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Cone dystrophy and supernormal dark-adapted b-waves in the electroretinogram

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Abstract. A male patient suffering from cone dystrophy was followed over 9 years. In addition to the typical clinical and electrophysiologic signs, supernormal b-waves were found in the dark-adapated electroretinogram. Our case is compared with 12 similar patients described in the literature. Our patient differed from the other patients in the following aspects: he was male and had a congenital stationary disease with a small pigment epithelial scar in the left eye only and no other fundus changes up to the age of 22 years. He did not complain of night blindness. The dark-adapted electroretinogram of our patient showed a normal b-wave threshold with increased b-wave amplitudes and markedly prolonged b-wave latencies and implicit times. This combination of signs has not been reported to date in any other patient and points towards a postreceptoral defect of the interneuronal connection.

Introduction

The electroretinogram enables differentiation of retinal degenerative diseases by their affected receptor systems. Therefore, cone or rod and combined cone-rod or rod-cone dystrophies can be distinguished. Cone dystrophies are differentiated clinically in stationary complete or incomplete rod monochromatism, blue cone monochromatism, and progressive cone dystrophies [2, 3, 9]. In cone dystrophies the electroretinogram shows reduced or missing potentials at light-adapted conditions and reduced photopic flicker frequencies. The dark-adapted electroretinogram is normal or slightly subnormal. However, some cases with cone dysfunction and supernormal dark-adapted potentials in the electroretinogram have been described [1, 4–6, 11]. We have followed a similar patient over 9 years. However, some of his clinical and electrophysiological findings were different from the patients described before.

Case report

At the time of the first examination our male Turkish patient was 13 years old. The family history was unremarkable; the parents and all siblings (one brother, two sisters) had no eye diseases. Our patient complained of decreased visual acuity without changes since childhood. Night blindness was not present.

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The visual acuity was OD 0.2, OS 0.3. A convergent alternating strabism was present. Fixation was central in both eyes. There were no morphological abnormalities in the anterior segments of both eyes. On ophthalmoscopy there were no abnormalities in both eyes. Especially the macular and foveal reflexes were normal. Fluorescein angiography of the left eye revealed a small parafoveolar pigment epithelial scar on the temporal side.

Color vision was severely impaired. Only the identification plate of the Ishihara plates could be read. The Panel-D-15-desaturé test gave no clues towards blue-cone monochromatism. The Farnsworth-Munsell 100 Hue test showed an elevated total error score with no specific axis. Testing with the Nagel anomaloscope revealed an achromatopsia. Large color plates held in the retinal periphery were named correctly.

Goldmann perimetry was normal. Although visual acuity suggested at least a relative central scotoma, the Amsler grid test showed no central scotoma. Adaptation to darkness, measured with the Goldmann-Weekers Ganzfeld adaptometer, showed a prolonged course with a borderline subnormal final outcome after 40 min. The electrooculogram, tested with the method of Rhode and Täumer [10] was normal (OD 178%, OS 160%). Pattern VECPs recorded under light- and dark-adapted conditions could not be evaluated because of small amplitudes and extensive artefacts. Nine years after the first investigation all clinical and electrophysiologic findings were unchanged.

Materials and methods

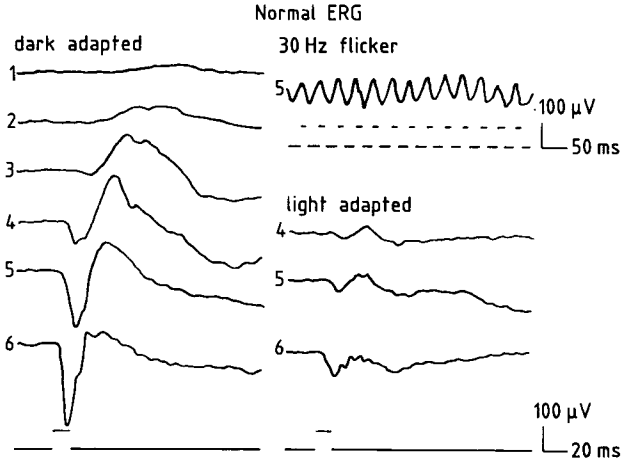
We used as a corneal electrode a modified Henkes contact lens; an indifferent electrode on the forehead and the preauricular skin served as the reference ground. All electrodes were connected wireless via electrolyte bridges (0.9% NaCl in 1.5% AgarAgar) to three nonpolarizing calomel half cells [7]. The signals were fed into an amplifier working either in AC or DC mode (Toennies DA II with DC preamplifier). The upper frequency limit was at 1000 Hz; the lower frequency limit was 0.3 Hz in AC mode.

