

SCIENTIFIC REPORT

Interocular amplitude differences of the full field electroretinogram in normal subjects

Y Rotenstreich, G A Fishman, R J Anderson, D G Birch

Br J Ophthalmol 2003;87:1268–1271

Aims: To determine the interocular amplitude response difference of the electroretinogram (ERG) in normal subjects.

Methods: 79 subjects, without retinal changes of clinical significance, underwent ERG testing. They included 63 men and 16 women, with a mean age of 44 (SD 12) years and range of 18–65 years. Isolated rod, scotopic maximal, dark adapted 30 Hz flicker, photopic single flash, and light adapted 30 Hz flicker responses were recorded in both eyes following the International Society for Clinical Electrophysiology of Vision (ISCEV) standard protocol. The interocular percentage differences of the ERG b-wave amplitudes were calculated and presented as percentiles (25th, 50th, 75th, 95th), means (SD), and medians.

Results: The median interocular percentage differences in the b-wave amplitudes for the above ERG stimulus responses were 10%, 8%, 10%, 11%, and 10%, respectively. The mean interocular percentage differences were 11%, 11%, 12%, 13%, and 14%. The 95th percentiles for the interocular percentage differences were 28%, 27%, 36%, 33%, and 35%, respectively.

Conclusions: The interocular percentage differences in the ERG b-wave amplitudes for five different stimulus responses were similar in our cohort of individuals without clinically significant retinal changes and ranged from a median of 8–11% and a 95th percentile of 27–36%. Our findings should be useful for determining sample sizes in future therapeutic trials on retinal diseases with monocular therapeutic strategies and may also have application for the more accurate detection of asymmetric retinal disease.

The full field electroretinogram (ERG) is a well established procedure for investigating retinal disease. Although a standard testing protocol has been recommended by the International Society for Clinical Electrophysiology of Vision (ISCEV),¹ there are limited data on the interocular difference that might be anticipated to occur with the use of the ISCEV testing protocol.^{2–5}

In this study, we calculated the interocular difference of the b-wave amplitude for various ERG stimuli in subjects primarily without or, in isolated instances, with only localised retinal changes. Measuring the range of normal interocular difference provides an important parameter for the clinical evaluation of patients with asymmetric retinal eye diseases, such as acute zonal occult outer retinopathy,⁴ retinal toxicity from an intraocular metallic foreign body,^{6–7} and carriers of X linked retinitis pigmentosa.^{8–9} Furthermore, knowledge of interocular ERG amplitude variability is important for determining sample size in treatment trials and for monitoring possible therapeutic effects in future clinical treatment trials for hereditary retinal diseases that utilise a monocular treatment protocol.

METHODS

ERG data were collected prospectively from 79 subjects, 63 females and 16 males, who were participants in a pharmaceutical study. The subjects included those being treated with either a proton pump inhibitor or a non-proton pump inhibitor for, predominantly, gastro-oesophageal reflux disease. They also included a group of normal control subjects. The medications used had no untoward effect on ERG amplitudes when compared to the control subjects. The study was carried out with approval from the institutional review board at the University of Texas, UT Southwestern Medical Center. Seventy two subjects were white, five black, and two Asian. The mean age was 44 (SD 12) years (range 18–65 years). Each subject underwent a full ophthalmological examination, visual field evaluation (Humphrey, 30-2 with standard full threshold technique), and ERG testing in both eyes. All participants had a normal visual field, normal ERG amplitude results, and none showed an asymmetric refractive error or strabismus. Of the 79 subjects, six had peripheral lattice degeneration, one showed mild bilaterally symmetric lens opacities, one was diagnosed with presumed bilateral ocular histoplasmosis, and one with limited, bilaterally symmetric macular drusen. None of the subjects had either a systemic disease or were on any medications known to affect ERG function.

