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Detection of Ophthalmic Impairments Indirectly with Electronystagmography

Gary P. Jacobson*
Devin L. McCaslin*

Abstract

The objective was to develop, from a pool of clinical electronystagmography (ENG) data, normal lower limits for the corneo-retinal potential (CRP). The CRP evaluated in the present study was derived as a byproduct of eye movement calibration with a computerized ENG system. The data set was collected from a cohort of patients without history of ophthalmic disease. This normative study was designed to develop upper and lower limits for the CRP recorded indirectly from ENG testing. Subjects were 107 consecutive patients (41 males, mean age 57 years). Subject age did not, but gender did affect significant changes in the CRP. Specifically women showed larger CRP values than men. Case studies are presented that support the contention that the dark-adapted CRP may be helpful in the identification of patients with ophthalmic diseases known to affect the CRP and, thus, augment information normally obtained in the course of the ENG examination.

Key Words: Electronystagmography, ophthalmic impairment

Abbreviations: CRP = corneo-retinal potential, EOG = electro-oculography, ENG = electronystagmography

Sumario

El objetivo fue desarrollar los límites normales inferiores del potencial córneo-retiniano (CRP), a partir de un agregado de datos de electronistagmografía clínica (ENG). El CRP evaluado en el presente estudio fue derivado como un sub-producto de la calibración del movimiento ocular con un sistema de ENG computarizado. La información fue recogida de una cohorte de pacientes sin historia de enfermedad oftálmica. Este estudio normativo fue diseñado para desarrollar los límites superiores e inferiores del CRP registrado indirectamente a partir de una evaluación por ENG. Los sujetos fueron 107 pacientes consecutivos (41 hombres con edad media de 57 años). El género pero no la edad afectó significativamente los cambios en el CRP. Las mujeres, específicamente, mostraron valores mayores de CRP que los hombres. Se presentan estudios de caso que apoyan la noción de que los CRP adaptados a la oscuridad fueron útiles en la identificación de pacientes con enfermedades oftálmicas afectan el CRP, y, por lo tanto, aumentando así la información normalmente obtenida en el curso de un examen ENG.

Palabras Clave: Electronistagmografía, trastorno oftálmico

Abreviaturas: CRP = potencial córneo-retiniano; EOG = electro-oculografía; ENG = electronistagmografía

*Division of Audiology, Vanderbilt University, Nashville, Tennessee

Reprint requests: Gary P. Jacobson, Ph.D., Director, Division of Audiology, Vanderbilt Clinic and Vanderbilt Balance and Hearing Center, 1500 21st Avenue South, Suite 2600, Nashville, TN 37212-3102; Phone: 615-322-4568; Fax: 615-343-0872; E-mail: gary.jacobson@vanderbilt.edu

The electronystagmography (ENG) test has become ubiquitous in audiology practices. Balance function testing has been included in the scope of practice statement of both the American Academy of Audiology and the American Speech-Language and Hearing Association. Vestibular system anatomy and physiology and ENG have been incorporated into Doctor of Audiology (Au.D.) training programs. The ENG examination consists of a series of subtests designed to assess the integrity of ocular motility subsystems (e.g., pursuit, gaze, and optokinetic subsystem tests) and the vestibular system (e.g., positional and caloric tests). Normal ocular motility is dependent on intact vision, which usually is not evaluated in the course of the ENG test. The electrical transducer of the visual system is the retina, which also serves as the source of the corneo-retinal potential (CRP). The CRP is a bioelectrical signal that is measured during electro-oculography (EOG), the recording technique used in ENG. The CRP has a dipolar orientation like a "battery" with the cornea being positively polarized and the retina negatively polarized. This standing potential is propagated through the eye by volume conduction where it is capable of being recorded with conventional surface electrodes. Contemporary ENG systems utilize computerization to digitize and then analyze voltage changes in the CRP generated by specific eye movements. Normative data for eye movement test results have been incorporated into many of the ENG software programs; however, little attention has been given to the actual voltage of the CRP on which these analyses are based.

