The electrically evoked response (EER) of the visual system

II. Effect of adaptation and retinitis pigmentosa

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In an attempt to learn the stimulus site of the EER, the following series of experiments was performed. (1) The effect of dark adaptation on EER and VER was determined. The effect was found to be negligible. (2) The effect of eliciting the electric phosphene on the course of dark adaptation was determined. Under our conditions there was no effect. (3) The effect of ambient light on amplitude of EER and VER was determined. Moderate levels of ambient light 7.0 foot-lamberts abolished the VER but $2 \times 10^2$ foot-lamberts decreased the EER only 20 per cent in one subject, less in others. (4) The determination of VER and EER on retinitis pigmentosa patients gave varied results. In some patients neither response could be elicited. In several others a sizeable EER could be obtained with our standard stimulus. To obtain a VER of the same subjective brightness a light level was required that was higher than for normal subjects. Since in all these instances the variables affecting the VER were not the same as those affecting the EER, it is assumed that the cell of origin is not the same for the two phenomena. If the cell of origin of the VER is the photoreceptor, it is probable that the cell of origin of the EER is more central than the photoreceptor.

Key words: Evoked electrical responses, visual evoked response, retinitis pigmentosa, light adaptation, dark adaptation, electric phosphene, flash stimulation, ambient light, retinal photoreceptor cells.

In a recent report we described the electrical evoked response of the visual system. We demonstrated that an electric current across the globe elicited a subjective electric phosphene and an evoked response which could be recorded from occipital scalp electrodes. We defined a number of conditions for obtaining the EER, but there are many questions yet unanswered. One of the most important of these deals with the excitability site stimulated by the electric current and responsible for initiating the response. If this site lies central to the visual cells, presumably the site of origin of the visual evoked response (VER), comparison of the two responses could provide valuable information on the state of the portion of the visual system lying between the two sites of
activation. Such a study is the object of the present report.

We have concentrated particularly on the effect of adaptation both to light and dark on the VER compared to the EER. We have also compared the nature of the two different responses when recorded in patients with known retinitis pigmentosa.

Methods

The electrical evoked response was obtained exactly as described in our previous publication. The EER was elicited by a current of 2 milliamperes for 5 milliseconds. The visual evoked response was obtained with Ganzfeld stimulation as described there also. Since the electric phosphene creates a sensation of light filling the whole visual field, it was considered desirable to compare the EER with a visual evoked response to a stimulus which also filled the entire field. The electrical evoked response was elicited with the cornea as the positive pole and alternatively as the negative pole in comparison to the large skin electrode. For the adaptation portion of the experiment a large number of determinations were made on a relatively small number of cooperative normal subjects. These results are presented below. With the retinitis pigmentosa cases, of course, no such stipulations on cooperation could be made, but in general we believe the results to be reliable.

Results

In Figs. 1 and 2, one may see the effect of dark adaptation on EER and on VER. Condition A is with the subject having been kept at normal room illumination of 7.0 foot-lamberts until initiation of measurements. For the 2.5 minutes of measurement room lights were off. Condition B is the determination made after 20 minutes in absolute darkness. It may be seen that the VER of the same subjective brightness as the EER shows less electrical response.
Fig. 2. Effect of dark adaptation on EER and VER, Subject C. A, Subject at normal room illumination; B, subject in darkness 20 minutes before determination.

for each subject as described previously. It is also evident that there is no greatly significant effect on either type of response as a result of dark adaptation.

A further ramification of this approach is the study of the effects of eliciting the electric phosphene on the process of dark adaptation. Experiments on four subjects are shown. Subjects A and B were examined with the pupils dilated; subjects C and D with the pupils undilated. In each case the electric phosphene was elicited on the test eye for a period of 2.5 minutes, two times, at 10 minutes apart after adaptation had reached its asymptotic phase. During the first period of stimulation the cornea was positive, during the second period of stimulation the cornea was negative. In each case the conditions were identical to those used for eliciting the EER. As can be seen from Fig. 3, there was no disturbance in the normal course of dark adaptation caused by the electrical stimulus. Figs. 4A, 4B, and 4C show the effect of light levels from darkness to much higher than the normal room illumination on EER and VER, and on two separate subjects. The four traces labeled A, B, C, and D in Figs. 4A and 4B represent responses obtained at light levels of A = 0, B = 5.0 × 10⁻³ foot-lamberts, C = 7.0 foot-lamberts, D = 2.0 × 10³ foot-lamberts. In the case of the EER, the maximum difference in response between the least intense and the most intense illumination of the surround was 22 per cent. In the other instances it was less than this. The range of light intensity from condition B to condition D was 400,000 times. In the case of the VER light intensity C was enough to
Fig. 3. Effect of producing electric phosphene on dark adaptation. Ordinate is relative intensity of threshold stimulus. Subjects A and B, pupils dilated; Subjects C and D, pupils undilated. Blocks on baseline indicate duration of phosphene production at one flash per second.

