FLICKER STIMULATION IN AMBLYOPIA*

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PROVIDED that the pathways are intact, it is possible to alter the normal electrical activity of the cerebral cortex by illuminating the retina with a flickering signal. The cortical responses are varied and depend upon the rate of the flicker. If the frequency of the stimulating signal is exactly the same as the patient's alpha rhythm, or harmonically related with it, the stability and voltage of the alpha rhythm will be enhanced. When there is only a small difference in rate between the flicker and the alpha rhythm, *e.g.*, one or two cycles, the alpha rhythm will follow the speed of the signal and be driven by it temporarily at the new rate. At other stimulating frequencies the response by the cortex varies from case to case. At some rates the cortex may be able to keep pace with the flicker, whilst at others this is not possible. Either the cortex appears to be able to ignore the flicker so that its normal activity continues, or else it resents the flicker and the alpha rhythm becomes suppressed. In certain cases very abnormal cortical rhythms may be produced. Thus, in those patients who have an abnormally low threshold to epilepsy, the typical high-voltage electrical outbursts of this condition may be evoked by flicker stimuli applied at certain rates which may be specific for each patient. Any lesion in the eye, optic nerve, tract, or cortex would modify these changes, and if gross enough would prevent them.

Wald and Burian (1944) considered that in amblyopic vision the entire apparatus of light perception and spatial localization is normal, whilst that part subserving the highest visual function of pattern vision is defective. They showed in severe cases of amblyopia that the absolute light threshold was normal both at the fovea and in the periphery, in light and dark adaptation, and that the capacity to localize luminous points was also normal. It has been shown that the activity of the cerebral cortex may be abnormal in patients suffering from neuro-ocular pathology (Levinson and others, 1951), and pathological cortical rhythms have been found in amblyopia (Dyer and Bierman, 1952; Parsons-Smith, 1953). In view of these facts, and of the known effects of flicker stimuli acting through the normal visual apparatus, it seems likely that flicker studies in patients with amblyopia may throw further light on the mechanism and site of the process which results in the visual extinction.

* Received for publication February 27, 1953

† In receipt of a grant from the Dan Mason Research Foundation, West London Medical School

Material

Fifty children suffering from strabismus with amblyopia have been subjected to flicker stimulation at various frequencies. The cases were consecutive ones attending the orthoptic department at the Western Ophthalmic Hospital (St. Mary's Hospital). Their ages ranged from 5 to 12 years. The children were all undergoing orthoptic treatment and had previously undergone routine electro-encephalographic study at the West London Hospital (Parsons-Smith, 1953).

Method

A standardized white light flicker routine was followed in every case. The electroencephalogram was recorded on a 6-channel Grass machine whilst the child lay in a quiet room. The eyelids were open between the various signals and were then closed at the same time as the stroboscope was switched on. The flicker signal was first directed at the amblyopic eye whilst the sound eye was covered with an opaque black eyeshield. The procedure was next reversed so that only the sound eye was stimulated. Finally both eyes were stimulated together. The length of each signal was approximately 5 seconds. The initial flicker frequency was chosen to be at twice the rate of the patient's alpha rhythm, and this had to be determined in each case. After a rest of 10 seconds the next signal was at twice the alpha rhythm minus three cycles per second (c/s). Another 10-second rest was followed by a signal of twice alpha + 3 c/s, and then twice alpha + 6 c/s. Thus, if the alpha rhythm was 9 c/s, the flicker signals were at frequencies of 18, 15, 21, and 24 c/s. Finally, in each position, the effect of a roving frequency signal was employed. This started at 2 c/s, increased to 24 c/s, and then returned to 2 c/s, the time taken for the scan being 20 seconds. Excerpts from E.E.G.s are seen in Figs 1 to 3. In each will be seen six lines, or leads. The top lead, Lead 1, indicates the speed of the flicker signal as picked up by a photo-electric cell placed on the child's forehead and then recorded on the E.E.G. The positions of the electrodes over the skull are indicated in the diagram in the top left hand corner, and the visual acuity of the eye at which the flicker signal is directed is recorded in the centre of this diagram. "B.E." indicates that both eyes were stimulated together. In every case Lead 2 records the potential differences between the two hemispheres, Leads 3 and 5 are from the right hemisphere, and Leads 4 and 6 are from the left. In the bottom left-hand corner the length of the horizontal part of the line represents a paper speed of 1 second, and the height of the standardized vertical line, a signal of 50 microvolts (μv).

Results

Four varieties of flicker response by the cerebral cortex of children suffering from amblyopia have resulted from this routine technique. Two of the responses are similar to those seen in normal subjects, whereas the other two have not been described previously and appear to be directly linked with the process of visual extinction.

In 34 cases (68 per cent), no unusual alteration of the cortical rhythms was produced when the flicker was directed at each eye in turn or at both eyes together. The cortical rhythms continued undisturbed, or occasionally showed a minimal follow, or at certain frequencies were suppressed symmetrically over both hemispheres. This is a normal finding and further commentary is unnecessary. In seven cases (14 per cent), the cortical frequencies followed exactly the rate of the flicker signal when applied to each eye in turn, and the cortical response was symmetrical. An example of this can be seen in Figs 1(a) and 1(b), where it can be observed that a flicker signal of 15 c/s directed first to the amblyopic eye

FIG. 1(a).—Girl aged 9 (16.7.51). Flicker stimulation at 15 c/s to amblyopic eye producing 15 c/s activity over occipital lobes. Electrode placing, standardization, etc., for all figures is described in the text.

FIG. 1(b).—Flicker stimulation to sound eye. Similar response.

