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Case report

ERGs in female carriers of incomplete Congenital Stationary Night Blindness (I-CSNB)

A family report

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Key words: female carriers, flicker ERG, Incomplete Congenital Stationary Night Blindness (I-CSNB), sum of the OPs amplitude

Abstract

ERG findings in five sisters are reported. By pedigree analysis, four of the five must be obligate carriers for I-CSNB since their sons were affected (impaired night vision, reduced visual acuity, variable ametropia, congenital nystagmus and ERG with both scotopic and photopic b-wave reduced amplitude). The fifth was childless at the time of examination and her ERG analysis was normal. Three of the four obligate carriers showed significant reduction in the sum of the OPs amplitude as previously reported as being an electrophysiological signs in female carriers: two without alteration in other ERG components and the third with association with a flicker ERG amplitude significantly increased. The fourth female carrier showed a normal sum of the OPs amplitude whereas the other b-wave ERG or flicker amplitudes were significantly decreased. These last two ERG results suggest a possible modifications of synaptic transmission at a post-receptoral site (outer plexiform layer or involvement of the bipolar pathways) in these two carriers.

Introduction

Female carriers of the complete CSNB X-linked type are usually reported as clinically normal [1],[2] although one study [3] conducted on a five generation pedigree, did identify symptomatic female carriers. It is however of interest to note that in Miyake's study [1], the sum of the oscillatory potentials amplitude was statistically lower than normal in 17/22 of the carriers (77%), a finding which was also confirmed by Young et al. [2]. The above could suggest some mild impairment of the synaptic interactions at the retinal inner plexiform layers, since it is at this level that the OPs are suggested to arise. The above contrasts with the more recent report of normal ERGs in obligate carriers of two pedigrees of the I-CSNB X-linked type [4]. These carriers did however demonstrate a sensitivity loss at 600 nm, a finding which the authors claimed to be a new carrier sign.

In this study, we report ERG findings in five sisters who are clinically normal. The youngest was childless at the time of examination and her ERG was normal. The other four had sons affected by I-CSNB i.e. they showed impaired night vision, reduced visual acuity, variable ametropia, congenital nystagmus. Their ERG results showed both scotopic and photopic b-wave reduced amplitude which is typical of the incomplete form whereas in the complete form, the scotopic b-wave amplitude is bearly recordable and the photopic ERGs are normal. These four sisters must be obligate carriers of the I-CSNB X-linked type. Two of them showed ERG results similar to that reported by Miyake et al. and Young et al.. The remaining two had different ERG anomalies which suggested a possible

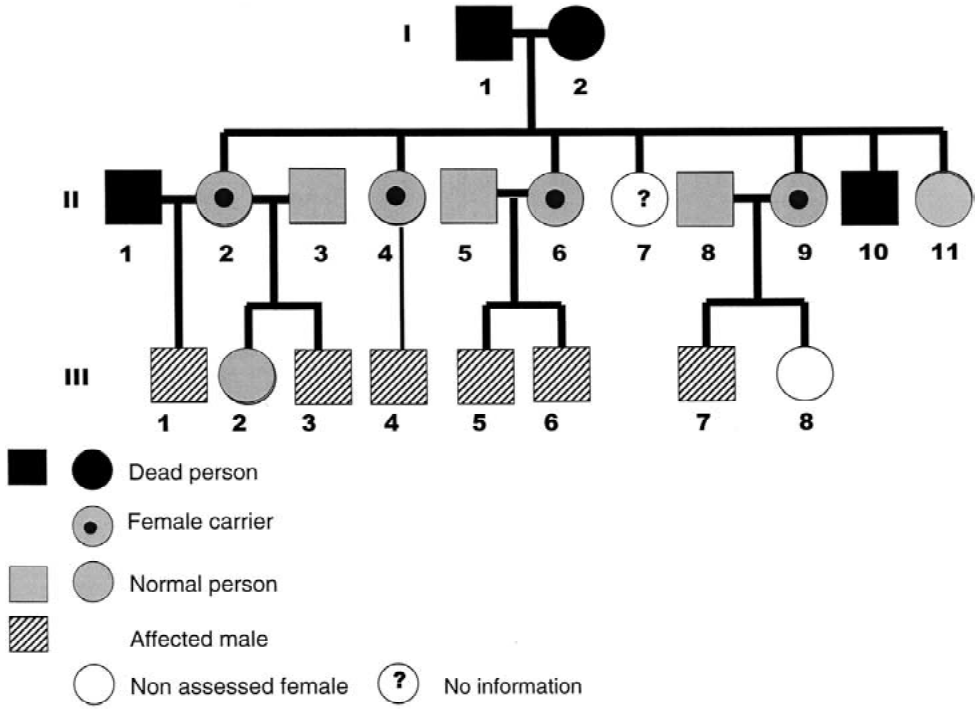

Figure 1. Pedigree of the assessed family in which six boys of the third generation had clinical and ERG findings suggestive of the I-CSNB form. Four sisters of the second generation (II-2, II-4, II-6, II-9) must be obligate carriers since their sons were diagnosed with I-CSNB.

dysfunction of the post-receptor synaptic transmission at the retinal outer plexiform layer or dysfunction of the bipolar pathways.

Subjects and methods

Fifteen of the twenty one member pedigree illustrated in Figure 1 were assessed. They underwent a complete ophthalmological examination prior to the recording of the ERG which was conducted according to the ISCEV standard [5].

