERG, indicates that the site of the deprivation effect in humans is higher up in the visual system.

Early in life, environmental conditions play a role in altering the structure and function of the visual system. This is reflected, for example, by the effects of early pattern deprivation on the visual system, causing neural changes and as a consequence to these a sharp decrease in pattern discrimination.4-6 The question asked is whether the cortical effects found2,4 are secondary to neural changes in the retina of the deprived eye.

The condition of pattern deprivation in humans is more suitable for investigation in comparison to the situations produced in animals by suturing technique1 since it is caused by various types of lens and corneal opacities. However, recording from single neurons in human retina, like in animal experiments, is almost impossible; therefore, the electroretinographic techniques used enable us to examine the neural elements of the deprived mammalian retina, i.e., the receptor layer and the bipolar cells.5

We characterized the complexity of the electroretinogram (ERG) wave-form of children deprived of pattern vision, mainly due to cataracts. Also, the relationship between the decrease in visual acuity of visually deprived eyes and the electrical changes in their retina was investigated. Furthermore, when the ocular media in these children became clear after removal of the cataract, we have been able to examine whether under normal conditions of light input to the retina the effect produced is in the previously deprived retina or higher up in the visual system.

Methods. Sixteen visually deprived children served for the electrophysiologic recordings; nine of them had unilateral or bilateral congenital cataracts, five had traumatic cataracts, and two had leukemia. Ten children's ages ranged between 2 months to 6.5 years and the other children's ages ranged between 7 and 12 years. Ten normal adult subjects served as comparisons. Refraction and visual acuity were measured concurrently. For several children, 2 to 4 electrophysiologic
Fig. 1. Temporal changes in visual acuity of a visually deprived child as a result of traumatic cataract at 4.5 years of age. Considerable improvement was seen after two operations following the initiation of the cataract (D-off). \( \Delta \) - - - \( \Delta \) Expected trend of the line. Full recovery of visual acuity could not be obtained because of the amblyopia developed while this eye was visually deprived.

Fig. 2. Relationship between visual acuity and the ERG in visually deprived (○) children and in normal subjects (●). ERG data from steady-state at dark adaptation were used.

tests were repeated during the period in which they underwent medical treatment.

Prior to the retinal examinations, the pupils were dilated with mydriaticum Roche or phenylephrine HCl 10 per cent (Neosynephrine). The corneas were anesthetized with oxybuprocaine 0.2 per cent (Novesine). Henkes contact lens electrodes were fastened to the cornea of each eye, and filled with methylcellulose 2 per cent in saline. An indifferent electrode was fastened to the skin at the mid-supraorbital rim above each eye and a ground electrode was attached to one ear. Recording was done from both eyes simultaneously. A Grass AC preamplifier (P511) was used with filters set between 0.1 C. and 1 Kc per second and the ERG's were photographed singly from the oscilloscope.

The subjects were examined in a recumbent
position in an electrically shielded room. A Grass photostimulator (PS-2) was used connected to a stroboscope, the flash duration of which was approximately 10 msec. The stroboscope was centered 20 cm. in front of the eyes. Relative intensities of 1, 2, 4, 8, and 16 were used. The electrophysiologic tests were carried out both in light (5 minutes of 230 foot candles) and during dark adaptation (30 minutes).

Amplitudes and peak latencies of the a- and b-waves of the ERG were measured. Statistical analysis was done using the t-test.

Results. The children with congenital cataract have been practically deprived of pattern vision for long periods of time. Due to the deprivation, the affected eye was of no use and became amblyopic, even after cataract extraction. However, the fact that the lens or cornea was opaque interfered only slightly with brightness as will be seen later by the slight and nonsignificant decrease of the ERG amplitude. A similar effect due to shorter periods of deprivation have been seen in children who had traumatic cataract. If recovery was seen due to treatment in the visual acuity of the deprived eye, despite the amblyopia, it never reached the level of the normal eye (Fig. 1).