After 40 min of dark adaptation and with maximal possible dilation of the pupil (phenylephrine 2.5%, tropicamide 1.0%) the ERGs were recorded in the dark. Stimulus duration was 10 ms. Six different light intensities (1–6) increasing by one logarithmic unit in steps from the b-wave threshold of the normal eye were used for the dark-adapted recordings. The maximum light intensity was 780 cd/m^2.

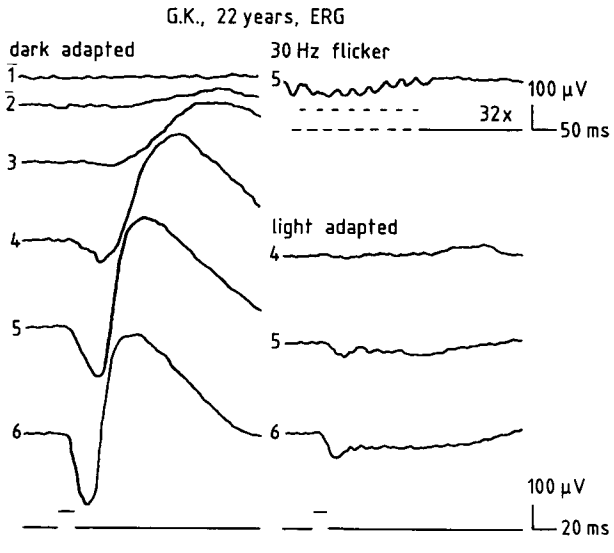
The light-adapted recordings were performed under adaptation to white light with 4.5 cd/m^2 and with the light stimuli 4–6. The 30-Hz flicker stimulus had the light intensity 5. White light from a filtered xenon light source served as stimulus in all examinations. The potentials were displayed on an oscilloscope, recorded on a paper writer, and stored digitally for later work-up on a computer disc. No computer averaging was used. The normal range is considered to be the mean of 40 normal eyes $\pm$ 2 SD.

Electroretinographic results

The electroretinogram was not markedly different between both eyes (Fig. 1). The a-wave amplitudes and latencies were in the upper normal range in both the dark- and light-adapted conditions. When dark-adapted the b-wave amplitudes were normal at stimulus intensities 1–3 and markedly elevated at stimulus intensities 4–6. The V/log I-plot of the dark-adapted b-wave had a steeper than normal slope (Fig. 2). When light-adapted the b-wave amplitudes were reduced and only at stimulus intensity 6 in the lower normal range. The b-wave latencies were prolonged at both dark and light adaptation. The b-wave implicit times were prolonged when dark-adapted and in the upper normal range when light-adapted. The T/log I-plot was parallel to the normal course at higher values (Fig. 3). The 30-Hz flicker response was reduced to 30 µV, less than the lower normal range of 50 µV. Oscillatory potentials were missing.



a



b

Fig. 1. a Normal electroretinogram: *Left*, the dark-adapted recordings; *lower right*, the light-adapted recordings with the stimuli below. *Upper right*, 30 Hz flicker response with stimuli below. *Numbers* at the beginning of every trace indicate the light intensity. **b** Electroretinogram of our patient. Compared with the normal electroretinogram the character of the b-wave is markedly changed at dark adaptation

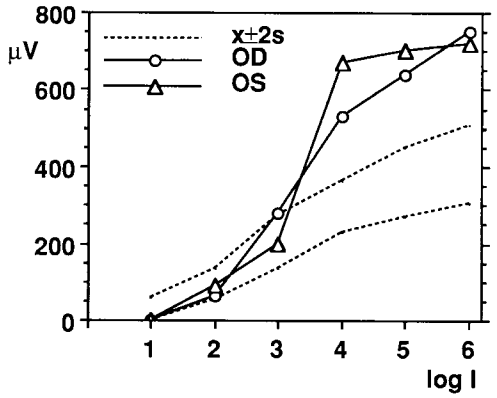


Fig. 2. b-Wave V/log I-function at dark adaptation. On the *x*-axis are the logarithmic stimulus intensities from 1 to 6. The space between the *dotted lines* is the normal range within 2 SD. The line with the *open circles* shows the values of the right eye and the line with *triangles* the values of the left eye