The electroretinograms were obtained with pupils fully dilated (Tropicamide-Faure 2 mg/0.4 ml, CIBA-vision, France, instilled 30 minutes before ERG recordings). Following a period of 20 minutes of dark-adaptation, the corneas were anesthetized with drops of Oxybuprocaine Chlorhydrate Faure (1.6 mg/0.4 ml - Novartis, 92 Reuil-Malmaison, France) and corneal contact lens electrodes (Dencott, 75 Paris, France) were used to record the responses from both eyes. The forehead was used as the reference electrode site and the two earlobes were connected to the ground.

After dark adaptation, the following ERG responses were obtained: rod response, maximal combined response. The subjects were then light-adapted to a background of 30 cd/m^2, for ten minutes after which the cone function was assessed with the following ERG responses: the oscillatory potentials (100 Hz-300 Hz), single-flash cone response and 30 Hz flicker response. Stimulus delivery and data acquisition were controlled with a *Moniteur Ophtalmologique* system (Métrovision, 59 Lille, France). Amplitudes and implicit times of the a-wave, b-wave, OPs (OP2, OP3, OP4), and flicker responses were measured as suggested by the ISCEV standard. Furthermore the amplitudes of the different OPs were summated to yield the variable sum of the OPs (OP2+OP3+OP4) amplitude, a method also suggested by the ISCEV standard. These results were compared to those of age-matched normal subjects. Data included within plus or minus two SD of the normal mean were considered as normal. As response amplitudes were superior to mean plus two SD or inferior to mean minus two SD, they were considered as increased or decreased respectively.

Six boys of the third generation (III-1, III-3, III-4, III-5, III-6 and III-7) had clinical signs (see Table 1) and photopic and scotopic ERGs altered (Figure 2) suggestive of the I-CSNB type according to Miyake

et al.'s classification [6] while patient III-2 (a female) was found normal. The other female offspring (III-8) was too young at the time of assessment to be examined. All fathers (II-3, II-5, II-8) had normal clinical and ERG results.

Based on the above, pedigree analysis strongly suggest that the condition is inherited as an X-linked trait and consequently, the five females of the second generation (which are sisters) could be carriers of this condition. In fact only four of them must be obligate carriers (II-2, II-4, II-6 and II-9) since their sons (III-1 & III-3, III-4, III-5 & III-6, III-7) were diagnosed with the condition.

Results

Clinical results

First generation: The two parents died prematurely, the father (I-1) at the age of 34 years and the mother (I-2), ten years latter at the age of 45 years. Unfortunately, there are no records available to attest to the visual health of either. In the s*econd generation,* six females (II-2, II-4, II-6, II-7, II-9, II-11) are still alive and five of them were examined. No clinical information could be obtained from female II-7. As shown at table 1, the five females tested were found to be clinically normal, with normal visual acuities, some light ametropia and no report of visual symptoms.

ERG results

The five ERG sequence results (amplitudes and implicit times) of the five females examined are compared to that obtained from an age-matched control group (see Table 2 and Figure 3). Three of the four female carriers (II-2, II-4, II-9) showed a variable decrease in the sum of the OPs amplitude with b/a ratios of the maximal combined and cone responses being within normal values or slightly decreased. The fourth female carrier (II-6) had a normal sum of the OPs amplitude. For all the four female carriers, no significant modifications of the OPs implicit times were observed. Examination of female carriers II-2 and II-6 revealed other electroretinographic anomalies which have not been previously described. Female II-2 associated to the decreased sum of the OPs amplitude a significant increased flicker amplitude (Figure 3) and female II-6 whose sum of the OPs amplitude was normal, showed a significant decrease in the amplitude of maximal