FIG. 2(a).—Girl aged 8 (18.6.51). Flicker stimulation at 15 c/s and 18 c/s to amblyopic eye does not alter alpha rhythm.

FIG. 2(b).—Flicker stimulation at 15 c/s and 18 c/s to sound eye has suppressed the alpha rhythm.

FIG. 3(a).—Girl aged 12 also suffering from epilepsy (23.10.51). Flicker stimulation at 15 c/s to both eyes has produced high voltage epileptic activity over cortex.

FIG. 3(b).—Flicker stimulation at 15 c/s to sound eye has produced epileptic activity.

FIG. 3(c).—Flicker stimulation at 15 c/s to amblyopic eye has produced no change in resting cortical activity.

and then to the sound eye resulted, on each occasion, in a symmetrical occipital response at the same frequency. This type of cortical follow is frequently evoked in normal subjects at certain frequencies. It appears to depend on a relationship between the signal and the alpha rhythm, the rates being specific in each patient. No significant connection was found between the various responses seen in the E.E.G. and the degree of the amblyopia. Thus, some children with severe amblyopia were found to have a good follow to the flicker signal either with the amblyopic or with the sound eye. Similarly, the abnormal cortical reactions which are to be described were evoked both in the presence of mild and severe degrees of amblyopia.

In four cases the alpha rhythm was suppressed when the sound eye was stimulated, but was able to persist when the flicker was directed at the amblyopic eye. An asymmetrical response of this sort does not occur in normal subjects. In Fig. 2(a) it can be seen that, when the flicker stimuli of both 15 and 18 c/s were directed at the amblyopic eye, the alpha rhythm arising over the posterior parts of both hemispheres persisted, whereas when the same signals were directed at the sound eye (Fig. 2b) the rhythm became suppressed. In a case with normal vision and intact pathways this suppression response may occur, but it will be the same whether the right or the left retina is stimulated. The fact that the alpha rhythm was suppressed over both hemispheres when the sound eye was stimulated, but persisted when the amblyopic eye was stimulated, would suggest that the flicker signal was blocked by a cortical or an extracortical lesion.

In three cases, who were known to have fits, outbursts of epileptic activity were evoked all over the cortex when the sound eye was stimulated, but the same signals

to the amblyopic eye caused little or no disturbance. This asymmetrical response, which has not been described previously, can be seen in Figs 3(*a, b, c*) which are excerpts from the records of one of these children.

Case Report

This child, a female aged 12, was first noted to have a squint at the age of 6 months. She was one of three siblings. There was no family history of strabismus or of epilepsy. She had always been of very unstable disposition and between the ages of 4 and 7 had at times been quite intractable in attacks, which from the clinical description, were epileptic equivalents. Except for these attacks of disordered behaviour, there was nothing to suggest epilepsy and no abnormalities were discovered on neurological testing. She first attended the orthoptic department at the Western Ophthalmic Hospital on 8.3.51. She did not have binocular vision, nor did she respond to occlusion therapy. The visual acuity in the right eye was 1/60, with eccentric fixation, and in the left eye 6/6. The asymmetry of the flicker studies which were made on 13.6.51 and on 23.10.51 was striking. Excerpts from the second experiment are seen in Fig. 3 (*a, b, c*). She clearly had a low threshold to epilepsy, as high-voltage bursts of epileptic activity were produced all over the cortex as soon as the signal of 15 c/s was directed at both eyes together (Fig. 3*a*). A similar response had been produced when the same signal was directed at the sound eye only (Fig. 3*b*), but when it was directed at the amblyopic eye only, the resting cortical activity continued unaltered and no epileptic bursts resulted (Fig. 3*c*).

Discussion

Flicker studies in this series of amblyopic children have shown that, in the majority of cases, the cortical response was the same whether the amblyopic or the sound eye was stimulated. Various types of response to the flicker signal were encountered, all of which must be dependent upon normally functioning pathways and connections. These findings would support the conclusions of Wald and Burian (1944) that in amblyopia the entire apparatus of light perception and spatial localization is normal, whilst that part subserving the highest function of pattern vision is defective.

In a smaller group of amblyopic patients, however, the response to flicker stimulation was different, and perception of light was involved in addition to the defect in pattern vision. No other clinical abnormality could be demonstrated in the affected eye in these children, and the cortical responses to flicker stimuli directed at both eyes simultaneously were symmetrical. Yet, when the stimulus was directed at each eye in turn, the cortical response was different. When the sound eye only was stimulated, either the excitatory or the inhibitory response described above was obtainable over both hemispheres but neither response was evoked when the signal was confined to the amblyopic eye.

Since it has been shown that the cortex was capable of responding to the signal if it received it, the light signal appears to be modified in certain amblyopic children, either by a diffuse cortical lesion directly connected with the affected eye or by a more discrete lesion within the pathways from that eye. Further study is required to determine the precise site of such a lesion.

Summary

Fifty children with amblyopia associated with strabismus were subjected to flicker stimulation.

In the majority of cases the visual extinction appeared to be brought about by active cortical suppression.

In some cases, however, a different mechanism exists.

REFERENCES

- DYER, D., and BIERMAN, E. O. (1952). *Amer. J. Ophthal.*, **35**, 66.
LEVINSON, J. D., GIBBS, E. L., STILLERMAN, M. L., and PERLSTEIN, M. A. (1951). *Pediatrics*, **7**, 422.
PARSONS-SMITH, B. G. (1953). *British Journal of Ophthalmology*, **37**, —.
WALD, G., and BURIAN, H. M. (1944). *Amer. J. Ophthal.*, **27**, 950.