Normal Values of Standard Full Field Electroretinography in an Iranian Population

Mohammad-Mehdi Parvaresh, MD; Leila Ghiasian, MD
Khalil Ghasemi Falavarjani, MD; Mostafa Soltan Sanjari, MD; Nadia Sadighi, BSc

Rasoul-Akram Hospital, Iran Medical University, Tehran, Iran

Purpose: To determine normal values of standard full-field electroretinography (ERG) and to evaluate their variations with age in an Iranian population.
Methods: Through convenient sampling, 170 normal subjects 1-80 years of age were selected from residents of Tehran. ERG amplitudes and implicit time values were measured according to recommendations by the International Society for Clinical Electrophysiology of Vision. Evaluations consisted of light-adapted ERG including single-white flash and 30-Hz flicker response; and dark-adapted ERG including rod, maximal dark-adapted and cone responses.
Results: No significant difference in ERG values was observed between men and women, or between right and left eyes. ERG amplitudes were lower (P=0.04) and implicit time values were greater (P=0.03) in subjects 70-80 years of age as compared to younger individuals.
Conclusions: ERG parameters are significantly diminished with age. Our results may serve as a reference against which standard ERG responses can be compared.

Key words: Electroretinography; Iran

J Ophthalmic Vis Res 2009; 4 (2): 97-101.

Correspondence to: Khalil Ghasemi Falavarjani, MD. Assistant Professor of Ophthalmology; Eye Research Center, Rasoul-Akram Hospital, Sattarkhan Ave., Niayesh St., Tehran 1445613131, Iran; Tel: +98 912 1725850, Fax: +98 21 66558811; e-mail: drghasemi@yahoo.com

Received: June 15, 2008 **Accepted:** October 26, 2008

INTRODUCTION

Full field electroretinography (ERG) is a well established diagnostic procedure employed in the evaluation of retinal disorders. It determines the functional integrity of the retina, including rods and cones in the outer retina as well as associated pathways in the middle and inner layers of the retina.[1-3] A standard ERG includes five recordings; response to dim stimulation in dark adaptation (scotopic rod response), response to a bright stimulus in dark adaptation (scotopic combined rod-cone response), oscillatory potentials, response to a bright stimulus in light adaptation (photopic single-flash cone response), and response to a flickering stimulus in light adaptation (photopic 30-Hz flicker cone response). Significant changes in the amplitude or implicit time of each response may indicate a distinct retinal disorder.[1-4]

Since 1989, the International Society for Clinical Electrophysiology of Vision (ISCEV) and the National Retinitis Pigmentosa Foundation (NRPF) have attempted to standardize ERG procedures.[4-6] The methodology is updated on a regular basis in order to standardize ERG responses and make them universally comparable. This standard provides simple recommendations on technical procedures to

record reproducible ERGs under defined conditions in patients of all ages.[6] However, despite unifying the practice, normal ERG responses may be influenced by other factors such as race, age, sex, medications, media clarity and refraction.[6-12]

The ISCEV recommends that each laboratory establish normal values based on its own equipment and patients.[6] In this study, we measured ERG responses based on ISCEV standards in ophthalmologically normal Iranian subjects of different ages while attempting to eliminate avoidable confounding factors by using strict inclusion criteria.

METHODS

One hundred seventy Iranian residents of Tehran aged 1 to 80 years were enrolled for the purpose of the study. We used convenient sampling and selected the study subjects among hospital personnel, clients seeking spectacle prescriptions and patients' attendants. The study subjects were asymptomatic with normal best-corrected visual acuity, normal color vision, normal eye examination, clear media, and low or insignificant refractive errors (myopia less than -6.00 diopters). In preverbal children, fixation behavior, preferential looking and Allen chart were used instead of Snellen visual acuity measurement. In order to avoid the influence of lenticular nuclear sclerosis, only patients with apparently clear lens on dilated biomicroscopy were included. Individuals with optic nerve disease, neurological impairment, systemic diseases, or a family history of heritable retinal disorders were excluded. No subject was on long-term medications. All ERG measurements were performed at the Visual Electrophysiology Unit of Rasoul-Akram Hospital. The Institutional Review Board of the hospital approved the study and informed consent was obtained from study subjects.

Recording procedures adhered to a recommended international standard for clinical electrophysiological measurements.[6] Pupils were fully dilated using 1% tropicamide and 2.5% phenylephrine eye drops. Silver/nylon fiber electrodes (DTL, Laird Technologies, Sauquoit Inc. Scranton, USA) were used. The active electrode was placed over the middle third of the lower eyelid of each eye. ERG recording in children was performed following oral intake of chloral hydrate for sedation. ERG recordings were obtained on both eyes. The ISCEV-ERG GF program which is an integrated part of the system (Roland Consult, Electrophysiologic Diagnostic Systems, Wiesbaden, Germany) was used to record standard ERGs. Stimulation was performed using a full field flash Ganzfeld stimulator (Roland Consult). All responses were differentially amplified, displayed on an oscilloscope, digitized and stored on a compact disc. An adjustable voltage window was used to reject records contaminated by artifacts. Dark adapted ERG responses were obtained after a minimum of 30 minutes of dark adaptation and included an isolated rod, standard flash (maximal) response, and oscillatory potentials. Light adapted responses included a single white flash and 30-Hz flicker.