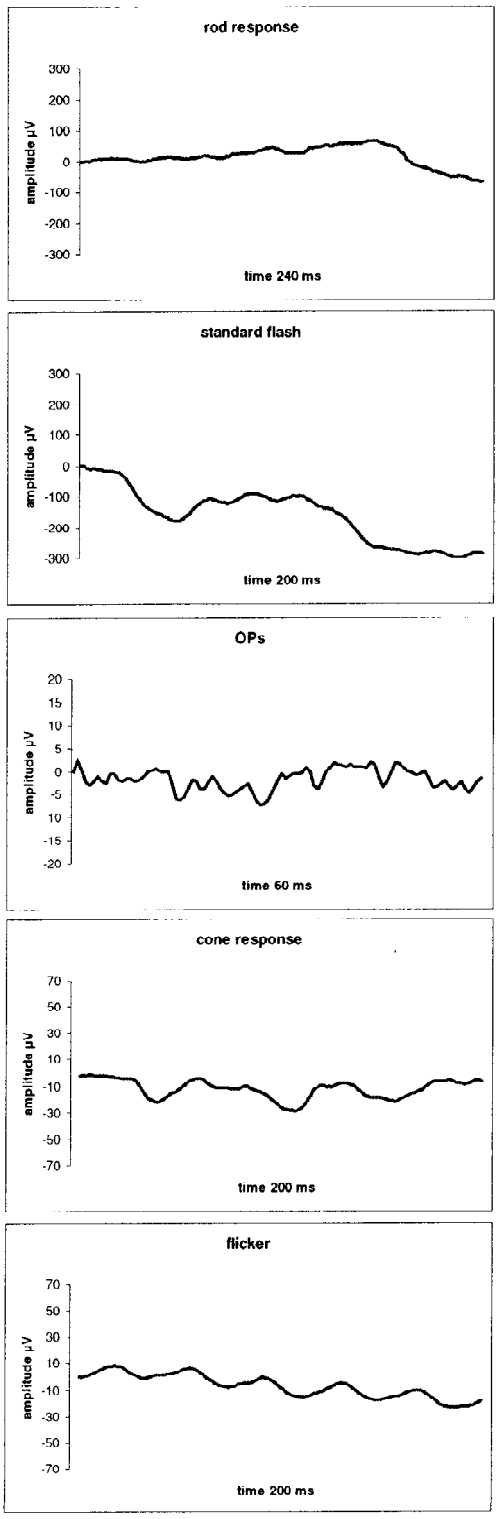

Figure 2. ERG responses of the affected boy III-1.

Table 1. Clinical results of the five sisters tested and the six affected boys

FEMALES	AFFECTED SONS	AGE as tested		REFRACTION	VISUAL ACUITY with correction	FUNDI	NYSTAGMUS	OTHERS
II-2		40	RE	$-0.50\,(80^\circ - 0.75)$	10/10 - P2	NORMAL		
			LE	$-1.25\,(85^\circ - 0.50)$	10/10 - P2	NORMAL		
	III-1	19	RE	$+2.25\,(75^\circ + 1.25)$	1.5/10	NORMAL	HORIZ/ROTATORY	ESOTROPIA
			LE	$+0.75\,(100^\circ + 1.75)$	2/10	NORMAL	HORIZ/ROTATORY	ESOTROPIA
	III-3	9	RE	$-0.50\,(30^\circ - 1.50)$	5/10	NORMAL	ROTATORY	
			LE	$-1.25\,(170^\circ - 1.50)$	5/10	NORMAL	ROTATORY	
II-4		38	RE	$-4.25\,(170^\circ - 0.50)$	10/10 - P2	NORMAL		
			LE	$-3.75\,(170^\circ - 0.50)$	10/10 - P2	NORMAL		
	III-4	1.5	RE	-10.5	non tested		LIGHT ROTATORY	
			LE	$-10.5\,(105^\circ + 2)$	non tested		LIGHT ROTATORY	
II-6		36	RE	-1	10/10 - P2	NORMAL		
			LE	-1	10/10 - P2	NORMAL		
	III-5	9	RE	-1	8/10	NORMAL	NO	
			LE	$-1\,(120^\circ - 1)$	8/10	NORMAL	NO	
	III-6	4	RE	-1	non tested	NORMAL	NO	
			LE	-2	non tested	NORMAL	NO	
II-9		33	RE	$-3\,(120^\circ - 1)$	10/10 - P2	NORMAL		
			LE	-1.25	10/10 - P2	NORMAL		
	III-7	7	RE	$-10.75\,(20^\circ - 2.50)$		NORMAL	HORIZONTAL	ESOTROPIA
			LE	$-10.25\,(160^\circ - 2.75)$		NORMAL	HORIZONTAL	ESOTROPIA
II-11		27	RE		12/10 - P2	NORMAL		
			LE	$(0^\circ - 0.50)$	12/10 - P2	NORMAL		

combined b-wave, cone b-wave and flicker responses with b/a ratios of the maximal combined and cone responses being decreased. For all the four female carriers, the implicit time of all ERG sequences were within normal values. Finally, female II-11 was found to have normal ERGs.

Comments

In the family presented, the five females including the four female carriers are clinically normal as previously reported for female carriers.

Of the five females examined, the four female carriers showed ERG anomalies (80%). The fifth (II-11) had normal ERG results, suggesting either that she is not a carrier having inherited a normal X chromosome from her father and one from her mother or that she has inherited an abnormal X chromosome from her mother with incomplete penetrance and no ERG expression.

Three of the four female carriers (75%) showed that the sum of the OPs amplitude was significantly decreased (II-2, II-4, II-9) with normal implicit time. This proportion is similar to that described by Miyake et al. [1] for the female carriers despite the fact the signal was filtered as recommended by the standard (i.e. between 100 and 300 Hz) and not filtered as recommended by Young et al. [2] (i.e. signal filtered around 130 Hz plus or minus 70 Hz range) which is claimed by these authors to be the most effective in this type of pathology to underscore the OPs.

Only two of the four female carriers (II-4, II-9) showed normal results except a decreased sum of the OPs amplitude which are ERG signs now admitted as being suggestive of an obligate carrier. In their study, Miyake et al. [1] made use of a very bright flash delivered to the dark-adapted eye and consequently both types of photoreceptors must have contributed to the OPs. Young et al. [2] recorded the OPs in light and dark-adapted conditions and showed that both

Table 2. Amplitudes and implicit times of all ERG sequences recorded in the five sisters tested

