

# The Effect of Fluorescein Angiography on Full-Field Electroretinography Parameters

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**Purpose:** To investigate the effect of simultaneously performed fluorescein angiography (FA) on full-field electroretinography (ffERG) parameters.

**Method:** Scotopic and photopic ffERG were performed immediately and 60 minutes after conventional FA in patients with retinal photoreceptor disorders; a- and b-wave amplitudes were compared between recordings obtained at the two time intervals in each patient.

**Results:** Ten eyes of five (3 male and 2 female) patients with mean age of  $19.6 \pm 3.8$  (range, 15-25) years were studied. Intravenous fluorescein administration caused an immediate reduction in ERG waves which was most prominent in rod and maximal combined responses. Mean a-wave amplitude in maximal combined response, rod response and cone response ERGs was  $46.0 \pm 18.8$ ,  $8.0 \pm 7.0$  and  $5.1 \pm 2.0$   $\mu\text{V}$  immediately after FA which was increased to  $79.0 \pm 30.0$ ,  $21.5 \pm 22.5$  and  $6.5 \pm 2.4$   $\mu\text{V}$  60 minutes afterwards, respectively ( $P < 0.005$  for all comparisons). Mean b-wave amplitude in the same order was  $91.0 \pm 17.5$ ,  $47.7 \pm 17.2$  and  $17.3 \pm 14.7$   $\mu\text{V}$  which was increased to  $145.0 \pm 54.3$ ,  $91.8 \pm 48.1$  and  $20.0 \pm 17.7$   $\mu\text{V}$  respectively, 60 minutes after FA ( $P < 0.005$  for all comparisons).

**Conclusion:** The amplitude of ERG a- and b-waves under scotopic and photopic conditions increased significantly one hour after FA. These changes may be explained by disappearance of phototoxic and bleaching effects of strong light exposure from the light source of the angiography machine and fluorescein molecule on retinal photoreceptors.

**Keywords:** Fluorescein Angiography; Electroretinography

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## INTRODUCTION

Fluorescein angiography (FA) and electroretinography (ERG) are two of the most important and common paraclinical tests employed for evaluation and diagnosis of retinal and choroidal disorders.<sup>1-4</sup> Simultaneous use of FA and ERG may sometimes be considered as the last resort for the diagnosis of these diseases.

Many factors such as stimulus duration, size of the illuminated retinal area, interval between stimuli, pupil size, circulation state, drugs, hyperventilation, retinal development, clarity of the media, age, sex, refractive error and anesthesia can affect ERG parameters.<sup>5,6</sup>

This study was aimed to evaluate the effect of simultaneously performed FA on Ganzfeld full-field electroretinography (ffERG) parameters.

**METHODS**

Five patients including 3 male and 2 female subjects with retinal photoreceptor disorders were enrolled in this study. Conventional FA with a stroboscopic lamp providing flashlight stimulation through a monochromatic blue filter was performed using the Heidelberg Retina Angiography system (Heidelberg Engineering, Germany). Photopic (cone response) and scotopic (rod and maximal combined response) ERGs were obtained according to the methods described by the International Society for Clinical Electrophysiology of Vision (ISCEV) using the Mono Elec2 system (Metrovision Inc., France) in all cases immediately and 60 minutes after FA. The pupils were fully dilated to a diameter of 8 mm with 1% tropicamide and 2.5% phenylephrine eye drops under topical anesthesia with 0.5% tetracaine. The ERGject contact lens electrode was used as the recording electrode and 0.5% methylcellulose was deposited into its concavity; the reference

electrode was placed in the center of the forehead and the ground electrode was attached to the ear lobe. The photopic response was recorded after 10 minutes of light adaptation and the scotopic and maximal responses were obtained following dark adaptation for at least 20 minutes. Amplitudes of a and b waves in these two conditions were measured and compared in each patient using Wilcoxon test with significance level set at 0.05.

**RESULTS**

Ten eyes of five (3 male and 2 female) consecutive patients with mean age of 19.6±3.8 (range, 15-25) years underwent FA in conjunction with ERG. Table 1 summarizes ERG data and clinical findings of the patients. The amplitude of a- and b- waves showed a remarkable decrease shortly after FA but increased significantly after one hour.