We studied the relationship between the retinal response and visual acuity in the visually deprived children. For the b-wave most of the data for low visual acuity were concentrated at amplitude ratios between 1.0 and 1.5 (1.0 on the abscissa indicates equal amplitudes in the normal and the affected eye) (Fig. 2, A). The latency results of the b-wave were similar to that of the amplitude data but were more clustered near ratio value 1.0 (Fig. 2, B). Similar results were obtained for the a-wave. These results indicate that the retinal elements which participate in the generation of the b-wave are influenced. However, the decrease in amplitude is not due to neural changes in the retina but is probably due to optical disturbances in the ocular media resulting from the cataract. In support of the latter is the lack of a certain function describing the b-wave/acuity ratio and, instead, a randomized spread of the points in Fig. 2 is found. The data presented in Fig. 2 for two normal subjects show some variability. It is also clear from Tables I and II that the amount of variability in normal eyes (six subjects) is similar to that of deprived eyes, indicating no essential differences between them. In addition to this, it was found that the complexity of the ERG wave-form was the same for the visually deprived eye and for the normal eye (Fig. 3). The photopic-scotopic relationship of the components of the ERG during the recovery in dark adaptation was found in the normal range.
Fig. 4. ERG's of a baby with bilateral congenital cataract before (A) and after (B) operation. ERG's of a normal subject under the same conditions are also presented (C). ERG's were recorded in the photopic phase of dark adaptation. Upper trace: right eye, lower trace: left eye. Calibrations 200 μV and 60 msec.

Table I: ERG responses of nine visually deprived children (in parenthesis are data for two children after cataract surgery)

<table>
<thead>
<tr>
<th></th>
<th>Light adaptation</th>
<th>Dark adaptation</th>
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<tbody>
<tr>
<td></td>
<td>2-5 mins.</td>
<td>2-5 mins.</td>
</tr>
<tr>
<td></td>
<td>a-wave</td>
<td>b-wave</td>
</tr>
<tr>
<td>Latency (msec):</td>
<td>Normal</td>
<td>11.4</td>
</tr>
<tr>
<td></td>
<td>Affected</td>
<td>(10.4)</td>
</tr>
<tr>
<td>Amplitude (μV):</td>
<td>Normal</td>
<td>43.1</td>
</tr>
<tr>
<td></td>
<td>Affected</td>
<td>(73.1)</td>
</tr>
<tr>
<td></td>
<td>(63.4)</td>
<td>(142.1)</td>
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</tbody>
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NS = Nonsignificant difference.

Discussion. While in species lower than primates, monocular deprivation produces either transitional or long-term diminution of the (ERG) b-wave in most cases, this was not observed in studies on primates, and in the present study on visually deprived children. In a recent study, however, a temporary depression of the b-wave was found in the deprived eye of monocularly patched children and a recovery occurred after the patching was discontinued. These differences among species may be explained by the greater involvement of the retina in visual
Table II. ERG responses in six normal adults

<table>
<thead>
<tr>
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<th>Light adaptation</th>
<th></th>
<th>Dark adaptation</th>
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<tbody>
<tr>
<td></td>
<td>2-5 mins.</td>
<td>2-5 mins.</td>
<td>25-30 mins.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a-wave</td>
<td>b-wave</td>
<td>a-wave</td>
<td>b-wave</td>
</tr>
<tr>
<td>Latency (msec.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>16.0</td>
<td>31.0</td>
<td>20.8</td>
<td>48.9</td>
</tr>
<tr>
<td>Left eye</td>
<td>11.4</td>
<td>28.0</td>
<td>20.4</td>
<td>46.7</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>64.6</td>
<td>93.3</td>
<td>140.5</td>
<td>369.3</td>
</tr>
<tr>
<td>Left eye</td>
<td>91.3</td>
<td>111.2</td>
<td>107.0</td>
<td>309.5</td>
</tr>
</tbody>
</table>

NS = Nonsignificant difference.

functions in lower animals related to specific structural differences. This reasoning has to be considered when deprivation effects reflected by the ERG are compared in humans and animals.

Our results make it unlikely that neuronal changes take place in the human retina due to deprivation. This was proved by the nonsignificant difference obtained between the ERG's of normal and cataractous eyes. Also, the pattern of the ERG is similar in its complexity in deprived and in normal eyes. In cases in which the ERG amplitude was smaller in the deprived eye it was interpreted either to variability within the responses as found in normal subjects, or to blocking of the light to the retina in cataractous eyes. That the differences in the ERG are due to optical reasons and not due to neural factors was suggested by Burian and Burns. They found that in patients with senile cataract the lower post-operative b-wave amplitude in two-thirds of their patients is explained by the action of the cataractous lens serving as a diffusing screen.