		Ops							ROD		Max combined					CONE					
		OP 2		OP 3		OP 4		Ops 2+3+4 Sum	b-wave		a-wave		b-wave			a-wave		b-wave			30 Hz FLICKER
		Ampl. microV	Impl. T ms	Ampl. microV	Impl. T ms	Ampl. microV	Impl. T ms	Ampl. microV	Ampl. microV	Impl. T ms	Ampl. microV	Impl. T ms	Ampl. microV	Impl. T ms	b/a ratio	Ampl. microV	Impl. T ms	Ampl. microV	Impl. T ms	b/a ratio	Ampl. microV
NORMES																					
MEAN +2 SD		17.3	29.5	18.3	36.8	18.6	47.3	49.8	312.4	129.3	−215.9	36.4	520.6	68.6	**2.4**	−47.1	36.1	103.1	55.0	**2.2**	63.6
MEAN		**12.3**	**27.3**	**12.9**	**34.6**	**11.8**	**44.3**	**37.0**	**206.9**	**112.9**	**−140.9**	**33.5**	**370.3**	**61.6**	**2.6**	**−26.7**	**28.4**	**70.2**	**49.5**	**2.6**	**42.0**
MEAN −2 SD		7.3	25.1	7.5	32.4	5.0	41.3	24.2	101.4	96.5	−65.9	30.6	220.1	54.6	**3.3**	−6.3	20.7	37.2	44.0	**5.9**	20.5
FEMALES																					
CARRIERS																					
II-2	RE	13.9	34	3.3	38	5.6	42	22.8	138.0	94	−156.0	34	293.0	59	**1.9**	−32.8	27	68.0	47	**2.1**	74.0
	LE	8.3	26	7.8	34	6.1	41	22.2	210.0	101	−186.0	33	352.0	57	**1.9**	−40.6	27	71.7	49	**1.8**	75.5
Affected sons III-1 III-3																					
II-4	RE	11.1	32	5.0	38	6.7	44	22.8	125.0	103	−143.7	35	293.6	57	**2.0**	−28.0	33	53.0	50	**1.9**	49.7
	LE	10.0	32	1.7	38	6.7	42	18.3	233.0	109	−171.8	35	299.8	59	**1.7**	−28.0	31	42.0	49	**1.5**	55.2
Affected son III-4																					
II-6	RE	9.1	26	14.4	33	13.0	42	36.4	124.8	120	−113.5	32	198.9	54	**1.8**	−26.0	28	36.0	43	**1.4**	20.4
	LE	14.7	26	8.1	34	12.6	44	35.4	116.8	118	−142.0	31	181.8	55	**1.3**	−22.3	25	30.3	42	**1.4**	19.8
Affected sons III-5 III-6																					
II-9	RE	7.4	28	5.6	32	7.8	42	20.8	200.0	120	−206.0	29	353.0	58	**1.7**	−23.4	24	51.4	49	**2.2**	44.7
	LE	2.8	25	4.4	32	8.3	39	15.6	188.0	115	−176.0	28	334.0	58	**1.9**	−26.5	28	46.7	49	**1.8**	38.0
Affected son III-7																					
II-11	RE	16.1	28	11.2	36	10.3	45	37.6	195.0	111	−125.2	33	278.5	55	**2.2**	−16.8	24	48.5	46	**2.9**	27.9
	LE	19.6	28	15.4	39	12.6	47	47.6	186.0	113	−153.7	33	318.6	56	**2.1**	−16.4	28	42.7	46	**2.6**	29.7

techniques yielded abnormal OPs, albeit the rod OPs appeared to be more affected. Our results thus confirm that not only the rod OPs are affected in carriers of I-CSNB (something that we already knew from previous studies) but also the cone OPs as well (as suggested by Young but not Miyake). Our findings thus suggest that, even in carriers of I-CSNB, the pathophysiology involves the rod as well as the cone pathway. Carriers of I-CSNB thus offer a unique opportunity to study the pathophysiological mechanisms involved in a more subtle model of this most interesting retinopathy. It should also be noted that, unlike in complete CSNB, the ERG of the affected males in I-CSNB is extremely reduced (especially the cone ERG) thus preventing an in depth analysis of the electrophysiological pathophysiological process involved. Examining the cone ERG and OPs in carriers of this condition thus offer the unique opportunity to postulate on what might be malfunctionning in the full blown (affected males) presentation of the same condition.

Female II-2 is an obligate carrier since she has two affected sons conceived from two different fathers II-1 (prematurely dead) and II-3. She had the previously described signs of the obligate carrier (decreased sum of the OPs amplitude) associated with a significant increase in amplitude of the flicker ERG. This sign has not been previously described in a female carrier of I-CSNB. It is reminiscent of that found in patients affected with I-CSNB in whom an exaggerated increase in the amplitude of the flicker ERG was reported during light adaptation [7]. Flicker ERG amplitude has been described as resulting from two post-receptor components, one issued from the ON pathway and one from the OFF pathway (probably at the cone bipolar cells level), the flicker response being the sum of both [8]. In case of partial blocking of one of these pathways and especially of the ON pathway, Kondo and Sieving [9] have demonstrated that flicker ERG amplitude increases. In this obligate female carrier, this sign could be interpreted in different ways. It could be in favor of a specific dysfunction of her ON-pathway in connection with a defect in neurotransmission of the photopic signal to the ON-pathway as it was suspected in a male affected with the complete form of CSNB [10]. It could also demonstrate a desynchronization or an abnormal delay between the signals delivered to the ON and OFF pathways which composed the flicker ERG response. This type of dysfunction was suggested by Alexander et al. [11] in patients affected with melanoma associated retinopathy (MAR syndrome) who reported symptoms of night blindness.