For each of the five stimuli, right and left eyes were individually tested and their data was processed separately. Thereafter, responses of both eyes for each stimulus were averaged to determine the individual subject's data. The subjects were divided into 8 age strata with 10-year intervals; within each age group, the median and range were calculated for each parameter. Average amplitudes and implicit times were analyzed using *t*-test and ANOVA.

RESULTS

Implicit times and amplitudes of ERG are stratified by gender and age groups in Tables 1 to 4. No significant difference was found between right and left eye measurements by gender and age. There was also no significant difference between male and female ERG amplitudes and implicit times within different age groups. However, amplitude values were significantly decreased and implicit time was significantly increased in both genders in the 70-80 year age group as compared to other age groups (P=0.04 and P=0.03 respectively).

Table 1 Median and 95% confidence interval for ERG amplitude (microvolt) in male subjects

Age (yr)	1-10		11-20		21-30		31-40		41-50		51-60		61-70		71-80	
Eye	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
a-wave rod response	72 42-95	69 45-92	74 48-92	75 46-97	73 41-92	71 43-89	76 48-96	74 41-89	72 39-94	74 42-96	77 38-88	72 38-91	73 37-99	71 41-89	65 34-82	66 36-84
b-wave rod response	159 85-270	157 98-280	168 102-290	167 105-308	166 105-310	164 95-320	135 82-50	132 81-262	128 85-292	131 81-305	145 85-301	142 87-265	143 92-251	144 89-249	125 71-225	128 69-235
a-wave max response	231 125-410	228 135-390	226 131-310	221 125-370	225 131-420	228 135-440	195 145-360	192 138-380	198 128-320	201 125-350	187 135-305	192 128-291	191 135-258	189 131-301	173 127-310	174 125-280
b-wave max response	380 275-520	382 285-530	390 305-610	385 295-630	405 315-790	402 305-810	390 295-710	398 305-740	408 295-590	410 285-610	412 305-591	415 301-605	398 298-450	402 282-585	375 295-510	378 285-521
OP_2	37 23-67	35 22-62	38 21-72	41 25-68	42 27-58	39 25-61	34 29-59	32 37-61	33 22-62	34 24-58	34 21-62	32 25-72	33 22-56	35 21-62	32 22-42	30 21-48
N_1-P_1	85 52-105	87 48-150	92 51-148	89 55-161	95 45-165	92 47-138	89 49-161	91 48-159	84 52-158	83 58-135	94 49-145	96 51-110	89 48-115	92 47-125	81 42-138	79 45-145
30-HZ flicker	95 51-201	97 58-195	105 62-210	103 57-198	112 51-205	110 54-215	107 48-217	109 51-205	99 47-201	98 49-182	102 51-175	101 48-201	95 48-165	98 47-175	85 45-151	83 48-161
a-wave cone response	37 22-75	38 21-69	36 25-85	35 22-87	38 25-79	37 31-67	34 29-71	34 28-75	33 21-82	34 24-65	30 25-75	31 23-73	31 25-69	31 27-79	29 21-49	30 23-51
b-wave cone response	157 88-240	160 87-225	161 89-285	162 81-245	148 89-251	149 95-245	158 85-225	157 87-231	156 91-245	155 92-251	161 87-215	162 89-225	153 75-215	152 71-210	140 55-195	138 58-192

ERG, electroretinogram; Max, maximum; OP, oscillatory potential; N_1-P_1, interval between first negative and positive waves.

Table 2 Median and 95% confidence interval for ERG amplitude (microvolt) in female subjects