The origin of the CRP is metabolic activity in the retina and primarily in the retinal pigment epithelium (RPE). This standing potential (i.e., the CRP) is generated by the transepithelial potential across the RPE (Marmor and Zrenner, 1993; Carl, 1997). The pigment epithelial cells located in the retina are spaced closely together, thereby allowing the RPE to maintain the positive and negative charges. When measured at the cornea, the strength of this potential may range from one to several millivolts (Marmor and Zrenner, 1993; Carl, 1997). In ophthalmology, the integrity of the RPE is assessed by recording the standing potential that exists between the cornea and the posterior pole of the eye. The EOG, which reflects RPE function, is the "gold standard" for evaluating vitelliform macular dystrophy (e.g., Best's disease). Since metabolic activity in the retina is affected by light, it is not surprising that the CRP varies across levels of illumination. In fact, when the potential is measured in an individual who has been light-adapted, there is a two-fold increase compared to the dark-adapted measurement. Dark-adapting a patient by placing them in a darkened room reduces metabolic activity in the RPE, thereby decreasing the CRP potential to its lowest magnitude. It is intuitive that retinal disease would also decrease the magnitude of the CRP due to the fact there are fewer functioning pigment epithelial cells to maintain the standing potential.

Contemporary ENG systems utilize automated eye movement calibration routines to ensure that one degree of eye deviation results in the equivalent of a 1 mm "pen" deflection. These automated calibration routines yield a gain value that can be used to approximate the number of microvolts of CRP associated with one degree of eye deviation. It was our empirical observation that occasionally (i.e., less than 10% of the time) patients were encountered in the clinic that demonstrated very "noisy" calibration traces. When the calibration values were obtained, it was clear that the "noisiness" occurred as a result of the recording system increasing its gain to a maximum to compensate for a very small CRP. These tracings appeared to represent the noise floor of the recording system superimposed on the eye movement tracing.

If this was true, then the magnitude of the CRP measured indirectly using EOG recording techniques might prove useful in the identification of ophthalmic diseases above and beyond that identified during ocular motility testing. If there was a relationship between eye function and the magnitude of the CRP measured during ENG calibration, then information above and beyond ocular motility and vestibular function could be derived from the ENG examination. A first step was to determine whether age and gender affected systematically the dark-adapted CRP measured using conventional electrode placements and instrumentation settings for ENG. Based on these findings, we sought to define the normal characteristics (i.e., normal lower limit) of the dark-adapted CRP.

MATERIALS AND METHODS

Subjects were 107 consecutive patients (41 male, mean age = 57 years ± 17 years) evaluated at the Henry Ford Hospital Balance Function Laboratory. The mean age of the group of males was 59.58 years (sd 18.98) and 55.57 (sd 16.23) for females (N = 66). None of these patients had a history of ophthalmic disease other than corrected or uncorrected refractive impairments. This was confirmed by a thorough search of the patient's medical record as well as through patient report. Each patient underwent a routine ENG examination consisting of subtests designed to assess ocular motility (i.e., assessments of gaze, saccade, pursuit, and optokinetic subsystem function) and vestibular system function (i.e., assessments of spontaneous nystagmus, positional and positioning nystagmus, and bithermal caloric testing).

Disposable silver/silver chloride surface electrodes were placed bitemporally at the outer canthus of each eye (i.e., to record horizontal versional eye movements), and then above and below the left eye (i.e., to record vertical versional eye movements). We chose bitemporal over monocular recordings to increase the generalizability of the data since bitemporal electrode placements are used commonly in clinical testing of dizzy patients. Electrode impedances were all less than 5000 ohm and interelectrode impedances were less than 3000 ohm. The electrical activity recorded during calibration at these inputs was digitized (120 Hz) and low-pass filtered DC-30 Hz. CRP measures were obtained after the patients had been dark-adapted for 10 minutes in the examination room. The level of illumination recorded at the patient's head with a light meter (Extech Inst. Corp, Waltham, MA, Model 401027) was 0.2 fc. Subjects were four feet from the visual target. All recordings were conducted using an ICS CHARTR computerized ENG system (ICS Medical, Schaumburg, IL). Although the international standard suggests that both light- and dark-adapted measures be obtained, it was our feeling that impairment of retinal function would be most apparent when the retinal potential was weakest. Additionally, Marmor and Zrenner state that "it is important to measure the standing potential amplitude in microvolts at the bottom of the dark trough … since low values may have clinical significance" (1993, p.6). Finally, we wanted to use data that were available during conventional ENG recordings.

As part of the calibration procedure, patients were asked to pursue a sinusoidal target that moved a total of 30 degrees (i.e., 15 degrees to the left and right of center). The ICS CHARTR system supplies sufficient amplification for the EOG signal so that one degree of eye deviation can be made equivalent to 1 mm deflection on the paper record. A byproduct of the calibration procedure is an estimate of the CRP (i.e., a derived value representing the number of microvolts of the CRP associated with each degree of eye excursion). We chose to obtain estimates of the CRP from horizontal as opposed to vertical calibration values.