Female II-6 is also an obligate carrier since she has two affected sons (III-5 and III-6). She doesn't show the classical sign of the obligate carrier i.e. sum of the OPs amplitude decreased. Her results show a normal sum of the OPs amplitude and a significant decrease of the maximal combined b-wave and cone b-wave amplitude and a flicker amplitude decreased lower than mean minus two SD, associated to a low value rod b-wave amplitude, between mean minus one SD and mean minus two SD. Krill [12] also found a mild decrease in rod b-wave amplitude in one female carrier, associated however with normal photopic results. These female (II-6) results approach more those of an affected I-CSNB person than of carriers. They could indicate a dysfunction of the post-receptor synaptic transmission, possibly to the ON bipolar pathway which contributes to the elaboration of the b-wave [13], with normal functioning at the photoreceptor levels as the a-wave amplitudes are normal.

These two obligate female carriers (II-2, II-6) seem to share some ERG signs of symptomatic and affected I-CSNB persons. In our opinion, these results found in two obligate carriers of the same family (in II-2: increase of amplitude of flicker ERG and in II-6: decrease of maximal combined b-wave, cone-b-wave and flicker amplitudes) beside the classical ones, could be signs of a more important dysfunction taking place at the retinal outer plexiform layer (post-receptor synaptic level and balance between bipolar ON and OFF pathways) indicating that these carriers are at the frontier of the symptomatic and asymptomatic affected person. These results could also be interpreted more as signs of functional disruptions than that of organic ones, similar to those observed in case of photopic system dysfunction in patients affected with X-linked retinoschisis [14].

Even if the study on the sum of the OPs amplitude suggested that they were significant markers of retinal dysfunction in CSNB carriers [1], their normality does not imply that the subject is not a carrier and it seems that the study of the photopic system in particular the cone b-wave amplitude and the flicker response is especially variable. It is possible that in order to ascertain a minimal photopic system dysfunction in female carriers, one could use chromatic flicker stimuli [15] to test separately the L and M cone pathways rather than the standard protocol ERG flicker (achromatic stimulus). This technique proved useful to ascertain specific dysfunction of pathways in particular modification of their respective phases, as in Retinitis pigmentosa [16], Stargardt's maculopathy

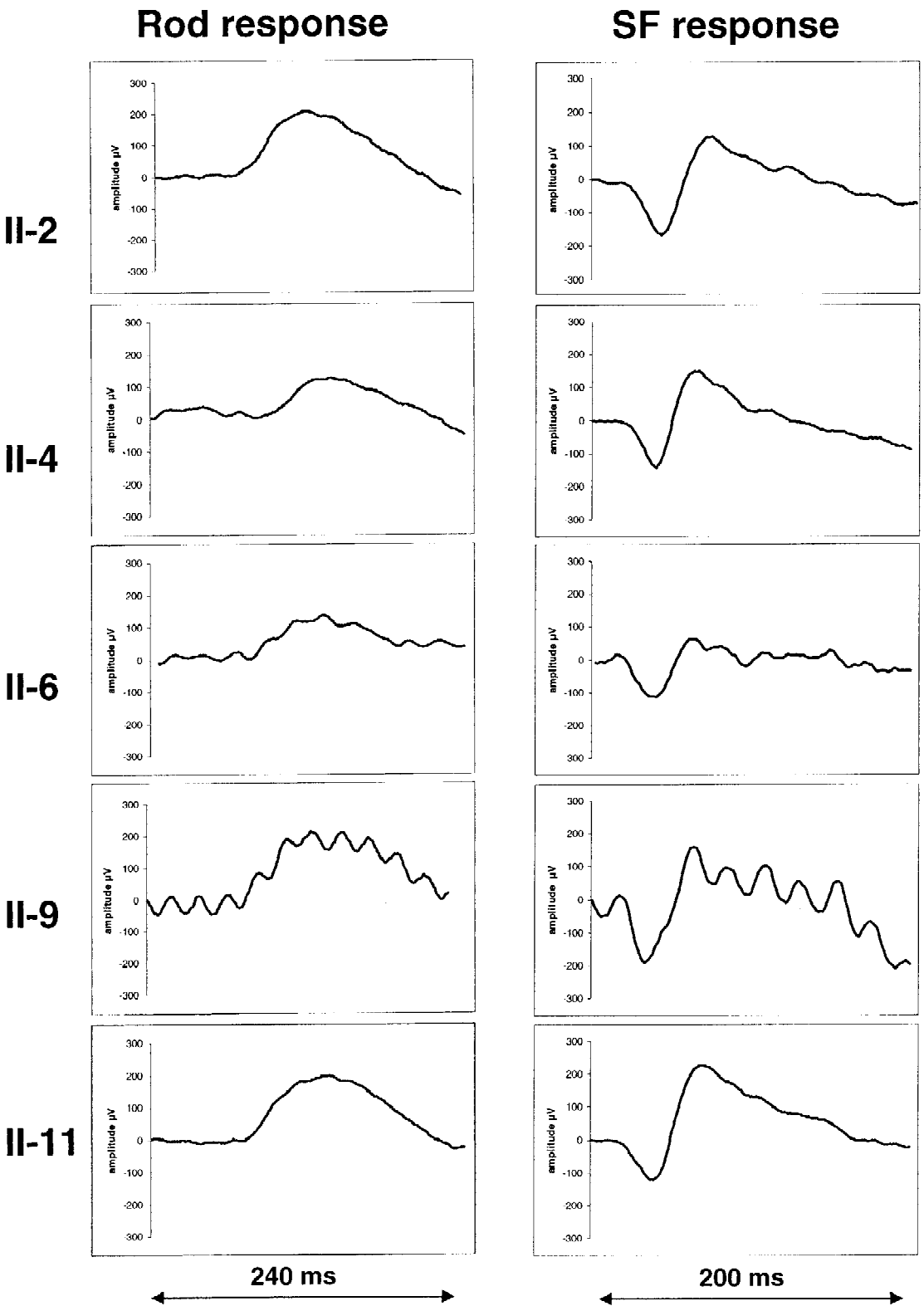

Figure 3a. ERG responses of the five sisters tested. The five ERG responses of subject II-11 are normal.

