PHYSIOLOGY

CONDITIONED REFLEX CHANGES IN THE HUMAN ELECTRORETINOGRAM

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The possibility of action of the higher nervous centers on processes taking place in the retina, has not yet been adequately established. E. M. Belostopkii, A. I. Bogoslovskii and E. N. Semenovskaya (1957) found in one case of traumatic encephalopathy, in which there was marked reduction in visual acuity and concentric reduction of the field of view to 10°, that the amplitude of the elctroretinogram (ERG) was greater than normal. They found however, that the amplitude of the b wave in subjects with normal vision varies from one experiment to another until it attains a fairly stable value. A. I. Bogoslovskii and E. M. Semenovskaya found in a case of complete blindness of one eye due to the growth of an intracranial tumor, that the amplitude of the b wave in this eye was greater than in the other, in which full vision was preserved and in which the ERG was normal. R. B. Zaretskaya [1] found that caffeine and bromine increase the human ERG. These facts lead us to suppose that although the ERG is most probably an expression of the electrical activity of the retina, and only arises from it, nevertheless it is under the control of the higher visual centers. This would certainly appear to be so from the theoretical point of view, but until recently the fact has not been demonstrated experimentally. Only I. Vaný̌sek [3] has described experiments from which it can be seen that the central nervous system influences the human ERG. He measured the ERG in 11 healthy subjects during the course of dark adaptation. He found that dark adaptation increases the amplitude of the b wave. At the 12th minute of dark adaptation, the subject was presented with a bright light. The light adaptation caused a reduction in the amplitude of the b wave in 6 out of the 11 subjects, and this reduction could be induced by one single presentation of the light. Vaný̌sek quite correctly concludes that the human ERG may be influenced by the central nervous system. Finally, in her article, A. V. Zonova [2] describes conditioned reflex changes in the ERG of the rabbit. The unconditioned stimulus used was subconjunctival injection of sodium chloride, and the conditioned stimuli were a sound and proprioceptive stimulation.

In the present investigation we have employed a different method of demonstrating the regulatory effect of the central nervous system on the ERG. We have tried to bring about conditioned reflex changes in the human ERG in response to an initially indifferent stimulus, while for the conditioned stimulus we have used the adequate stimulus – light.

METHOD

The electroretinogram was recorded using a silver electrode fixed to a contact lens. A silver disk fixed by a plastic clip to the lobe of the homolateral ear was used as the indifferent electrode. Simultaneous recordings were made of the elctroencephalogram (EEG) of both occipital areas. To record ERG and EEG an MPO-2 string oscillograph and the six-channel amplifier system of Peimer and Ul't were used.