Tables 2 and 3 compare a- and b-wave amplitudes shortly and 60 minutes after FA

**Table 1.** Clinical data and electrophysiological findings of patients following fluorescein angiography

Eyes	Patients	Age (yr)	Sex	Laterality	a-wave Amplitude (µv)						b-wave Amplitude (µv)					
					Maximal Combined Response		Rod Response		Cone Response		Maximal Combined Response		Rod Response		Cone Response	
					Early	Late	Early	Late	Early	Late	Early	Late	Early	Late	Early	Late
					1	1	15	M	OD	60.9	72.9	6.3	10.4	3.1	3.1	85
2				OS	65.5	106	26	80.1	2.7	3	89	125	52.1	85.1	2.7	3.5
3	2	17	F	OD	27.1	40.6	7.8	17.2	5.9	6.1	70.2	126	22.6	60.8	5.1	6.1
4				OS	22.8	48.4	2.9	8.8	4.4	6.7	60.4	126	17.1	67.1	2.8	13.1
5	3	20	M	OD	63.5	146	10.4	37.5	6.3	10.7	110	292	58.2	213	40.2	60.4
6				OS	65.5	80.5	1	14	4.7	6.9	110	162	47.8	134	33.8	35
7	4	21	M	OD	46	68.3	4.3	7.2	9.8	8.9	89.2	152	65.6	92.7	9.2	11.3
8				OS	57	72.7	4.7	8.6	4.7	7.9	114	119	72	70.7	31	20.7
9	5	25	F	OD	18.8	68	6.3	10.2	4.1	5.2	89	99.9	44.9	57.8	17.4	18.1
10				OS	34	91	10	21	5.2	6.1	101	125	53.6	70.1	28	29.1

F, Female; M, Male; OD, right eye; OS, left eye; Early, electoretinography (ERG) immediately after fluorescein angiography (FA); Late, ERG 60 minutes after FA

**Table 2.** a-wave amplitude (microvolts) immediately (early) and one hour after (late) fluorescein angiography

Response	M±SD; Median (range)		M±SD (95%CI) Median (95%CI)	M±SD Median (95%CI)	*P-value
	Early	Late	Change	% of change	
	Maximal combined	46.1±18.8; 51.5 (18.8-65.5)	79.4±30; 72.8 (40.6-146)	33.3±23.5 (16.5-50.1) 24 (12-82.5)	
Rod	8±7; 6.3 (1-26)	21.5±22.5; 12.2 (7.2-80.1)	13.5±16 (2.1-2.5) 7.7 (2.9-54.1)	248±376 115 (62-1300)	0.005
Cone	5.1±2; 4.7 (2.7-9.8)	6.5±2.4; 6.4 (3-10.7)	1.4±1.6 (0.2-2.5) 1 (-0.9 to 4.4)	29±29 22 (-9 to 70)	0.004