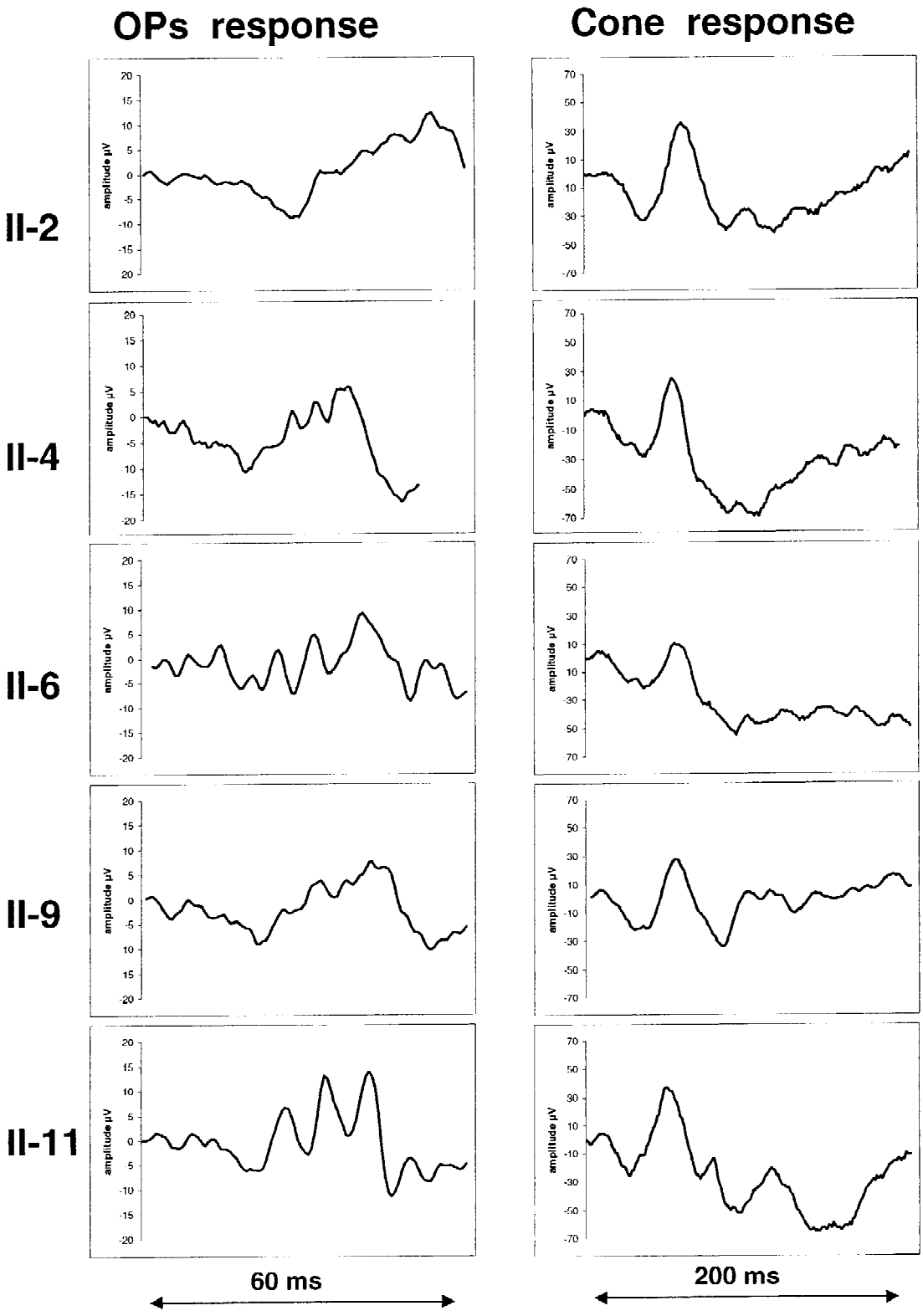

Figure 3b. ERG responses of the five sisters tested. The five ERG responses of subject II-11 are normal.