Since deprivation of pattern vision during development was responsible in most of our subjects for a very low level of visual acuity, a higher level of the visual system than the retina is involved. This assumption is supported by the fact that we found no relationship between changes in the level of visual acuity and changes in amplitudes and latencies of the a- and b-wave of the ERG. This assumption can hardly be concluded for strabismic amblyopia or amblyopia ex anopia since the cause of the defect is not clear as in the case of deprivation amblyopia (lenticular or corneal opacity). Additional evidence for localization in the brain is the fact that in children who underwent a partial recovery, a clear increase was observed in the visual acuity while in the ERG no change was observed. On the other hand, since we have used full-field stimulus the relationship between neural changes in the retina affecting the macular region and visual acuity is not clear. Further studies with macular ERG's in deprived retina are of great importance for this question.

In the retina of cats, no changes were found in the response of ganglion cells of the deprived eye in comparison to the seeing eye. However, because of the remarkable dissimilarity in retinal organization in cats and other species, the question as to whether macular changes exist has to be investigated specifically on the unitary level in the primate retina.

We are grateful to Dr. F. Abraham, Dr. M. Machlin, Mrs. Y. Basher, Mrs. S. Ben-Hanoch, and Mr. C. Shaw for their helpful assistance and advice.

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Key words: pattern deprivation, electroretinogram, visually deprived children, corneal opacity, congenital cataract, traumatic cataract, visual acuity.

REFERENCES

Volume provides an excellent review of prior studies as well as his own observations. This information was studied in detail by other means and Ruskell-vessels is delineated by selective injection. 

The circulation of the rabbit eye has been demonstrated in vitro using soft x-rays. 

A detailed in vitro demonstration of the ocular circulation using soft x-rays is presented. The contribution of individual vessels is delineated by selective injection. In addition, a preliminary in vivo study of the anterior ciliary circulation is included; and the potential for in vivo radiographic study of ocular circulation is discussed.

Soft x-rays have been used to demonstrate the microcirculation of the human eye in vitro. The purpose of the present work is to extend this method to the study of the rabbit eye in vitro and to use this as a background for development of in vivo radiologic studies of the ocular circulation. The circulation of the rabbit eye has been studied in detail by other means and Ruskell provides an excellent review of prior studies as well as his own observations. This information was used to evaluate the accuracy of our radiographs. In vitro, we have found it possible to demonstrate circulation at the level of large capillaries. In addition, a preliminary in vivo study shows some promise for usefulness with further refinement of technique.

**Technique.** The animals used in the in vitro experiments were male albino rabbits weighing 2 to 3 kilograms. Prior to death all animals were anticoagulated with 1,000 units of intravenous heparin. Thirty minutes after heparinization, the animals were killed with intravenous sodium pentobarbital.

One group of animals was injected with contrast via the common carotid artery. Immediately after death, one of the common carotid arteries was isolated in the neck and cannulated with a No. 4 French polyethylene catheter. The jugular vein on that side was then opened and the circulation flushed with room-temperature saline. Warm colloidial barium gel with a particle size of 0.1 to 0.5 μ was then injected with a plastic syringe; the injection was monitored by observation of the conjunctival and iris vessels. The animals were then decapitated and the heads placed in refrigeration to allow the gel to harden. After approximately 24 hours, the injected eye was enucleated and placed in a 10 per cent formalin solution. After fixation, the globes were dissected to allow radiography of the optic nerve, retina, choroid, and anterior segment separately.

In a second group of animals the eyes were enucleated immediately after death and major vessels of the globe were selectively cannulated following the method of Johnson and Grant. The warmed colloidial barium gel was injected and allowed to set in refrigeration. The eyes were fixed in 10 per cent formalin, and dissection was carried out to isolate the circulation of the cannulated vessel.

The dissected specimens were sealed in envelopes of plastic (0.004 μ in thickness) using a Futura Portable Heat Sealer. This served to immobilize the specimens for filming and to maintain them in a formalin atmosphere. Radiographs were made using a water-cooled unit with a chromium-copper target with a 0.2 mm. by 1.0 mm. focal spot and a thin beryllium window. Exposures in the range of 20 KVP and 20 ma. were used, the time of exposure being varied with the thickness of the specimen. Kodak Type R film was used. The radiographs were hand-processed in D19 Developer at 68° F. for eight minutes, fixed for sixteen minutes, and washed for one-half hour. A more detailed description of the barium suspension and the radiographic technique is presented in a separate communication.

In vivo studies were carried out on male albino rabbits anesthetized with intravenous sodium pentobarbital and periorbital injection of 2 per cent lidocaine. Injections of Renografin 60 were made either via a No. 4 French catheter in the common carotid artery or via a small polyethylene catheter in a long posterior ciliary artery. Two to