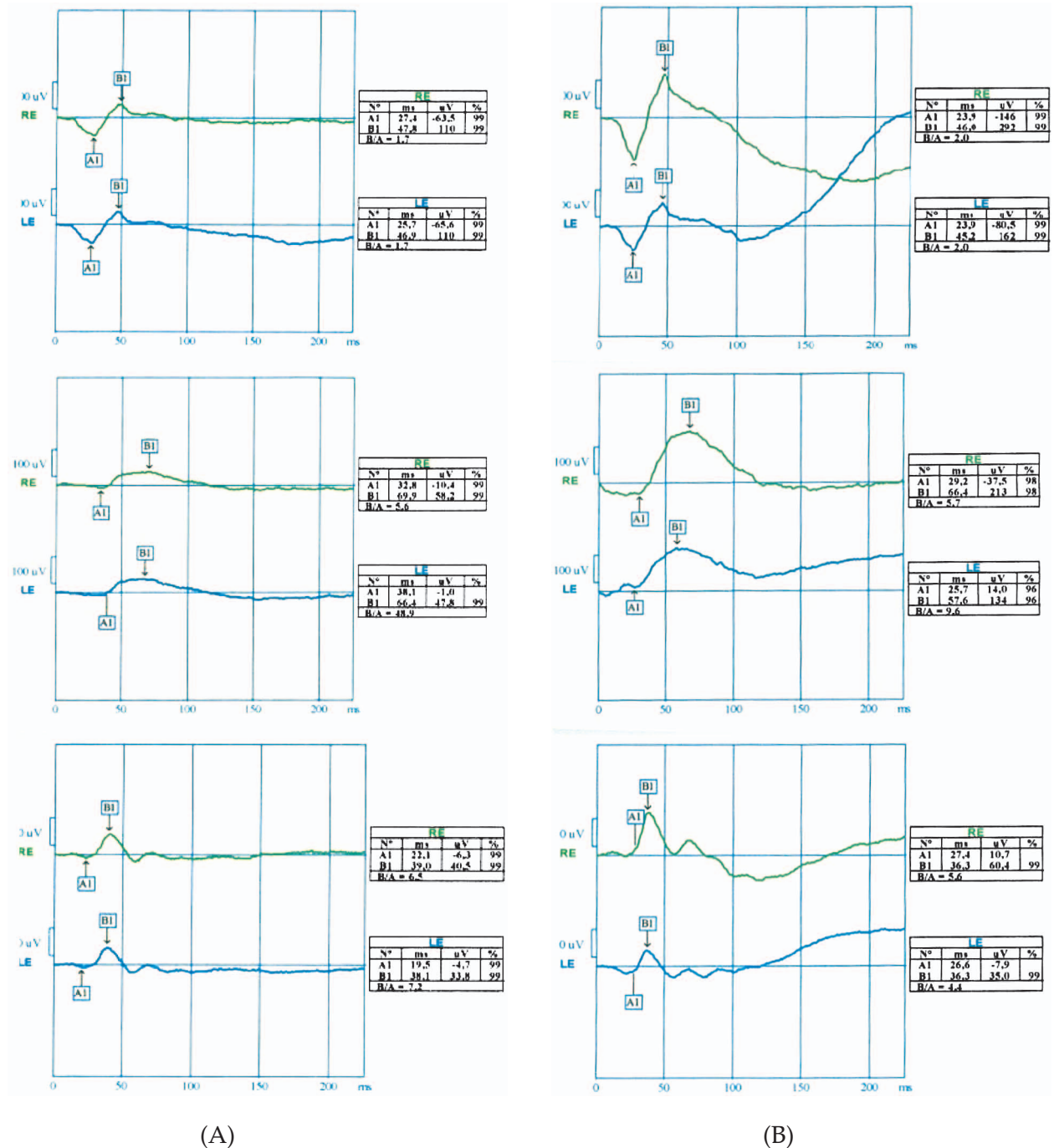
M, mean; SD, standard deviation; CI, confidence interval

\* Wilcoxon signed rank test

in terms of maximal combined, rod and cone responses. All changes were statistically significant ( $P < 0.005$ ) under all conditions.

A representative case (#3) demonstrates low a- and b-wave amplitudes shortly after FA in

maximal combined, rod, and cone response ERGs (Fig. 1A). ERG in the same patient one hour after FA demonstrated a significant increase in a- and b-wave amplitudes in all three settings (Fig. 1B).



**Figure 1.** (A) A representative case (#3) demonstrates low a- and b-waves amplitudes shortly after fluorescein angiography in maximal combined response, rod response, and cone response ERGs (upper, middle and lower printouts, respectively). (B) Electroretinography in the same patient 60 minutes after fluorescein angiography shows a significant increase in both a- and b- wave amplitudes.

**Table 3.** b-wave amplitude (microvolts) immediately (early) and one hour after (late) fluorescein angiography

Response	M±SD; Median (range)		M±SD (95%CI) Median (95%CI)	M±SD Median (95%CI)	*P-value
	Early	Late	Change	% of change	
Maximal combined	91.8±17.5; 89.1 (60.4-114)	145.3±54.3; 126 (99.9-292)	53.5±49.7 (17.9-89.1) 46.5 (5-182)	60±49 48 (4-165)	0.005
Rod	47.7±17.2; 50 (17.1-72)	91.8±48.1; 70.4 (57.8-213)	44.1±45.6 (11.5-76.7) 30.1 (-1.3 to 154.8)	112±106 59 (-2 to 292)	0.007
Cone	17.3±14.7; 13.3 (2.7-40.2)	20±17.7; 15.6 (3.1-60.4)	2.7±7.9 (-2.9 to 8.3) 1.1 (-10.3 to 20.2)	47±115 12 (-33 to 368)	0.075

M, mean; SD, standard deviation; CI, confidence interval

\* Wilcoxon signed rank test

## DISCUSSION

Electrophysiological testing at two time points following FA seem to have different results due to the effect of fluorescein.<sup>7,8</sup> The idea that repeated recording of ERG together with FA may provide information on dynamic aspects of retinal damage has already been proposed.<sup>9</sup> Ophthalmologists, however have generally been discouraged because of the phototoxic and bleaching effect of the strong light emitted from fluorescein molecules.