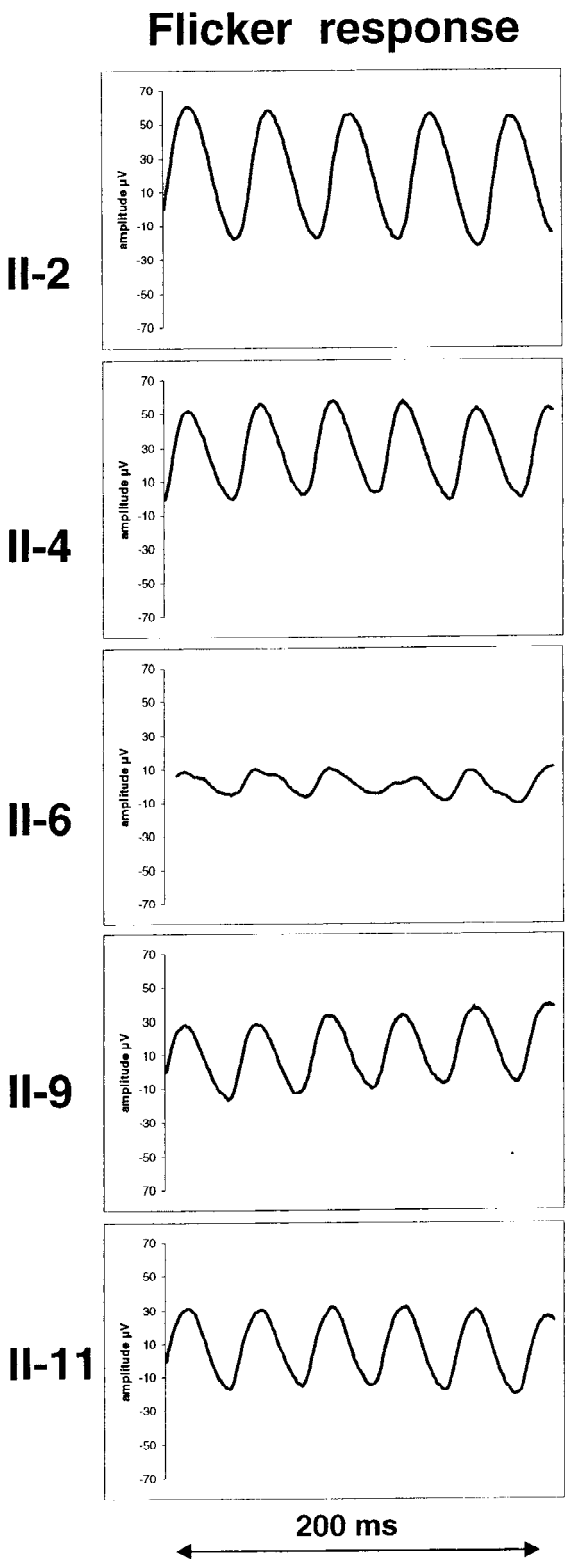

Figure 3c. ERG responses of the five sisters tested. The five ERG responses of subject II-11 are normal.

[17] or to a lesser degree, in Best's disease [18]. This could eventually better bring to light a dysfunction of the ON or OFF pathway or a phase shift between the two systems.

The genetic of X-linked I-CSNB is heterogeneous [19]. Gene disorders accounting for I-CSNB (CSNB2) have been localized in locus within Xp11.23 [20]. Mutations in the calcium-channel CACNA1F [21],[22] cause X-linked I-CSNB with considerable clinical variability [23]. This strongly suggests that I-CSNB is an example of human channelopathy disorder of the retina. The flicker hyperamplitude recorded in our female carrier II-2 may be an indirect demonstration of a minimal channelopathy disorder.

In animal models, despite the fact that visual function is difficult to evaluate, clinical findings similar to I-CSNB were reported in Appaloosa horses [24],[25] and in Briard dogs [26]. The proposed cause of equine night blindness in Appaloosa horses is a neural transmission defect in the region of inner segments of the photoreceptors or in the region of the bipolar cells [27] a localisation similar to that suggested for our carriers II-2 and II-6. Recently two spontaneous models were described in mouse [28] and rat [29] with in both cases, a normal dark-adapted a-wave but neither b-wave nor oscillatory potentials recorded. Despite the ERG abnormalities recorded in these animal models, the laminar structure and cytoarchitecture of the retina of the latter animal model seemed normal under light and electron microscopy, supporting the above idea that the origin of the dysfunction signs could reflect a major dysfunction in signal timing, a factor impossible to ascertain from histological studies.

Conclusion

Our results demonstrated that in five females assessed in this study, four of the five who are female carriers show clear electrophysiological signs of a retinal dysfunction. In three of the four, we saw significant reduction in the sum of the OPs amplitude with or without alteration in other ERG components, while in the fourth carrier the sum of the OPs amplitude were not affected whereas the other ERG components were. The above variability in the electrophysiological phenotype of our carriers could possibly be accounted for by the lyonisation hypothesis.