Pupils were dilated to at least a 7 mm diameter with 2.5% phenylephrine hydrochloride and 1% cyclopentolate hydrochloride. ERG amplitudes on both eyes of each subject were obtained. Dark adapted ERG responses after a minimum of 45 minutes for dark adaptation included an isolated rod, maximal response, and 30 Hz flicker. Light adapted responses included a single white flash and 30 Hz flicker. These recording procedures adhered to a recommended international standard for clinical electrophysiological measurements.¹

For each of the five stimuli, the percentage difference between right and left eyes for the ERG b-wave amplitudes in

Table 1 The interocular percentage difference in b-wave amplitude for each ERG stimulus

	Photopic		Scotopic		
	Single flash (%)	30 Hz flicker (%)	Isolated (blue) (%)	Maximal white (%)	30 Hz flicker (%)
Mean (SD)	13 (10)	14 (11)	11 (9)	11 (9)	12 ± 9
Range	0–54	0–57	0–34	0–33	1–44
Percentile*					
25th	≤ 6	≤ 6	≤ 4	≤ 4	≤ 6
50th†	≤ 11	≤ 10	≤ 10	≤ 8	≤ 10
75th	≤ 18	≤ 20	≤ 17	≤ 17	≤ 15
95th	≤ 33	≤ 35	≤ 28	≤ 27	≤ 36

*A percentile represents the maximal interocular percentage difference in the percentile of the population.

†The 50th percentile represents the median.

Table 2 The number of individuals (%) at different levels of percentage difference

	Photopic		Scotopic		
	Single flash	30 Hz flicker	Isolated (blue)	Maximal white	30 Hz flicker
10% difference or lower	35 (44)	40 (51)	44 (56)	46 (58)	41 (52)
20% difference or lower	67 (85)	61 (77)	66 (84)	66 (84)	66 (84)
30% difference or lower	74 (94)	69 (87)	76 (96)	77 (97)	73 (92)

The interocular percentage difference for the above five stimuli had no statistically significant relation with age (Spearman rank order p values from 0.471 to 0.806), or with the averaged b-wave amplitude for the two eyes (Spearman rank order p values from 0.070 to 0.441).

each subject was calculated. This difference was computed by dividing the ERG b-wave amplitude difference between the eyes by the higher amplitude. The effect of the b-wave amplitude on the interocular percentage difference was evaluated by analysing the relation between the average amplitude of both eyes to the interocular percentage difference in each subject.

RESULTS

The median percentage interocular differences of the b-wave amplitudes were similar for the photopic single flash, light adapted 30 Hz flicker, isolated rod, maximal scotopic, and dark adapted 30 Hz flicker responses (11, 10, 10, 8, and 10 respectively). The maximal interocular percentage differences

observed were 54, 57, 34, 33, and 44, respectively. The 95th percentiles for the percentage difference were 31, 34, 28, 27, and 34, respectively (Table 1). The number of individuals and percentage with ERG b-wave interocular amplitude differences at $\leq 10\%$, $\leq 20\%$, or $\leq 30\%$ as well as the median differences and 95th percentile interocular ERG b-wave amplitude differences for the five stimulus conditions are shown in Tables 1 and 2. Of all the participants, only one subject had a 21% difference or greater for each one of the stimuli.

The distribution and the cumulative curves of the interocular differences for the b-wave amplitudes obtained with the five different stimuli are presented in Figures 1–5. The cumulative curves represent the percentage of the study

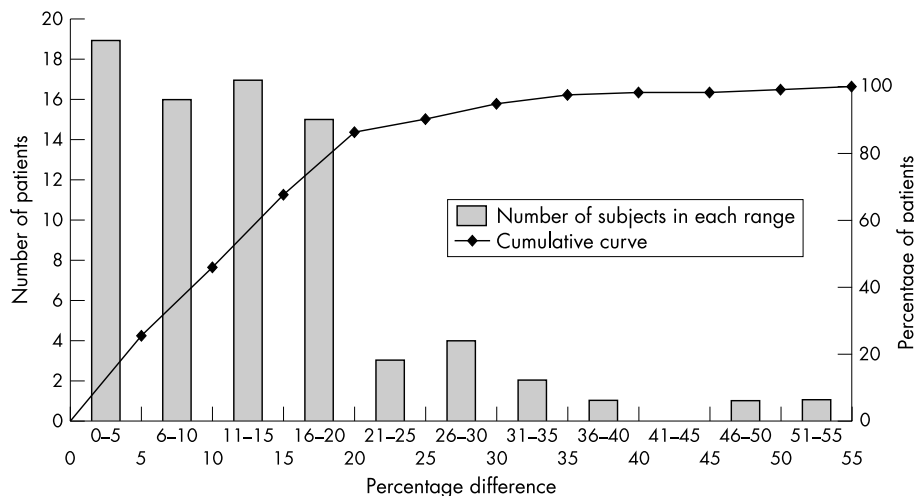


Figure 1 The columns represent the interocular percentage difference distribution in 5% intervals of the ERG b-wave amplitude responses for the single flash photopic stimulus. The line demonstrates the cumulative curve for this stimulus in 5% difference increment steps.

