ACTIVITY OF THE CEREBRAL CORTEX IN AMBLYOPIA*†

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The site of the lesion which determines the loss of vision in amblyopia ex anopsia in children has not been demonstrated, but existing evidence would suggest that the visual extinction is effected by the brain, since, even in the most profound case of amblyopia associated with strabismus, no abnormality is demonstrable within the eye. The loss of sight of one eye appears to result from the arrival at the cerebral cortex of two separate images instead of one. This produces visual confusion which brings an active inhibitory process into play whereby the vision from the squinting eye is suppressed. If the condition is recognized early in its development, and treated appropriately, the process is reversible. If untreated the extinction of vision becomes permanent.

Keiner (1951) postulated that all children are born with a potentiality for squint, that correct ing influences make themselves felt at about the sixth month of life, and that the cause of the condition is to be sought in some disturbance of the physiological processes through which all children have to pass during a certain period of their development. He assumed this disturbance to be a delay in the myelination of the visual pathways, a process which is usually not complete at birth, so that if myelination is far from complete the child is born blind. If myelination is delayed the chances are that the infant will squint early in life, whereas, if myelination is completed at, or soon after, birth, the possibility of squint can be excluded. This delayed myelination has been termed "myelogenesis retardata". For obvious reasons, this thesis is difficult to prove, but supportive evidence for such a cerebral explanation for the evolution of squint, and hence for the associated amblyopia, can be found in the electroencephalogram (E.E.G.). Levinson and Stillerman (1950) and Levinson and others (1951), in E.E.G. studies, have described the presence of abnormal slow wave and spike foci over the occipital regions in patients suffering from neuro-ocular pathology. They found that only 0.5 per cent. of 180 normal children displayed occipital abnormalities, whereas 30 per cent. of 36 children apparently otherwise normal but suffering from strabismus showed these focal abnormalities. The same authors described the E.E.G. findings in 460 cases of cerebral palsy. In those children who also had some neuro-ocular pathology the incidence of the occipital foci was twice that in the group without eye involvement. Dyer and Bierman (1952) have studied the E.E.G. in cases of suppression amblyopia. They consider that if the E.E.G. is abnormal the

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case will respond to occlusion therapy, whilst those children who have normal brain wave patterns may or may not be improved with this treatment.

During occlusive therapy for amblyopia, particularly in the early stages, it is frequently noticed by orthoptists and parents that certain children become unduly irritable, and subject to temper tantrums and even petit mal during the period of occlusion. Some patients cannot tolerate the exercises with the synoptophore. Lyle and Jackson (1949) state that for children who stammer, or have nervous habits, or who suffer from fits of any sort, orthoptic treatment may have to be modified because it may exacerbate these conditions. It is already known that disorders of behaviour in children are frequently associated with generalized abnormalities in the E.E.G., and that when the behaviour is in fact epileptic the gross and classical dysrhythmias of this condition will be seen to occur frequently in larval bursts all over the cerebral cortex. The frequency of the bursts is enhanced by biochemical changes, and by certain stresses. In view of the close relationship which is known to exist between vision and the normal electrical function over the occipital cortex, it would seem probable that by examination of the E.E.G. in cases of amblyopia, especially when associated with cortical dysfunction, light may be thrown on the mechanism of the disorder.

The work described below has been carried out to investigate whether there is any relationship between the variety of the cortical rhythms and the degree and aetiology of the amblyopia. Resting E.E.Gs in a series of amblyopic children have been assessed and the results correlated with the general clinical state and with the ophthalmic condition. The value of the E.E.G. investigation in the management of amblyopia has been studied, and an attempt made to see whether it is possible to differentiate those children who should respond to treatment from those in whom difficulties may be expected.

Material

Fifty cases of amblyopia ex anopsia have been investigated. The cases were consecutive ones attending the orthoptic department at the Western Ophthalmic Hospital (St. Mary's Hospital, London). No child under the age of five was included in the series because of the great difficulty in assessing the E.E.G. records of children under this age. The oldest patient in the series was aged twelve. The E.E.Gs. were performed at the West London Hospital, with the child lying on a couch, with the eyelids closed, in a quiet room. Tracings were made on a six-channel Grass machine. The recordings were made in every patient towards the end of a course of active orthoptic treatment.