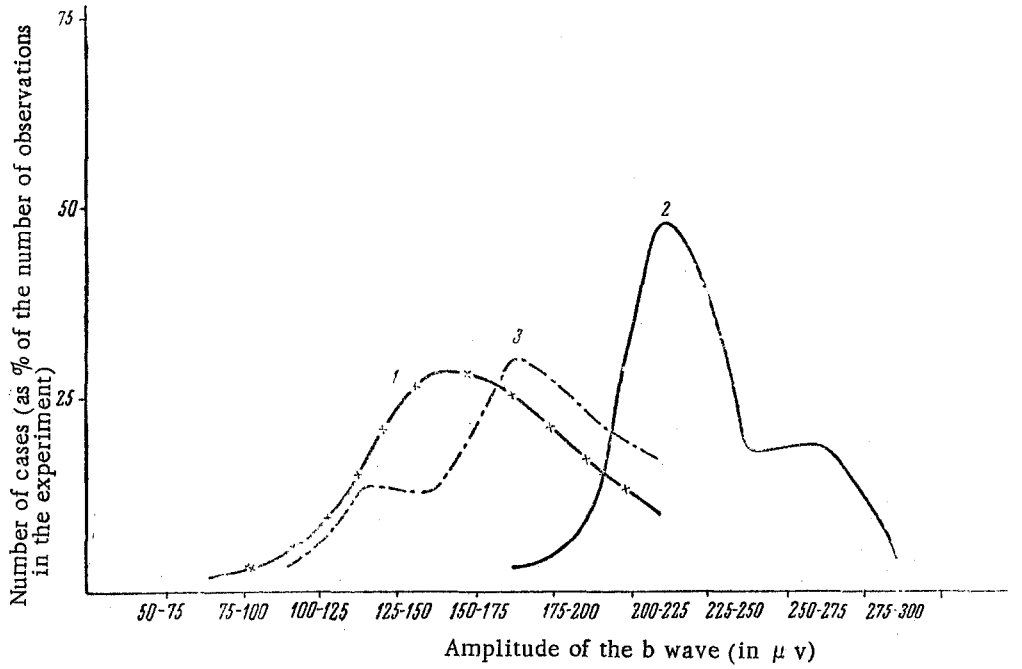

Fig. 1. Distribution curves for the amplitude of the b wave of the ERG.
1) In response to light giving a brightness at the eye of approximately 80 lux (weak light); 2) in response to combined sound + strong light stimulus (giving a brightness at the eye of about 600 lux); 3) in response to combined stimulus of sound + weak light (80 lux).

The light stimulus subtended about 1.5° at the eye. Two different brightnesses of stimulus were used, the weaker giving a brightness of 80 lux at the pupil, and the stronger a brightness of about 600 lux. As an auditory stimulus, we used the sound of a ZG-10 generator having a loudness of 60 decibels above threshold, and a frequency of 250 c/s. The sound was emitted from a loudspeaker placed 1 m in front of the subject. It had no direct effect on the ERG. Two subjects were used for the experiments: a woman M, of 45 years, and a man O, 30 years old. Neither had any ophthalmological defect. The visual acuity in both subjects was 1.0.

In preliminary experiments, we determined the qualitative and quantitative features of the ERG and EEG in response to the weak light of 40 milliseconds duration, and to the strong light, using the same exposure, and to the combined stimulus of sound + strong light. Initially the sound was switched on and maintained for 30 seconds, and during the 15th second of the sound, the strong light of 40 milliseconds duration was presented. The experiment was conducted as follows: The electrodes were placed in position. The subject was placed in total darkness for 3 minutes; while sitting comfortably in an armchair, he directed his attention to a red fixation point placed adjacent to the test field.

Preliminary tests showed that the response of the ERG and EEG to these stimuli was very constant during the single experiments, and showed very little variation from one experiment to another. For instance, for the subject M, on stimulating with the weak light, the ERG produced a b wave with an average amplitude of 135 μv; the latent period of the b wave was about 60 milliseconds; the duration of the b wave was, on average, about 200 milliseconds. On stimulating with the strong light, the amplitude of the b wave was about 225 μ v; the latent period was about 40 milliseconds, and the total duration about 160 milliseconds. When the sound was given together with the stronger light stimulus, the ERG was the same as to the strong light alone. After the preliminary tests had been concluded, we proceeded to the main experiment.

Here the sequence was as follows. After the subject had been in darkness for 3 minutes, and while fixating the red point, the following stimuli were presented in a random order at intervals of 30 seconds: weak light (80 lux; 2-3 presentations at intervals of 15 seconds) or a 15-second sound stimulation on which were superimposed 2-3-4 strong light flashes of 600 lux at intervals of 15 seconds. This procedure is called "elaborating aconditioned reflex" to sound; it was repeated many times during the experiment, which lasted altogether about 2 hours. Each time recordings of both ERG and EEG were made.