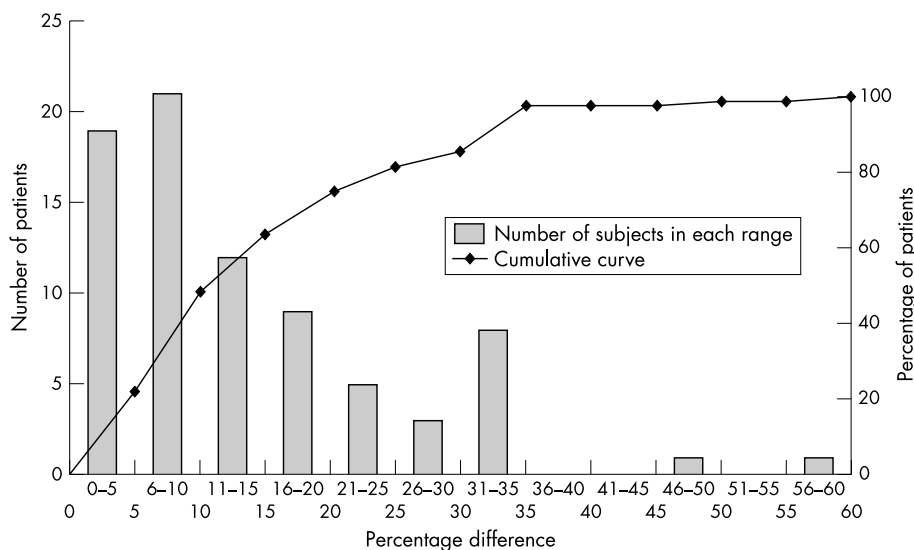


Figure 2 The columns represent the interocular percentage difference distribution in 5% intervals of the ERG b-wave amplitude responses for the light adapted 30 Hz flicker stimulus. The line demonstrates the cumulative curve for this stimulus in 5% difference increment steps.

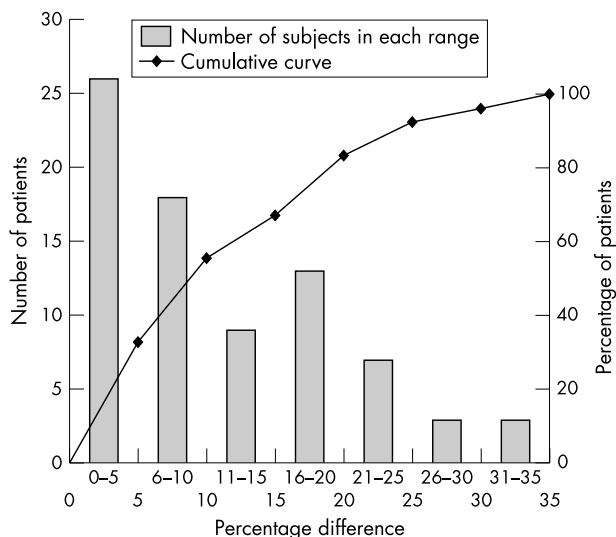


Figure 3 The columns represent the interocular percentage difference distribution in 5% intervals of the ERG b-wave amplitude responses for the scotopic isolated rod stimulus. The line demonstrates the cumulative curve for this stimulus in 5% difference increment steps.

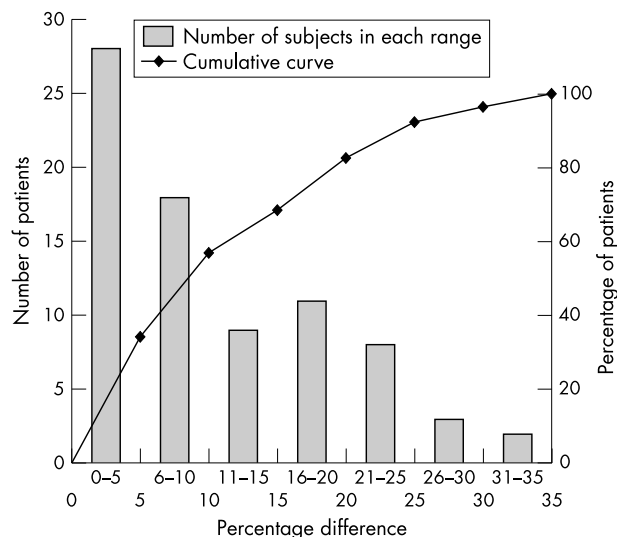


Figure 4 The columns represent the interocular percentage difference distribution in 5% intervals of the ERG b-wave amplitude responses for the scotopic maximal stimulus. The line demonstrates the cumulative curve for this stimulus in 5% difference increment steps.

population at various levels of interocular percentage difference.

