

Acquired cone dysfunction

J. H. KELSEY AND G. B. ARDEN

Moorfields Eye Hospital, City Road, London E.C.1

A reduction of visual acuity is probably the most common presenting symptom in ophthalmology and either a refractive error or a lesion of the eye or the visual pathways can generally be found to account for it. Occasionally no cause for the poor vision can be found by routine clinical techniques, but more sophisticated methods of examination may reveal other evidence of retinal dysfunction allowing a diagnosis to be made. Sloan and Brown (1962) described five patients with poor vision in whom psychophysical and, to a lesser extent, electrophysiological tests demonstrated a specific defect of the photopic (cone) visual system. Goodman, Ripps, and Siegel (1963) presented a large series of such cases and noted that, although the condition may be congenital, it can develop postnatally. They recognized three grades of severity of the condition and remarked on the wide variety of diagnoses that had been applied to these patients. Berson, Gouras, and Gunkel (1968) described a family in which a progressive dysfunction of the cone system was dominantly inherited. Goodman, Ripps, and Siegel (1966) described a patient in whom the condition was markedly asymmetrical although abnormalities in the more normal eye could be demonstrated.

This paper, which reviews a series of patients referred for the investigation of unexplained loss of visual acuity, emphasizes the importance of electroretinography in the demonstration of a specific disorder of the photopic visual system.

Materials and methods

(1) SUBJECTS

These were patients referred to the Electrodiagnostic Clinic of Moorfields Eye Hospital for the investigation of an unexplained loss of visual acuity, which was the presenting symptom in 298 of the first 2,000 patients referred to the clinic. The results of the tests showed that fifteen of these patients had a defect of the photopic system, affecting both eyes in thirteen of them and one eye only in two. The salient findings in the patients with both eyes affected are shown in the table. The patients in whom one eye was affected are not described as they were inadequately studied.

The visual acuity and visual fields of these patients were assessed by the referring clinicians and a wide variety of testing conditions were therefore involved. In no case was there a significant ametropia nor a significant defect of the visual field.

(2) COLOUR VISION

This was tested separately in each eye using the Hardy-Rand-Ritter (HRR, American Optical Company) pseudo-isochromatic test plates. The illumination was the battery of fluorescent tubes ('Warmlight', Crompton) used as the light source for electro-oculography. The colour defect was recorded according to the test plate instructions and when there was no colour discrimination this was recorded as 'none'.

(3) DARK ADAPTATION

The Goldmann-Weekers Dark Adaptometer was used. The test was preceded by an instruction period, and both eyes were then adapted for 5 minutes by illuminating the globe with two 60-watt bulbs. One eye was then occluded and then threshold measurements for the central 11 degrees of the other eye were determined using a variable stimulus flashing once a second. Measurements were made every few seconds for 25 minutes and at the end of this time the final threshold of the occluded eye was determined. The test was done once only in each subject. It was not repeated in an attempt to monitor more accurately the cone part of the curve and the cone/rod break.

(4) ELECTRO-OCULOGRAPHY (EOG)

The method used was that introduced by Arden, Barrada, and Kelsey (1962), which has been fully described by Kelsey and Arden (1969) and by Kelsey (1969).

(5) ELECTRORETINOGRAPHY (ERG)

The method used was based on that introduced by Karpe (1945), which has been described by Kelsey and Arden (1969). Amplification and recording were done through a modified Schwartz PE₄ physioscript. The stimulus was a modified Xenon flash stroboscope (Dawe).

For single stimuli the amplifier was set with a time constant of 2 sec. and a top cut of 30 c.p.s. For flicker studies the top cut was increased to 200 c.p.s. The paper speed was 5 cm./sec. and the stimulus was also recorded. Flicker records were produced by increasing the stimulus rate until discrete responses could no longer be recognised and were then decreased until they were again recognized.

Results

The salient clinical features are summarized in the Table.