In 1981, Tamai and Mizuno<sup>10</sup> attempted to detect impairment of retinal vessels with "fluorescein ERG". They expected to obtain information on the microvascular lesion in the immediate vicinity of the vessels. The basis of their experiment was the assumption that during ERG examination after FA, photoreceptors might be stimulated not only by the blue light (480 nm) flashed onto the retina, but also by the green light (520 nm) emitted by fluorescein which may reflect impairment of blood retinal barrier, damage to photoreceptors and alterations in ERG response.

In an animal study by Bloom and Burian<sup>11</sup> using large doses of orally administered fluorescein in rabbits, there were no significant changes in fundus, ERG or histopathological retinal sections. A similar effect has been reported by fluorescein and indocyanine green angiography on subsequent dark adaptation and ERG.<sup>12,13</sup>

In the current study, ERG recording revealed considerable amplitude changes at different time points following fluorescein administration. An initial and transient decrease of a- and b-wave amplitude was noted immediately after

administration of the dye in all cases which increased one hour thereafter. We can therefore conclude that the initial amplitude reduction may be due to the bleaching and phototoxic effects of the light source of the FA machine or due to the transient phototoxic effect of the fluorescein molecules. In cases requiring both FA and ERG, ERG could be performed prior to FA. However when FA is performed prior to ERG, it is prudent to postpone ERG for at least one hour to avoid the effects of FA on the electrophysiological response.

## Conflicts of Interest

None.

## REFERENCES

1. Berkow JW, Flower RW, Orth DH, Kelley JS. Fluorescein and Indocyanine Green Angiography. 2nd ed. San Francisco: American Academy of Ophthalmology; 1997.
2. Marmor MF, Holder GE, Seeliger MW, Yamamoto S; International Society for Clinical Electrophysiology of Vision. Standard for clinical electroretinography (2004 update). *Doc Ophthalmol* 2004;108:107-114.
3. Fishman GA, Birch DG, Holder GE, Brigell MG. Ophthalmology Monograph 2- Electrophysiologic testing in disorder of the retina, optic nerve, and visual pathway. 2nd ed. San Francisco: American Academy of Ophthalmology; 2001.
4. Heckenlively JR, Arden GB. Principles and practice of clinical electrophysiology of vision. St Louis: Mosby; 1991.
5. Carr RE, Siegel LM. Electrodiagnostic testing of the visual system: a clinical guide. Philadelphia: FA Davis; 1990.

6. Marmor MF, Arden GB, Nilsson SE, Zrenner F. Standard for clinical electroretinography. *Arch Ophthalmol* 1989;107:816-819.
7. Kuwabara T, Gorn RA. Retinal damage by visible light. An electron microscopic study. *Arch Ophthalmol* 1968;72:69-78.
8. Valenzano DP, Pooler JP. Phototoxicity. The neglected factor. *JAMA* 1979;242:453-454.
9. Putting BJ, Zweydfenning RC, Vrensen GF, Oosterhuis JA, van Best JA. Blood-retinal barrier dysfunctions at the pigment epithelium induced by blue light. *Invest Ophthalmol Vis Sci* 1992;33:3385-3393.
10. Tamai M, Mizuno K. Electroretinogram changes after fluorescein injection: a new method to evaluate blood retinal barrier dysfunction. *Invest Ophthalmol Vis Sci* 1981;20:272-276.
11. Bloome MA, Burian HM. Chronic fluoride ingestion in rabbits. Absence of ocular effects. *Arch Ophthalmol* 1970;83:354-356.
12. Bartz-Schmidt KU, Walter P, Krott R, Brunner R, Esser P, Heimann K. Effect of fluorescein and indocyanine green angiography on subsequent dark adaptation and the electroretinogram. *Klin Monbl Augenheilkd* 1996;208:224-228.
13. Wen F, Yu M, Wu D, Ma J, Wu L. Effect of indocyanine green angiography using infrared fundus camera on subsequent dark adaptation and electroretinogram. *Doc Ophthalmol* 2002;105:51-56.