DISCUSSION

The determination of interocular difference in ERG b-wave amplitude responses in visually normal subjects has provided useful information for comparison with the retinal function of patients with different asymmetric retinal diseases.⁴⁻⁹ The aim of this study was to establish the degree of the interocular percentage difference in subjects with, at most, mild retinal changes using the ISCEV¹ recommendations for various stimulus conditions. In our study, interocular percentage differences are presented as percentiles (25th, 50th, 75th, 95th), medians, and means (SD). Among our 79 subjects, the median interocular percentage differences of the ERG b-wave amplitude responses in the five different stimuli were similar. Fifty per cent of our cohort subjects had an interocular percentage difference of from 8% to 11% for different stimuli, which is consistent with an interocular amplitude difference of within 10%, previously cited by

Fishman *et al.*³ Ninety five per cent of our cohort had interocular percentage differences in the five stimuli that ranged from 27–36% or less. The average interocular percentage difference ranged from 11–14% for the five different stimuli (Table 1).

For comparison, we calculated the interocular percentage differences in ERG b-wave amplitude from the 22 normal individuals in studies by Jacobson *et al.*^{4,5} (Table 3). We found that the interocular percentage differences in the same normal population reported in these studies were, overall, comparatively smaller than in our subjects (compare Tables 1 and 3). Fifty per cent of their cohort had interocular percentage differences that ranged from 4–8% or less while 95% had a range of 12–16% or less for different stimuli. The mean interocular percentage difference ranged from 5% to 8%.

In our study, we also chose arbitrary levels of percentage interocular b-wave amplitude differences (10%, 20%, and 30%) to compare among different stimuli (Table 2). For the different stimulus responses, generally over 90% of our

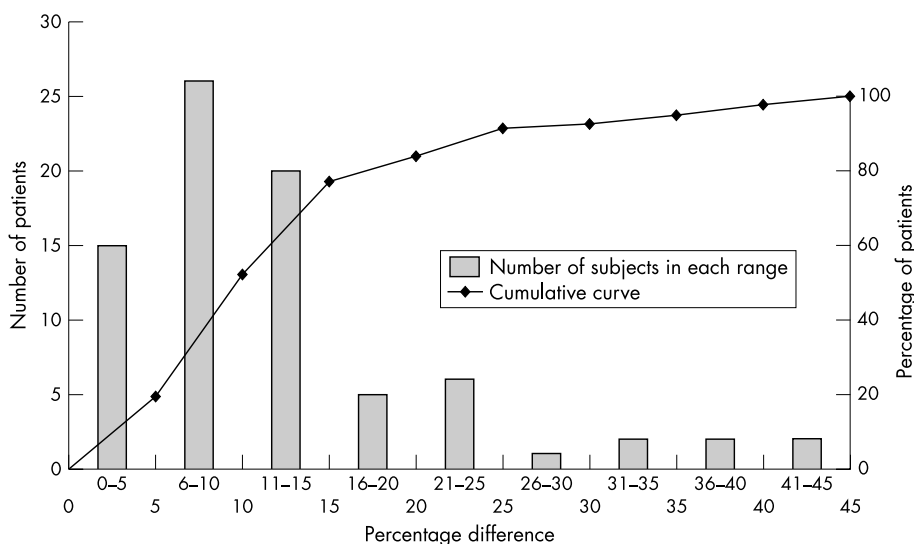


Figure 5 The columns represent the interocular percentage difference distribution in 5% intervals of the ERG b-wave amplitude responses for the dark adapted 30 Hz flicker stimulus. The line demonstrates the cumulative curve for this stimulus in 5% difference increment steps.