Table Findings in thirteen patients

Med. no.	Sex	Age (yrs)	Age at onset	Diagnosis on referral	Visual acuity		Colour vision	EOG		Photo-phobia	Nystagmus	Family history
					Right	Left		Right	Left			
419	M	22	20	Macular degeneration	6/18	6/18	R/G defect	170	170	No	No	No
651	F	19	Child	Congenital bad sight	6/24	6/24	None	170	170	Slight	No	Brother; sister
1024	F	28	?18	Poor vision	6/24	6/24	None	150	160	Slight	No	Father; paternal grandmother
1069	F	37	24	Macular degeneration Optic atrophy	6/60	6/60	—	Flat	Flat	—	—	—
1072	M	9/12		Status epilepticus	—	—	—	—	—	—	—	—
1178	F	22	Child	Defective vision	6/60	6/60	None	200	200	Slight	Slight	Brother
1524	M	57	?45	Miner's nystagmus	6/36	6/60	—	175	170	No	Fine	No
1556	M	24	?14	Tapeto-retinal degeneration	6/24	6/24	R/G defect	180	170	No	No	No
1572	M	54	50's	Tobacco amblyopia	6/18	3/60	Presumed R/G defect	185	200	No	No	No
1790	M	10	Child	Optic nerve lesion or Tapeto-retinal atrophy or Macular degeneration	6/60	6/60	R/G defect	Flat	Flat			
1792	M	17	Child	Macular degeneration	6/24	6/24	None	Flat	Flat	No	No	Adopted
1921	M	26	Child	Macular degeneration	6/60	6/60	None	200	200	Slight	No	Large pedigree with dominant inheritance
1981	F	12	10	Macular degeneration	6/60	6/60	—	Flat	Flat	No	No	Father has cerebro-macular degeneration

The clinical course is very variable. A wide variety of diagnoses is evident emphasizing the lack of unequivocal retinal change. Where a diagnosis of a macular degeneration was made, the referring clinicians noted either granularity of the macula or a loss of the foveal reflex, and the interpretation of this picture may well have been influenced by the abnormal visual acuity. Most patients seem to fall between the Groups I and II of Goodman and others (1963, 1966), in that although some had no colour discrimination photophobia was not a troublesome symptom.

Other features in the series may be noted. When tested the colour vision was found to be abnormal with either a severe red/green defect or no colour discrimination. The EOG was normal in only three patients with light rises of 185 per cent. or more. The rest had low EOGs, four being flat.

The abnormality common to all patients was that in the ERG. In this clinic the amplitude of the b-wave after 10 minutes of dark adaptation is used as a measure of retinal function and all the patients described had normal responses. Flicker fusion studies were carried out at the end of this period and a normal response is shown in Fig. 1. It will be seen that discrete responses can be identified with a stimulus rate of almost 70 per second.

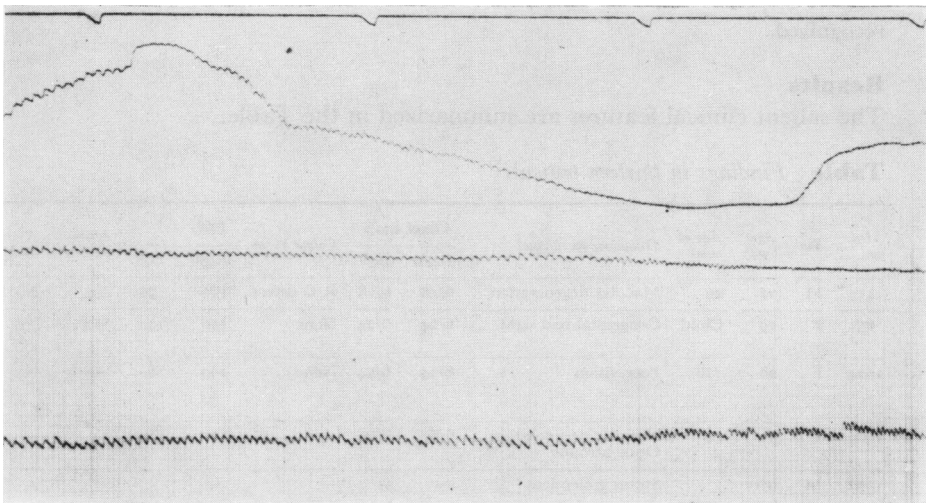


FIG. 1 *Flicker fusion in normal eye*

Top line marks second intervals and thicker vertical lines half-second intervals
Top trace is from right eye and middle trace from left eye.
Bottom trace is stimulus marker

The response from an eye with cone dysfunction is shown in Fig. 2. There are two characteristic changes in the flicker response. Fusion of the responses occurs at a low stimulus rate, in this case 16 c.p.s. The responses themselves are altered. The waveform to a single stimulus is the same as that from a normal eye. With the start of repetitive stimuli, the angular trace produced by the normal eye to give a serrated pattern is not found. Instead the responses are rounded and an undulant trace is produced which decreases in amplitude until fusion occurs.

Dark adaptometry was done in several of the patients; in all cases a normal final sensitivity threshold was achieved in 25 minutes.