Results

Of the fifty amblyopic patients only twelve (24 per cent.) had the normal records of childhood; considerable doubt existed whether the records of seven patients were normal or not, and 31 (62 per cent.) had grossly abnormal records. In eight cases (16 per cent.) the resting E.E.G. showed an epileptic dysrhythmia and in only one of these was there a family history of this condition. In 21 cases there was a family history of strabismus, generally in parents or in siblings, and only five of these cases had normal E.E.G. records. Not including frank epileptic discharges,
the most frequently encountered abnormalities were bursts of 18-22 cycle per second (c/s) activity, and runs of high voltage 6-7, 4-6, and 2-4 c/s waves. Marked asymmetry between the two hemispheres due to immaturity was seen in six cases.

The most significant abnormality was the presence in the E.E.G. of fast activity at 18-22 c/s. It occurred in twelve cases and not one of them had been considered to be normal clinically. All twelve gave a history of undue nervousness and had previously attended psychiatrists, child guidance clinics or speech therapy clinics, etc. All had been found difficult in the orthoptic department. Three had suffered from epilepsy. It should be mentioned, since these drugs do cause this type of cortical abnormality, that not one of the twelve patients was receiving treatment with sedatives or anticonvulsants. Another important abnormality encountered was the occurrence of bursts of 5 c/s waves over the occipital lobes in fourteen (28 per cent.) patients, and over the parietal areas in 21 (42 per cent.). In six cases the bursts occurred in both areas. There was no significant connection, other than amblyopia, between this 5 c/s activity and the neurological and visual states. No relationship was found to exist between the degree of visual loss and the incidence of the abnormalities in the E.E.G. These results are detailed in Table I. The incidence of clinical states of undue irritability, epilepsy, and so-called epileptic equivalents was unrelated to the degree of amblyopia.

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>E.E.G.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abnormal</td>
</tr>
<tr>
<td>6/9 to 6/24</td>
<td>20</td>
</tr>
<tr>
<td>6/24 to 6/60</td>
<td>18</td>
</tr>
<tr>
<td>6/60 to P.L.</td>
<td>24</td>
</tr>
</tbody>
</table>

It has been customary, on clinical grounds, to consider amblyopia in childhood to be either congenital or acquired. Adhering to this classification, the amblyopia in thirteen of the fifty cases studied here was congenital and in 37 it was acquired. Examination of the relevant clinical features in the two groups shows a marked correspondence. The only significant difference, in fact, lay in their response to occlusion: the congenital cases showed a 100 per cent. failure rate, whilst failure occurred in only 54 per cent. of the acquired cases (Table II).

<table>
<thead>
<tr>
<th>Clinical Abnormalities (per cent.)</th>
<th>Amblyopia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Congenital (13)</td>
</tr>
<tr>
<td>None apart from amblyopia</td>
<td>38.5</td>
</tr>
<tr>
<td>Undue nervousness</td>
<td>30.7</td>
</tr>
<tr>
<td>Temper tantrums</td>
<td>7.7</td>
</tr>
<tr>
<td>Left-handedness</td>
<td>15.3</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>15.3</td>
</tr>
<tr>
<td>Abnormal electroencephalogram</td>
<td>61.5</td>
</tr>
<tr>
<td>Total failed occlusion</td>
<td>100</td>
</tr>
</tbody>
</table>
A severe disorder of behaviour is frequently found to be associated with maturation defects in the E.E.G. In some cases actual epileptic discharges may be recorded, and these generally arise over one or other of the temporal lobes. The age when the E.E.G. maturation occurs varies from case to case and in some patients may take place at an early age, as in the following child, in whom, on all clinical grounds, a very abnormal E.E.G. was to be expected:

**Case 1, male, aged 7**, had suffered from severe convulsions in infancy, but had since been free from clinical attacks. He was left-handed. There was a strong family history of epilepsy, left-handedness, and strabismus. His squint was first noticed at the age of four, and orthoptic treatment was begun 2 years later. He was not disturbed by the treatment, but his response to it was poor. His corrected visual acuity was 6/60 in the right eye and 6/6 in the left. His E.E.G. was remarkably mature and quite normal.

In only half of the patients who had been disturbed by orthoptic treatment was an abnormal E.E.G. record found during the period of treatment. Records were taken at intervals in many of the children during the year following the completion of the orthoptic treatment, but no significant alteration occurred either in those patients who had responded to the occlusion or in those who had failed to do so.