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References

1. Miyake Y, Kawase Y. Reduced amplitude of oscillatory potentials in female carriers of X-linked recessive congenital stationary night blindness. Am J Ophthalmol 1984; 98(2): 208–215.
2. Young RS, Chaparro A, Price J, Walters J. Oscillatory potentials of X-linked carriers of congenital stationary night blindness. Invest Ophthalmol Vis Sci 1989; 30(5): 806–812.
3. Ruttum MS, Lewandowski MF, Bateman JB. Affected females in X-linked congenital stationary night blindness. Ophthalmology 1992; 99(5): 747–752.
4. Lorenz B, Andrassi M, Miliczek KD. Incomplete congenital stationary night blindness (CSNB). An important differential diagnosis of congenital nystagmus. Klin Monatsbl Augenheilkd 1996; 208(1): 48–55.
5. Marmor MF, Zrenner E. Standard for clinical electroretinography (1999 update). Doc Ophthalmol 1999; 97: 143–156.
6. Miyake Y, Yagasaki K, Horiguchi M, Kawase Y, Kanda T. Congenital stationary night blindness with negative electroretinogram. A new classification. Arch Ophthalmol 1986; 104: 1013–1020.
7. Miyake Y, Horiguchi M, Ota I, Shiroyama N. Characteristic ERG-flicker anomaly in incomplete congenital stationary night blindness. Invest Ophthalmol Vis Sci 1987; 28(11): 1816–1823.
8. Bush RA, Sieving PA. Inner retinal contributions to the primate photopic fast flicker electroretinogram. J Opt Soc Am A 1996; 13(3): 557–565.
9. Kondo M, Sieving PA. Primate photopic sine-wave flicker ERG: vector modeling analysis of component origins using glutamate analogs. Invest Ophthalmol Vis Sci 2001; 42(1): 305–312.
10. Barnes CS, Alexander KR, Fishman GA. A distinctive form of congenital stationary night blindness with cone ON-pathway dysfunction. Ophthalmol 2002; 109(3): 575–583.
11. Alexander KR, Barnes CS, Fishman GA, Milam AH. Nature of the cone ON-pathway dysfunction in Melanoma-Associated Retinopathy. Invest Ophthalmol Vis Sci 2002; 43(4): 1189–1197.
12. Krill AE. X-chromosomal linked diseases affecting the eye. Status of the heterozygote female. Trans Am Ophthalmol Soc 1969; 67: 535.
13. Karwoski CJ, Xu X. Current source-density analysis of light-evoked field potentials in rabbit retina. Visual Neuroscience 1999; 16: 369–377.
14. Alexander KR, Fishman GA, Grover S. Temporal deficits in the electroretinogram of the cone system in X-linked retinoschisis. Vision Res 2000; 40: 2861–2868.
15. Usui T, Kremers J, Sharpe LT, Zrenner E. Response phase of the flicker electroretinogram (ERG) is influenced by cone excitation strength. Vision Res 1998; 38(21): 3247–3251.
16. Scholl HP, Kremers J. Large phase differences between L-cone and M-cone-driven electroretinograms in retinitis pigmentosa. Invest Ophthalmol Vis Sci 2000; 41(10): 3225–3233.
17. Scholl HPN, Kremers J, Vonthein R, White K, Weber BHF. L- and M-cone-driven electroretinograms in Stargardt's macular dystrophy-fundus flavimaculatus. Invest Ophthalmol Vis Sci 2001; 42(6): 1380–1389.
18. Scholl HPN, Kremers J, Apfelstedt-Sylla E, Zrenner E. L- and M-cone-driven electroretinograms are differently altered in Best's macular dystrophy. Vision Res 2000; 40: 3159–3168.
19. Boycott KM, Pearce WG, Musarella MA, Weleber RG, Maybaum TA, Miyake Y, Young RS, Bech-Hansen NT. Evidence for genetic heterogeneity in X-linked congenital night blindness. Am J Hum Genet 1998; 62(4): 865–875.
20. Bech-Hansen NT, Boycott KM, Gratton KJ, Ross DA, Field LL, Pearce WG. Localization of a gene for incomplete X-linked congenital stationary night blindness to the interval between DXS6849 and DXS8023 in Xp11.23. Hum Genet 1998; 103(2): 124–130.
21. Bech-Hansen NT, Naylor MJ, Maybaum TA, Pearce WG, Koop B, Fishman GA, Mets M, Musarella MA, Boycott KM. Loss-of-function mutations in a calcium-channel alpha-1-subunit gene in Xp11.23 cause incomplete X-linked congenital stationary night blindness. Nature Genet 1998; 19: 264–267.
22. Nakamura M, Ito S, Terasaki H, Miyake Y. Novel CACNA1F mutations in Japanese patients with incomplete congenital stationary night blindness. Invest Ophthalmol Vis Sci 2001; 42(7): 1610–1616.
23. Boycott KM, Pearce WG, Bech-Hansen NT. Clinical variability among patients with incomplete X-linked congenital stationary night blindness and a founder mutation in CACNA1F. Can J Ophthalmol 2000; 35(4): 204–213.
24. Witzel DA, Smith EL, Wilson RD, Aguirre GD. Congenital Stationary Night Blindness: an animal model. Invest Ophthalmol Vis Sci 1978; 17: 788-795.
25. Rebhun WC, Loew ER, Riis RC, Laratta LJ. Clinical manifestations of night blindness in the Appaloosa Horse. Comp of Cont Ed Vet 1984; 6: 103–106.
26. Narfström K, Wrigstad A, Ekesten B, Nilsson SE. Hereditary retina dystrophy in the Briard dog: clinical and hereditary characteristics. Vet and Comp Ophthalmol 1994; 4(2): 85–92.
27. Witzel DA, Joyce JR, Smith EL. Electroretinography of congenital night blindness in an Appaloosa filly. J of Equine Med Surg 1977; 1: 226.
28. Pardue MT, McCall MA, LaVail MM, Gregg RG, Peachey NS. A naturally occurring mouse model of X-linked Congenital Stationary Night Blindness. Invest Ophthalmol Vis Sci 1998; 39: 2443–2449.
29. Zhang Z, Gu Y, Li L, Long T, Guo Q, Shi L. A spontaneous gene mutant rat model of CSNB. ISCEV 2002; Abstract p. 65.

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