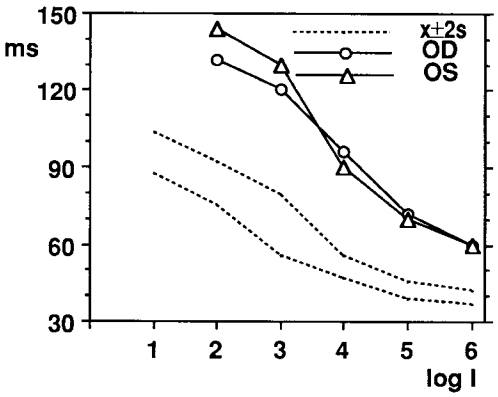


Fig. 3. b-Wave implicit T/log I-function at dark adaptation. For further explanation, see Fig. 2

Discussion

The clinical findings of our patient, including nonprogressive reduced visual acuity since childhood, alternating strabism, and achromatopsia, indicated a congenital rod monochromatism. The ability to identify large color plates indicated the incomplete form [8]. This was verified by the electrophysiologic findings: there were still potentials at light-adapted conditions, but the b-wave amplitude was reduced as was the 30-Hz flicker response. The electrooculogram was normal, which we would expect in rod monochromatism [8].

Table 1. Clinical data on 12 patients described in the literature and our patient

Case	Age	Sex	Course	VA	Fundus	Color vision	Perimetry	Fluorescein angiography	Night blindness	Dark adaptation	EOG	Author
1	15	M	Progressive	0.3	Pigm irreg	Protan	Central scotoma	Normal	Yes	2.0 log Elevated	Normal	Gouras
2	11	F	Progressive	0.3	Pigm irreg	Deutan	Central scotoma	–	Yes	1.9 log Elevated	Normal	Gouras
3	14	F	Progressive	0.2	Bull's eye	Protan	Normal	–	Yes	–	–	Alexander
4	30	F	Progressive	0.1	Bull's eye	Nearly normal	Central scotoma	–	No	–	–	Alexander
5	31	F	Progressive	0.2	Bull's eye	Tritan	Central scotama	Fenestrations	No	–	–	Alexander
6	15	F	6 years	0.05	Bull's eye	Achromatopsia	Normal	Bull's eye	Yes	3.0 log Elevated	–	Yagasaki
7	11	F	Congenital?	0.07	Golden reflex	Achromatopsia	Normal	Normal	Yes	1.5 log Elevated	Normal	Yagasaki
8	22	F	?	?	Pigm irreg	?	?	–	–	–	–	Fishman
9	27	F	?	?	Pigm irreg	?	?	–	–	–	–	Fishman
10	33	F	?	?	Pigm irreg	?	?	–	–	–	–	Fishman
11	7	F	Congenital	0.3	Pigm irreg	Disturbed	?	Fenestrations	–	Elevated	–	Francois
12	17	F	Congenital	0.05	Pigm irreg	Disturbed	?	–	–	Elevated	–	Francois
13	13	M	Congenital	0.3	Small pigm scar	Achromatopsia	Normal	–	No	Borderline	Normal	Our patient

VA, Visual acuity; Pigm irreg, extensive pigment irregularities

An indicator of an additional retinal defect was the borderline subnormal adaptation to darkness without symptoms of night blindness. The electroretinogram also showed a defect in the rod system. There was a marked change in the characteristic of the dark-adapted b-wave. The amplitudes were nearly twice the normal value at higher stimulus intensities. The latencies and implicit times were prolonged in the same range. Because the a-waves were normal, these changes indicate a defect in the postreceptoral intraretinal transmission of the rod potentials.

In the literature, 12 patients with supernormal b-wave amplitudes in cone dysfunction have been described [1, 4–6, 11]. Only seven cases were well documented [1, 6, 11]. An overview of the clinical and electrophysiologic data is given in Tables 1 and 2.

Of the 12 patients nine were female, one was male, and in two cases the sex is unknown. The age of the 12 patients was between 7 and 33 years. The two cases presented by Francois and the two patients of Gouras were familial. All other patients were single occurrences in the different traits.

The course of the disease was progressive in six of 12 cases, congenital and stationary in three cases, and unknown in three cases. The visual acuity was between 0.3 and 0.05. In three cases it is not documented.

Perimetry was normal in three of seven tested patients. The other four patients had a central scotoma. Color vision was tested in nine patients. It was nearly normal in one of them and more or less impaired in the other eight patients. Five out of seven patients complained of difficulties with seeing at night. In four of them and two other patients adaptation to darkness was tested and showed an increased final threshold. The electrooculogram was normal in the three patients tested.

The results of electroretinography were documented in various ways (Table 2). Moreover, the method of ERG recording was different between all investigators. Normal values for comparison were missing in some cases, and in other cases two normal persons served as a comparison.