In certain circumstances, the E.E.G. has proved to be of value in prognosis, but the appearances per se are not specific. Twelve patients had normal records. In four of these the amblyopia, which was only mild, responded well to orthoptic treatment, whilst in eight, in whom the amblyopia was severe, there was no response to occlusion. Of 31 patients with abnormal E.E.Gs., six, all mild amblyopes, responded to treatment. Of the twenty who failed to respond to orthoptic treatment, eight had severe, eight moderate, and four mild amblyopia. These results indicate that a normal E.E.G. associated with a severe degree of amblyopia carries a poor prognosis for recovery of vision. No further conclusions seem possible. The assertion of Dyer and Bierman (1952) that an abnormal E.E.G. carries a good prognosis was not confirmed.

**Discussion**

This study has confirmed the findings by earlier workers that the E.E.G. is abnormal in certain ophthalmic conditions in childhood which have been considered on clinical grounds to result from developmental defects. Many of the non-specific and generalized E.E.G. changes which have been described in these cases are compatible with undue delay in cerebral maturation. It is usual for maturation changes to be present in the E.E.G. of childhood, the records being, quite unlike the adult record, very unstable and irregular. In this group of cases, however, just as in those described elsewhere, gross and unusual electrical changes have been encountered in a higher proportion than could be expected in an otherwise normal group of normal children. The changes indicate that the cerebral cortex is functioning abnormally, and although there are no known E.E.G. appearances specific for demyelination, these abnormalities would support such a theory as that propounded by Keiner (1951).

The electrical activity of a child's cortex can be observed to change con-
considerably over the years. It gradually loses its instability and eventually matures to produce the normal stable adult E.E.G. The age when this maturation takes place cannot be anticipated in any one case, and occasionally it does not occur at all. It seems that once the appearances of cortical immaturity have been replaced by stable adult rhythms, any associated physical defect is unlikely to be corrected.

The E.E.G. abnormalities which we have found in this group of fifty amblyopic children fall into two classes. First, non-specific cortical dysrhythmias, of which bursts of fast activity or occipital slow waves are the commonest, and second, larval bursts of epileptic discharges. Clinically, the most significant non-specific cortical abnormality appears to be the presence of generalized fast rhythms, since the children thus affected were all unduly nervous and had been disturbed by the orthoptic treatment. Since we have noted this association it has proved possible, by giving small doses of sedatives (e.g. phenobarbite gr. 1/4-1/2, two or three times a day) to cause this type of child to become more amiable, and thus better able to co-operate during treatment. Abnormal occipital bursts were described by Levinson and his co-workers (1951) in 30 per cent. of their cases of strabismus, and a similar figure (28 per cent.) was found in the present group of amblyopic children. It is significant that the abnormality was over the visual cortex, as this would suggest that a localized underlying cortical abnormality is the basis for the strabismus in these cases. No connexion has been found to exist between the severity of the cortical abnormality and the degree and stage of the amblyopia.

Epileptic records were found in 16 per cent. of the children, a remarkably high incidence in a group of children in which this disorder was not suspected. Seven of the eight children were suffering from clinical petit mal and all were disturbed by orthoptic treatment, particularly by occlusion. Beyond stating that the threshold for epileptic dysrhythmia was, for constitutional reasons, unduly low, no further conclusions regarding the aetiology can be offered. The condition is likely to be only transient since no known connection exists between these visual defects and epilepsy in other age groups. Clinically it is important to recognize this group, since such children resent orthoptic treatment and are those in whom actual clinical epileptic fits may be evoked. The prescription of anticonvulsants will, however, permit the continuance of orthoptic treatment without risk. Further study of these children, with particular reference to the effects of flicker stimulation, has already been carried out and will be reported in a later communication.

Summary

A high proportion of children undergoing orthoptic treatment for amblyopia were found to have severe E.E.G. abnormalities.

The disturbance of the cortical rhythms supports the thesis that abnormalities are present in the central nervous system in amblyopia associated with strabismus.
The neurological and E.E.G. findings are similar in congenital and acquired amblyopia.

From the E.E.G. appearances, it is possible to select those children who are likely to be disturbed by orthoptic treatment so that they may be treated appropriately with sedatives or anticonvulsants.

In certain cases, a normal E.E.G. carries a poor prognosis for recovery of vision in the amblyopic eye.

I am indebted to the Surgeons of the Western Ophthalmic Hospital for allowing me to investigate the cases under their care, and particularly to Mr. McIver Paton, F.R.C.S., in charge of the Orthoptic Clinic. I am grateful to Miss Helden, senior orthoptist at the Western Ophthalmic Hospital, and to Mrs. Arundel, E.E.G. recordist at the West London Hospital, for their help.

REFERENCES