Age (yr)	1-10		11-20		21-30		31-40		41-50		51-60		61-70		71-80	
Eye	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
a-wave rod response	70 40-97	71 42-93	72 47-94	74 46-97	70 41-100	73 40-97	75 45-97	73 41-92	71 38-95	73 39-96	71 37-91	72 39-95	74 38-92	73 41-96	67 32-92	65 31-96
b-wave rod response	157 85-281	159 92-275	166 102-295	168 97-310	165 97-312	163 98-322	141 85-272	144 87-305	132 89-292	134 91-310	141 87-298	138 85-265	141 91-278	143 89-257	127 71-251	125 69-261
a-wave max response	234 118-398	229 125-405	222 138-345	226 121-375	229 135-440	224 128-425	199 125-375	201 119-385	201 125-352	203 127-345	191 125-315	189 128-310	189 132-298	192 125-297	175 125-305	171 135-295
b-wave max response	375 225-531	380 275-525	392 302-625	387 295-625	407 295-791	401 295-810	395 285-712	397 275-745	407 285-610	409 280-625	415 275-615	410 295-595	395 285-550	399 282-610	374 285-525	387 275-521
OP2	36 21-65	37 22-67	39 24-72	39 25-68	42 21-67	41 24-71	35 23-69	32 21-71	32 23-68	33 21-69	33 22-59	34 23-63	31 21-58	33 22-56	34 21-45	32 21-46
N1-p1	87 52-110	86 48-158	94 48-165	91 47-159	93 51-165	90 46-162	88 48-148	91 51-161	83 55-149	84 48-158	93 47-161	98 48-175	90 51-158	91 52-161	83 41-148	79 45-145
30-HZ flicker	94 48-210	97 52-197	104 51-211	105 49-215	114 47-195	110 52-215	106 54-225	110 47-201	97 49-98	99 47-211	103 52-217	100 47-175	98 48-185	95 49-165	84 44-165	85 45-171
a-wave cone response	36 21-78	38 22-69	37 24-87	36 22-91	36 24-82	35 32-65	33 29-78	34 26-78	34 22-85	33 23-66	29 22-74	30 22-75	31 24-71	31 24-79	28 21-52	31 21-49
b-wave cone response	156 85-245	159 84-239	162 84-262	161 85-252	149 79-251	151 86-245	156 87-235	158 85-241	157 251-79	158 89-242	160 91-258	162 85-245	155 87-235	151 78-215	138 58-198	139 56-197

ERG, electroretinogram; Max, maximum; OP, oscillatory potential; N_1-P_1, interval between first negative and positive waves.

Table 3 Median and 95% confidence interval for ERG implicit time (milliseconds) in male subjects

Age (yr)	1-10		11-20		21-30		31-40		41-50		51-60		61-70		71-80	
Eye	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
a-wave rod response	39 29-63	40 28-65	43 31-62	42 28-61	38 29-66	37 27-64	42 27-64	44 29-71	43 31-68	42 32-71	41 31-68	44 29-66	42 30-69	41 31-68	46 28-72	47 32-71
b-wave rod response	86 68-98	88 59-105	79 72-99	81 69-98	83 71-102	82 72-98	88 69-96	86 68-97	92 70-98	95 72-102	88 68-98	96 72-105	89 71-101	92 72-99	99 75-105	99 78-108
a-wave max response	19 15-25	20 14-24	16 13-33	18 14-25	20 15-24	21 15-26	22 14-24	21 14-25	24 15-26	23 14-25	22 15-24	21 15-24	24 14-26	23 18-26	25 20-28	25 20-27
b-wave max response	41 32-45	43 33-46	39 34-43	41 33-48	42 32-49	41 34-49	45 32-51	42 32-49	44 33-51	43 32-51	42 34-50	43 33-48	44 34-51	42 35-51	48 36-54	49 37-54
OP N_2	13 12-16	14 12-16	14 12-15	15 13-17	14 12-16	13 12-15	15 13-16	14 12-16	16 13-18	15 13-17	15 13-16	15 13-17	16 14-18	15 13-17	17 14-19	18 15-20
OP P_2	31 28-32	30 28-32	29 28-31	31 29-32	28 27-31	30 28-31	29 28-32	30 29-32	31 29-33	32 30-33	30 28-32	29 27-32	30 29-32	31 29-33	32 30-34	32 30-35
a-wave cone response	15 13-16	14 13-16	14 13-16	15 13-17	15 12-17	16 13-17	15 13-17	16 14-18	15 13-16	14 13-17	15 13-17	15 14-17	15 13-17	16 14-18	16 14-18	17 14-19
b-wave cone response	30 28-32	31 28-33	31 29-32	30 28-31	32 30-33	31 29-32	32 30-33	31 28-32	31 28-32	30 28-31	31 29-32	31 29-33	31 28-32	28 23-30	32 28-33	32 29-33
30-HZ N_1	14 12-15	13 12-16	13 12-16	12 11-15	13 12-14	14 12-15	13 12-15	14 12-16	14 13-16	14 12-16	13 12-16	14 13-16	14 13-16	14 13-16	15 13-17	14 13-17
30-HZ P_1	26 23-28	26 23-29	26 25-29	26 24-29	27 24-31	25 23-29	26 23-30	26 24-29	27 24-31	27 25-31	26 24-29	27 25-31	26 24-29	30 24-36	27 25-32	28 25-32

ERG, electroretinogram; Max, maximum; N_1, first negative wave; P_1, first positive wave; OP N_2, oscillatory potential-second negative wave; OP P_2, oscillatory potential-second positive wave.