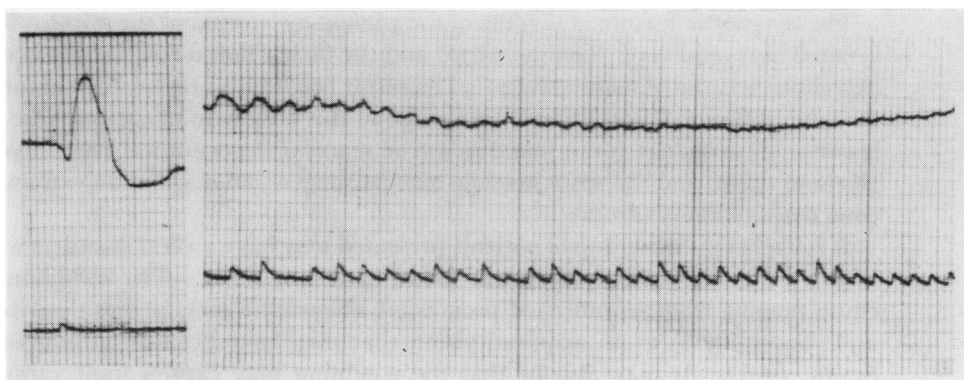


FIG. 2 Flicker fusion in cone dysfunction

Single response is normal
 Upper trace is flicker response from left eye
 Lower trace is stimulus marker
 Thicker vertical lines are at half-second intervals

Discussion

Several diagnostic criteria have been proposed for the diagnosis of a cone dysfunction syndrome. The main ones are loss of visual acuity with an even more marked defect in colour vision, abnormalities in the early stages of dark adaptation, loss of peripheral colour vision, and loss of the photopic elements of the ERG (Sloan and Brown (1962); Goodman and others, 1963). Zweifach and Wolf (1968) purported to show that similar changes could be due to optic nerve disease, but their report was too sketchy in both the description of methods and results to sustain this contention.

The simplest test to use in the early stages of the condition is that of colour vision. François and Verriest (1961) showed that, in acquired loss of colour vision, lesions of the deeper retinal layers produces a blue-yellow defect whereas a red/green defect indicates a lesion affecting the ganglion cell layer or optic nerve. They used a battery of tests, including the H-R-R plates, and these results are at variance with ours. Goodman and his colleagues had findings similar to ours in that the more severe cases had achromatopsia and the less severely affected had various degrees of red/green abnormality. The test may therefore help in the differential diagnosis of a macular degeneration. A feature of note in this small series is that the patients with a red/green defect were male. In view of the frequent occurrence of this condition as an *X*-linked condition, the validity of a colour vision defect as a diagnostic criterion is less than has been generally accepted.

A surprising finding was the frequently abnormal EOG. This is a mass retinal response and, although a cone contribution has been demonstrated (Elenius and Karo, 1966), it is overwhelmingly rod-mediated (Arden and Kelsey, 1962). Other apparently focal disorders of the retina may affect the EOG, leaving the ERG intact. François, de Rouck, and Fernandez-Sasso (1967) showed that a vitelliform macular degeneration selectively depresses the EOG. Kelsey (1969) showed that this tends to occur in any form of macular degeneration affecting the young. This overlap rules out the use of the EOG as a differential diagnostic test and indeed some patients with a cone dysfunction syndrome have changes sufficient to merit the ophthalmoscopic diagnosis of macular degeneration. As with the young patients with macular degeneration, it suggests that the cone dysfunction symptoms are the manifestation of a more generalized retinal disorder.

The diagnostic feature is the loss of the photopic elements of the ERG. These may be isolated in several ways (Gouras, 1970) and the flicker fusion method has been adopted in this clinic because of its simplicity. The result has been to reveal both an abnormality in the rate of flicker fusion and also a change in the waveform of the response before fusion occurs. This change is not found in a true macular degeneration even in young patients (Kelsey, 1969), and therefore juvenile macular degeneration is not an extreme variant of a cone dysfunction syndrome.

It is likely that the group of patients presented may have several disorders which manifest in this way. A family history was found in five of them. The condition may have a cause ranging from an inherited progressive abiotrophy such as that described by Berson and others (1968) to an acquired vision that may have been drug-induced (Siegel and Smith, 1967). It may also be that the condition may express itself variously, ranging from a mere defect of colour vision to an overt macular degeneration. Even more sophisticated tests of cone activity may reveal different degrees of severity of the condition. Dodt and Wadensten (1954) studied the relation of flicker fusion rate and stimulus intensity. They showed that, in a normal person, a rod and cone contribution could be recognized, but that in a cone-blind subject only the rod part was present. It would be interesting to learn if part of the cone section can be demonstrated in subjects not severely afflicted.

Summary

Poor visual acuity may be due to an acquired defect in the cone system. A variable clinical picture is presented but a diagnosis may be made by flicker electroretinography.

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