Values were tabulated for this sample of 107 subjects. These data were then evaluated in an attempt to determine whether age and gender systematically affected the dark-adapted CRP, and to determine the lower limits of the magnitude of the CRP.

RESULTS

The CRP grouped across AGE and GENDER was 16.4 μV (sd 5.24 μV) per degree of eye deviation. These data were analyzed with an analysis of variance with CRP serving as the dependent measure, and patient AGE (i.e., "young" = <60 years vs. "old" = ≥60 years) and GENDER (i.e., male v. female)

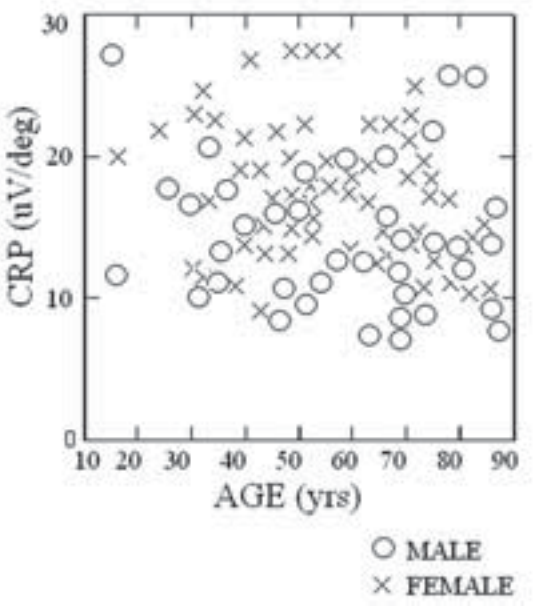


Figure 1. Scatterplot of the data set for this investigation. Shown are corneo-retinal potential values plotted against patient age.

Table 1. Percentile Values Associated with CRP Values Corresponding to One Degree Eye Deviations from Midline

Gender	1st	5th	10th	15th	20th	50th	80th	85th	90th	95th	99th
Male	7.1	8.2	9.2	9.5	10.4	13.8	17.3	19.1	19.9	21.8	25.8
Female	9.0	10.8	11.4	13.0	13.2	17.2	21.7	22.2	24.5	27.3	28.2

serving as grouping factors. Results of these analyses demonstrated that although subject AGE did not affect systematic changes in the CRP ($p = 0.23$), subject GENDER did affect significant differences in the magnitude of the CRP ($F = 253.66 = 3.71$, $df = 1$, $p = 0.001$). A scatterplot of corneo-retinal potential values plotted as a function of age is shown in Figure 1. Females demonstrated significantly larger amplitude dark-adapted CRPs than did males. The mean CRP was 17.5 (sd 4.55 μV) per degree of eye deviation for females and 14.1 (sd 4.54 μV) per degree of eye deviation for males.

The data set was analyzed by gender separately in an attempt to define percentiles that might be used clinically to define potentially normal and abnormal CRP values. The 1st through 99th percentile values associated with the CRP for males and females are shown in Table 1.

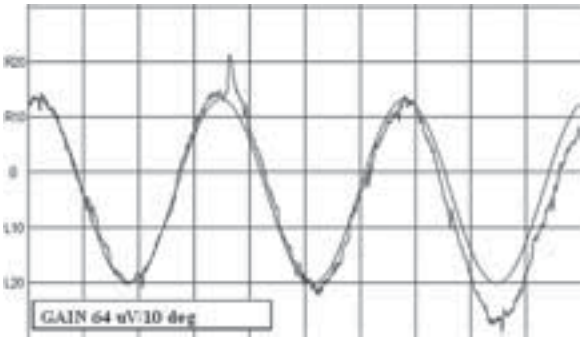
The following are two case studies that illustrate the potential usefulness of this data for the detection of ophthalmic disease.

Case 1

Case 1 is a 69-year-old male patient who was evaluated for dizziness and unsteadiness. The calibration trace for this patient is shown next to that of a normal patient in Figures 2a and 2b. Notice that there is inherent "fuzziness" or "noisiness" in the calibration tracing of this patient. This noise is occurring because the patient's CRP is so small (6.4 μV/degree of eye deviation) that the amplifier has been deattenuated so that we are viewing the noise floor of the recording system superimposed on the eye position tracing. This CRP value was below the 1st percentile value that was derived from the normative data pool. The inherent noisiness of this tracing interfered with automated identification of nystagmus slow phase during caloric testing. This patient was found to have diabetic retinopathy.