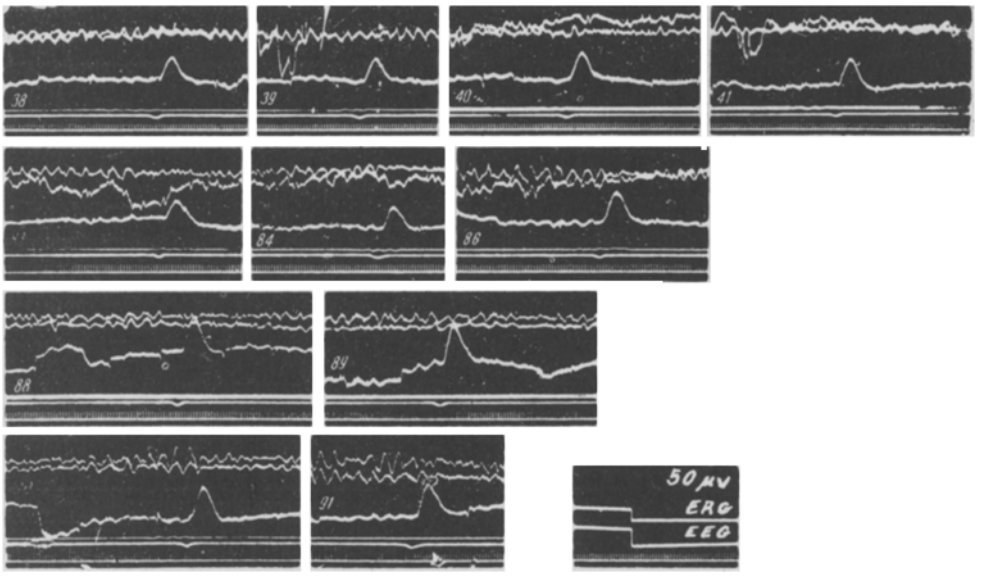

Fig. 2. Changes in the ERG in response to conditioned reflex stimulation.
Curves, from above downwards: EEG of right occipital area, EEG of left occipital area, ERG, trace of sound signal (switching on sound causes broadening of line. See traces 40, 41, 88, and 89), record of light stimulus (downward displacement at time of light stimulus). Time marking 40 milliseconds. Calibration 50 μv; upper cal. for ERG, lower, for EEG.

After a few coincidences of the bell + strong light, instead of the strong light being superimposed on the 15-second sound stimulation, the weak light was substituted. This procedure was known as "testing the conditioned reflex". Both before and after this testing of the reflex, the weak light was presented alone as control.

We assumed that if it were possible to elaborate a conditioned reflex change in the ERG, then such a procedure would produce a change in the ERG in response to the combination of sound + weak light which would approximate that of the ERG in response to the combination of sound + strong light. Since a simultaneous record of the EEG was made, it would be expected that the response in it to the sound would also show conditioned reflex changes; however, we did not investigate this point, since such changes have been known for a long time (G. Jasper, I. S. Beritov, A. Gasteau, V. S. Rusinov, and others).

RESULTS

We will give the detailed results only for the subject M, since those obtained with subject O were similar. With subject M, we carried out a total of 15 experiments during July of 1957. 628 separate ERG and EEG recordings were obtained, and of these 242 were recordings of the combined effect of sound + strong light ("development of the conditioned reflex"), 71 showed the response to sound + weak light ("testing the conditioned reflex"), and 315 were recordings of the response to weak light alone (control).

In examining the results, we first paid attention to the amplitude of the b wave of the ERG, then to its latent period, time to reach maximum value, and to its total duration. With the combined stimuli of sound and strong light, the b wave amplitude had an average value of 207 μv, in response to the weak light alone the value was 144 μv, and to the combined stimulus of sound and weak light ("testing the conditioned reflex") it was 158 μv. A still greater difference was shown between the second and third combinations, as can be seen by comparing the results of the first and of the second sets of experiments. In the first set, the amplitude of the b wave in response to the weak light alone was, on average, 135 μv, while to the combination of sound + weak light the average value was 139 μv. However, in the second set, the corresponding values were 140 and 166 μv. Fig. 1 shows curves giving the variation in amplitude of the b wave for the three conditions used. Despite the comparatively small number of readings, the curves show a fairly typical Gaussian distribution. The modal value for curve 1 is 138, for curve 3 – 167, and for curve 2 – 225 μv.

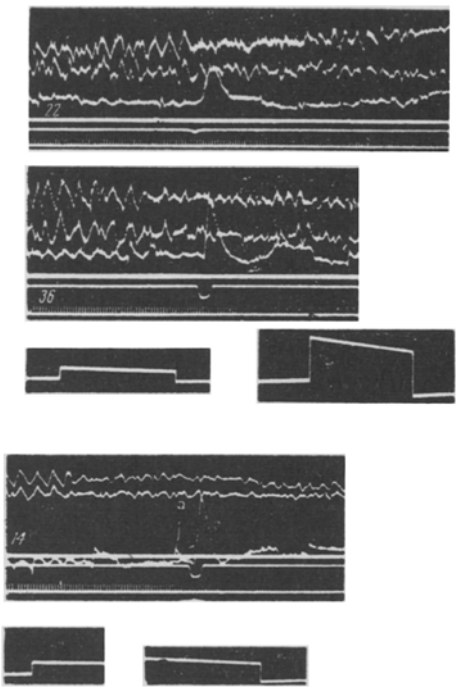

Fig. 3. EEG during elaboration of conditioned reflex changes in the ERG. Sequence of traces as in Fig. 2. In response to the combination of a strong light and a sound stimulus, the α-rhythm is arrested before the light flash is given (see curve 36 and 14). Calibration 50 μv, left cal. for ERG, right, for EEG.