Table 4 Median and 95% confidence interval for ERG implicit time (milliseconds) in female subjects

Age (yr)	1-10		11-20		21-30		31-40		41-50		51-60		61-70		71-80	
Eye	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
a-wave rod response	40	39	42	42	21	21	21	20	44	43	41	43	42	41	47	46
	30-65	28-64	28-62	28-65	15-24	16-25	15-26	14-25	28-64	29-71	28-69	28-66	31-65	31-62	30-69	31-72
b-wave rod response	86	87	80	79	83	83	87	86	92	95	97	97	90	91	98	98
	68-97	67-105	71-98	69-97	72-103	71-99	69-97	70-99	72-103	67-98	72-106	71-99	72-99	78-105	75-106	76-108
a-wave max response	20	20	17	18	21	21	20	23	24	24	21	21	24	24	25	25
	15-24	16-26	14-20	14-22	16-25	15-26	14-25	16-25	14-27	14-27	17-24	15-25	14-26	16-26	19-29	20-28
b-wave max response	42	43	39	41	41	42	45	43	44	44	43	42	43	43	48	48
	32-46	25-47	34-45	33-45	34-48	33-49	32-48	34-51	35-51	34-50	36-48	33-49	34-51	35-53	37-55	36-54
OP N_2	14	14	13	14	15	14	14	15	13	15	16	15	16	15	16	18
	12-17	12-16	12-16	12-17	13-18	12-16	12-16	14-17	12-15	13-18	13-17	14-16	13-17	13-16	15-19	15-20
OP P_2	30	30	29	31	29	30	29	29	31	31	31	32	30	29	32	32
	8-33	28-32	28-32	27-33	28-32	29-31	28-31	28-33	28-32	28-33	29-33	09-33	29-32	28-32	29-34	30-34
a-wave cone response	14	14	14	15	15	14	15	15	16	15	14	14	14	15	17	17
	13-17	12-16	13-18	14-17	14-16	13-17	13-18	14-18	14-18	13-18	13-16	13-17	13-16	13-18	14-19	14-18
b-wave cone response	30	30	30	31	31	32	32	31	31	30	31	30	32	31	33	32
	28-31	24-33	28-33	28-33	29-33	29-34	29-33	29-32	28-32	28-32	29-33	29-33	30-34	29-33	30-34	30-33
30-HZ N_1	14	14	13	13	13	13	14	13	14	14	13	13	14	13	15	15
	12-17	12-16	12-16	11-15	12-14	12-15	12-15	12-15	13-15	12-16	12-16	12-16	12-15	13-17	13-17	12-17
30-HZ P_1	25	25	26	26	29	26	25	26	26	27	26	26	27	26	28	27
	23-28	23-29	24-29	24-28	27-32	23-28	24-30	25-29	25-31	24-30	24-29	24-29	24-30	25-30	25-32	25-32

ERG, electroretinogram; Max, maximum; N_1, first negative wave; P_1, first positive wave; OP N_2, oscillatory potential-second negative wave; OP P_2, oscillatory potential-second positive wave.

DISCUSSION

This study provides normal ranges for ERG responses in different age groups in an Iranian population. All procedures were performed as recommended by the International Standardization Committee.[6] Our study size (170 individuals) was much larger than certain studies reporting normal ERG values.[13] ERG measurements obtained herein show a difference of 5-15% in amplitude and 15-20% in implicit time in comparison to ISCEV reported normal values.[13] Since we eliminated confounding factors affecting ERG amplitude and implicit time such as refractive errors, intraocular pressure, media clarity, systemic medications and retinal diseases,[6-11] the ethnicity of studied subjects may account for the observed difference.

We paid particular attention to age as a variable reported to be associated with a decrease in full-field ERG responses.[11,12] The reason for decrease in ERG amplitude in the elderly is not well understood. Although our study subjects were clinically normal, subclinical pathologic conditions cannot be ruled out. Factors such as subtle preretinal media changes or reduction in photopigment optical density[11], and bipolar or Muller cell death in the ageing retina could be the reason for the decline in amplitude with increasing age.[14]

A statistically significant effect of gender on ERG recordings has been reported[8,11] but, we did not observe any difference between male and female subjects in our study. Many technical factors such as electrode placement, integrity of the ocular surface and pupil size may affect interocular difference in ERG amplitudes, however, in our series no significant difference was found between right and left eyes. Our results support the findings of Rotenstreich et al[15] who found small interocular differences in ERG b-wave amplitudes for five different stimulus responses.

Specific amplitude and implicit time values for ERG will probably differ among different laboratories due to minor variations in recording electrodes, equipment and protocol.[6] Nevertheless, the present data were obtained under rigidly controlled conditions and can be used as a basis for comparison in our country.

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