The dark-adapted a-wave was normal in amplitudes (seven cases) and latencies (three cases). The dark-adapted b-wave threshold is known in eight cases and was elevated in six of them. The dark-adapted b-wave amplitudes were reported in all 12 cases. They were reduced at low stimulus intensities and supernormal at high stimulus intensities in six cases. The b-wave responses were supernormal at high stimulus intensities in five cases. One of them had a normal b-wave amplitude at lower stimulus intensities and in four the response to lower stimulus intensities is unknown. In one case the b-wave amplitudes were supernormal at all stimulus intensities.

The b-wave latencies were never mentioned. The b-wave implicit times were given in seven cases. They were prolonged at all stimulus intensities in two cases, normal in three cases, and prolonged only at low stimulus intensities in the remaining two cases.

The light-adapted recordings were normal in three of 12 cases, missing in two cases and reduced or subnormal in the remaining seven cases. Responses to flicker stimuli were recorded and reduced in two patients. Oscillatory potentials were reduced in the same two patients and not reported in the others.

All of the 12 patients had morphologic changes of the retina. Eleven patients revealed distinct macular pathology. One patient had only a golden appearing reflex in the retinal

Table 2. Electrophysiological data of 12 patients described in the literature and our patient

Case	Dark adaptation						Light adaptation					30 Hz	Osc Pot
	a-Wave		b-Wave				a-Wave		b-Wave				
	Amplitude	Latency	Threshold	Amplitude	Latency	Imp	Amplitude	Latency	Amplitude	Latency	Imp		
1	–	–	Elevated	L-Red/H-Inc	–	Prol	Red	Prol	Red	–	Prol	–	–
2	–	–	Elevated	L-Red/H-Inc	–	Prol	Red	Prol	Red	–	Prol	–	–
3	N	N	Elevated	L-Red/H-Inc	–	N	N	Prol	Red	–	Prol	–	–
4	N	N	N	Increased	–	N	N	N	N	–	N	–	–
5	N	N	N	H-Inc	–	N	N	N	N	–	N	–	–
6	N	–	Elevated	L-Red/H-Inc	–	L-Prol/H-N	Red	–	Red	–	Prol	Red	Red
7	N	–	Elevated	L-Red/H-Inc	–	L-Prol/H-N	Miss	–	Miss	–	–	Red	Red
8	–	–	–	Increased	–	–	Red	–	Red	–	–	–	–
9	–	–	–	L-Red/H-Inc	–	–	Red	–	Red	–	–	–	–
10	–	–	–	Increased	–	–	N	–	N	–	–	–	–
11	–	N	–	H-Inc	–	–	–	–	Red	–	–	–	–
12	–	N	–	H-Inc	–	–	–	–	Miss	–	–	–	–
13	N	N	N	Increased	Prol	Prol	N	N	Red	Prol	(Prol)	Red	Miss

Osc Pot, Oscillatory potentials; Imp, implicit time; N, normal; Miss, missing; Red, reduced; Prol, prolonged; Inc, increased; L, Low stimulus intensities; H, high stimulus intensities

periphery. Of the 11 patients four had bull's eye lesions in both maculae. The other seven patients had extensive irregularities of the retinal pigment epithelium in the macular area without peripheral changes.

None of these 12 patients were comparable to our patient in all clinical and electrophysiologic data. He differed from the other patients in the following aspects: he was male and had a congenital stationary disease with a small pigment epithelial scar in the left eye only and no other fundus changes up to the age of 22 years. He did not complain of night blindness. The dark-adapted electroretinogram showed a normal b-wave threshold with increased b-wave amplitudes and markedly prolonged b-wave latencies and implicit times, a combination of signs that was not seen in any other patient.

Our patient and all of the 12 patients previously described had a cone dysfunction. They differ from each other in the course of the disease and the severity of the deterioration of visual acuity, color vision disturbances, macular pathology, and changes of the light-adapted electroretinogram. In contrast to patients with a simple cone dystrophy, the dark-adapted potentials in the electroretinogram were not normal or subnormal. Instead the amplitudes of the b-wave were increased and in some cases the implicit times were markedly prolonged. Only some of these patients had clinical symptoms of impaired rod function. Though all 13 patients were very heterogeneous in the course of the disease, and in their clinical and electrophysiologic findings, all seem to have a defect in the postreceptoral transmission of the rod potentials. The location of the defect must therefore be within the inner retinal layers. Different defects in the inner retina presenting with similar electrophysiologic changes may be the reason why in some patients the disease is congenital and stationary while in others it is progressive.

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