Fig. 4A. Effect of light on EER. Subject B. Condition A, complete darkness; B, $5.0 \times 10^{-3}$ foot-lamberts illumination of field; C, 7.0 foot-lamberts; D, $2.0 \times 10^{-3}$ foot-lamberts.
Fig. 4B. Effect of light on EER, Subject C. Condition A, complete darkness; B, $5.0 \times 10^{-5}$ foot-lamberts illumination of field; C, 7.0 foot-lamberts; D, $2.0 \times 10^{3}$ foot-lamberts.

Fig. 4C. Effect of light on VER, Subjects B and C. Brightness of stimulus flash when subject is in total darkness is subjectively equal to brightness of EER sensation in Figs. 4 and 5, condition A. A, Visual field in complete darkness; B, field at $5.0 \times 10^{-5}$ foot-lamberts; C, field at 7.0 foot-lamberts.
completely abolish the response. Hence intensity D was not shown in Fig. 4C.

In an attempt to apply the EER to the study of disease, examinations were done on eight individuals who had unequivocal retinitis pigmentosa. Although most of the histological material in our possession suggests that there is complete destruction of retinal organization in the later stages of the disease, there is reason to believe on histological grounds that retinitis pigmentosa might be a disease whose initial effects are restricted to the receptor cells. If this were the case, one might find diminished VER and intact EER in such individuals. However, in five of eight cases there was parallelism in the diminution of the two measurements. Where EER was of normal size, the VER was also intact; where VER was diminished, EER was also diminished. In three cases of the eight the VER was diminished disproportionately to the EER. These findings are shown in Figs. 5A and 5B.

Discussion

On the basis of the above findings on light adaptation particularly, it is reasonable to conclude that the structure sensitive to the electrical pulse of the EER lies proximal to the photoreceptor portion of the visual system. There is an increasing body of opinion which believes that the initial response to light stimulation by a photoreceptor is a change in membrane permeability and alteration of the potential across a membrane of the receptor cell. Thus adaptation to various levels of illumination from absolute darkness for 20 minutes to light of the intensity of \(2.0 \times 10^3\) foot-lamberts should represent the gamut of response of which the receptor cell is capable in terms of permeability and potential change, or firing rate or both. If the EER were indeed acting on the receptor cell itself, one would expect that this response caused by changing the potential across the retina would be markedly influenced by the level of adap-
tation to light. As was shown in our experiments, this is not the case. Similarly if the potential change causing the EER were acting on the receptor cell, it is improbable that the course of dark adaptation would proceed unperturbed by elicitation of the EER, as it in fact does. This in terms of potential change considerations would be the converse of the light adaptation situation described above. Thus it seems reasonable for us to assume that the EER acts at a site central to the place where the change in membrane potential of the receptor causes alteration in bipolar cell response. This site may be as close as the dendrites of the bipolar cells. It may have to do with horizontal or amacrine cells. It seems improbable that it would have its locus in the receptor cell.

Our study of the retinitis pigmentosa patients was done in the hope that at least some of these would represent a situation where receptor cells were destroyed and the rest of the retina left intact. We had hoped that the total retinal destruction, seen on histological examination, was only a late phase of the disease. Our finding that there was very good parallelism between VER and EER in five of our series of eight patients suggests to us that the receptor cell, presumably the site of the VER, and the more central site of action of the EER are both damaged in the advanced cases. The existence of three cases where the VER is disproportionately lower than EER (even though large amounts of light are required to match the brightness of the phosphene) suggests that our assumption is correct. In general these three cases had less damage as measured by visual field and electro-retinogram than the others. However, such an experiment without histological confirmation must remain equivocal. To gain histological infor-
mation to match our electrical information experiments are under way in rabbits treated with selective retinal poisons.

REFERENCES