From Fig. 1 it can be seen that the whole of the curve and the mode for the combination of sound + weak light is displaced in the direction of the maximum of the curve for sound + strong light. This indicates that in our experiments, the sound has acquired the significance of a signal, and that it affects the ERG by changing the amplitude of the b wave in accordance with the principles of conditioned reflex action. This change was not great, but it was greater than any experimental error. The conditioned reflex change in the ERG can be seen still more clearly in the curves obtained when the sound had already come to acquire the significance of a signal (Fig. 2). All these curves were obtained from an experiment made on 7/19/1957. Here it emerges very definitely that the amplitudes of the b wave in the ERG obtained in response to sound + weak light (curves 40, 41, 88 and 89) are greater than the control recordings in response to the weak light alone (curves 38, 39, 83, 84, 90 and 91), which were obtained both before and after testing the conditioned reflex; here, if we compare curves 38 and 39 with curves 40 and 41 obtained after 164 reinforcements of the conditioned reflex, the difference amounts to approximately 25 μv, but when comparing curves 83-84-86 (weak light without sound) and curves 88-89 (weak light + sound) after 173 reinforcements, the difference now amounts to as much as 60-110 μv; again, when we compare curves 88-89 with the control curves 90 and 91 (experiment without sound, and weak light used alone) it amounts to about 50 μv. Other ERG parameters, such as the latent period of the b wave, time to attain the maximum and total duration, all showed less change.

A more detailed analysis of the different experiments showed that the sound does not immediately acquire the significance of a signal. Only after 50-60 coincidences was it possible to observe its conditioned reflex action and at this stage it was still weakly shown. The effect was very much better shown after 100-125 combinations, and the reflex was found to become extinguished very rapidly, and as a rule, on the following day, it either did not appear or else was shown very weakly. This feature of the formation of the conditioned reflex as affecting the ERG differs sharply from the behavior of sensory conditioned reflexes elaborated in connection with vision, where conditioned reflexes are elaborated very rapidly, after 2-5 coincidences, and are maintained for a long time (A. I. Bogoslovskii, E. N. Semenovskaya, R. B. Zaretskaya, and others).

While inducing conditioned reflex changes in the ERG, we incidentally observed similar alterations in the EEG. As would be expected, these developed considerably earlier than the corresponding ERG changes; the α-rhythm ceased in response to the sound somewhat before the light stimulation was given.

In this connection we investigated the possibility of an orienting reaction (arrest of α-rhythm by sound); the reaction was rapidly extinguished even in the first experiments and had no effect on the conditioned reflex extinction of the α-rhythm.

In the experiment performed on 10/7/1957, after the first 9 reinforcements of the conditioned reflex we observed no extinction of the α-rhythm to sound before the light stimulus was presented (see Fig. 3, trace 22), but in this same experiment (trace 36) after 36 reinforcements, before the strong light stimulus was given and at the moment of the sound stimulus, a well-marked depression of the α-rhythm was observed, showing that the sound stimulus was acting as a signal for the light. In the experiment performed on 16/7/1957 (see Fig. 3, trace 14), after 70 reinforcements of the conditioned reflex, this anticipatory arrest of the α-rhythm was still more pronounced: it began about 1 second before the strong light stimulus, 14 seconds after the sound had been turned on.

Our experiments are provisional, and are being continued. We think it worth while to publish some of them, as these observations are of importance in determining the part played by the central nervous system in the development of the human ERG and in connection with the problem of the interaction of central and peripheral processes in the visual analyser as a whole.

SUMMARY

The conditioned reflex changes were formed in the human electroretinogram. The ERG was registered with the aid of an active electrode soldered into the contact lens. The EEG of both occipital regions was registered simultaneously. Light (which gave about 600 lux illumination on the pupil) served as an unconditioned stimulus. Sound served as conditioned stimulus (60 decibel over the threshold of hearing, 250 cycles per sec) which had no effect by itself on the ERG. Numerous combinations of this sound with the light stimulus brought about the development of conditioned reflex changes in the ERG. This was manifested by the fact that in response to the mild light stimulation, preceded by sound, the amplitude of the electroretinographic wave "b" became higher than in response to the weak stimulation by light alone. In both cases the light which was employed as a stimulus gave an illumination on the pupil equal to about 80 lux and the wave "b" the amplitude of which was much lower than in light stimulus with 600 lux. The conditioned reflex changes were simultaneously observed in the EEG.

LITERATURE CITED

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[3] J. Vaný sek, Csl. opthal. t 12, N. 4, 233-238 (1956).

* In Russian.