Table 3 Data from Jacobson *et al*⁵ analysed for interocular percentage difference

	Photopic		Scotopic	
	Single flash (%)	30 Hz flicker (%)	Isolated (blue) (%)	Maximal white (%)
Mean (SD)	7 (6)	7 (4)	5 (4)	8 (9)
Range	1–25	1–15	1–15	1–33
Percentile*				
25th	≤3	≤4	≤2	≤3
50th†	≤5	≤8	≤4	≤6
75th	≤8	≤10	≤7	≤9
95th	≤16	≤13	≤12	≤16

*A percentile represents the maximal interocular percentage difference in the percentile of the population.
 †The 50th percentile represents the median.

population had a 30% or less interocular difference. Our findings are consistent with a previous citation indicating that a normal interocular b-wave amplitude difference should be no greater than 20–24%.³ Figures 1–5 show the quantification of our population at various continuous levels of interocular percentage differences.

In a study of 95 healthy individuals, Ayres *et al*² showed that the difference between the two eyes of the same subject was smaller than the difference between the eyes of different subjects. They demonstrated that the maximal interocular difference in the ERG b-wave amplitude for the maximal scotopic response was 144.58 μ V, which was 29% of their maximal intersubject b-wave amplitude range. For comparison, in our study these values were 163.38 μ V and 31%, respectively.

Various technical factors, such as contact lens placement, the structural integrity of the corneal surface, pupil size, among others, may impact on the interocular difference in ERG amplitudes. Regardless of the explanation, our findings can be applied in the design of future therapeutic trials,

which implement monocular therapeutic strategies for various retinal diseases, and define more accurate criteria for the detection of asymmetric retinal disease.

Authors' affiliations

Y Rotenstreich, G A Fishman, Department of Ophthalmology and Visual Science, University of Illinois at Chicago, Chicago, IL, USA

R J Anderson, Division of Epidemiology and Biostatistics, University of Illinois at Chicago, Chicago, IL, USA

D G Birch, Retina Foundation of the Southwest, Dallas, TX, USA

Correspondence to: Professor Gerald A Fishman, 1855 W Taylor Chicago, IL 60612, USA; gerafish@uic.edu

Accepted for publication 21 January 2003

REFERENCES

- 1 **Marmor MF**, Zrenner E. Standard for clinical electroretinography (1999 update). International Society for Clinical Electrophysiology of Vision. *Doc Ophthalmol* 1998;99;97:143–56.
- 2 **Ayres LM**, Caruso RC, Lopez P, *et al*. Diagnostic significance of interocular differences in Ganzfeld electroretinogram (ERG) amplitude. *Invest Ophthalmol Vis Sci* 1998;39:B235, S972.
- 3 **Fishman GA**, Birch DG, Holder GE, *et al*. *Electrophysiologic testing in disorders of the retina, optic nerve, and visual pathway*. 2nd ed. San Francisco: The Foundation of the American Academy of Ophthalmology, 2001:10–11.
- 4 **Jacobson SG**, Morales DS, Sun XK, *et al*. Pattern of retinal dysfunction in acute zonal occult outer retinopathy. *Ophthalmology* 1995;102:1187–98.
- 5 **Jacobson SG**, Yagasaki K, Feuer WJ, *et al*. Interocular asymmetry of visual function in heterozygotes of X-linked retinitis pigmentosa. *Exp Eye Res* 1989;48:679–91.
- 6 **Schechner R**, Miller B, Merksamer E, *et al*. Long term follow up of ocular siderosis: quantitative assessment of the electroretinogram. *Doc Ophthalmol* 1991;76:231–40.
- 7 **Fishman GA**, Birch DG, Holder GE, *et al*. *Electrophysiologic testing in disorders of the retina, optic nerve, and visual pathway*. 2nd ed. San Francisco: The Foundation of the American Academy of Ophthalmology, 2001:115–16.
- 8 **Fishman GA**, Weinberg AB, McMahon TT. X-linked recessive retinitis pigmentosa. Clinical characteristics of carriers. *Arch Ophthalmol* 1986;104:1329–35.
- 9 **Berson EL**, Rosen JB, Simonoff EA. Electroretinographic testing as an aid in detection of carriers of X-chromosome-linked retinitis pigmentosa. *Am J Ophthalmol* 1979;87:460–8.



Interocular amplitude differences of the full field electroretinogram in normal subjects

Y Rotenstreich, G A Fishman, R J Anderson, et al.

Br J Ophthalmol 2003 87: 1268-1271

doi: 10.1136/bjo.87.10.1268

Updated information and services can be found at:

<http://bjo.bmj.com/content/87/10/1268.full.html>

These include:

References

This article cites 7 articles, 1 of which can be accessed free at:

<http://bjo.bmj.com/content/87/10/1268.full.html#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

[Retina](#) (1217 articles)

[Epidemiology](#) (766 articles)

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>