Case 2

Case 2 is an 80-year-old female who was evaluated for episodic dizziness. The calibration tracing for this patient is shown in Figure 3a. Again, the calibration tracing shows the same noise artifact shown in Figure 2a. In this case, the patient's CRP was 5.3 μV per degree of eye deviation that is reduced beyond the 1st percentile derived from the



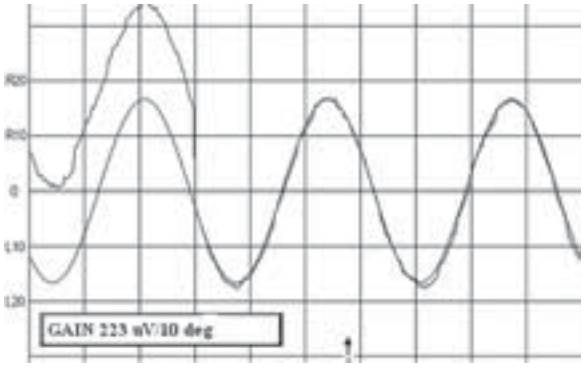


Figure 2. (a) Horizontal (i.e., bitemporal electrode derivation) calibration tracing obtained from 69-year-old male with diabetic retinopathy. Notice the noise superimposed on the eye movement recording. This patient's calibration values fell below the 1st percentile for a cohort of men. (b) Shows a horizontal calibration tracing obtained from a normal patient.

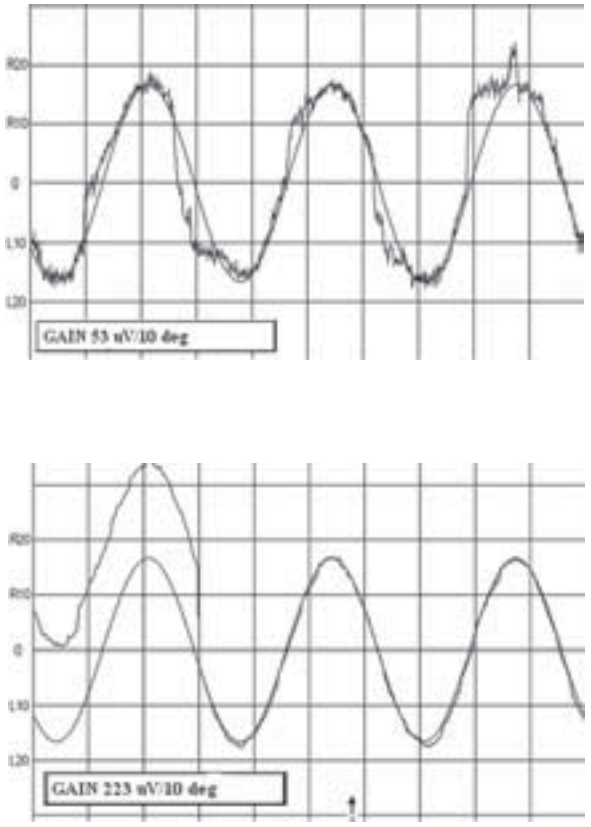


Figure 3. (a) Horizontal (i.e., bitemporal electrode derivation) calibration tracing obtained from an 80-year-old female patient with advanced glaucoma and hypertensive retinopathy. Notice the noise superimposed on the eye movement recording. This patient's calibration values fell below the 1st percentile for a cohort of men. (b) Shows a horizontal calibration tracing obtained from the same normal patient as in Figure 2b.

normative data set for women. This patient has a diagnosis of advanced glaucoma with hypertensive retinopathy.

DISCUSSION

The objective of the present investigation was to develop, from a pool of clinical electronystagmography (ENG) data, normal lower limits for the corneo-retinal potential (CRP). The CRP evaluated in the present study was derived as a byproduct of eye movement calibration with a computerized ENG system. The data set was collected from a cohort of patients without history of ophthalmic disease. This normative study was designed to develop lower limits for the CRP recorded indirectly from ENG testing. The results of this investigation have suggested that while subject age did not, subject gender did affect significant differences in the CRP magnitude. Women generated significantly larger dark-adapted CRP values than men. A finding similar to this has been reported previously (Krogh, 1976, 1977). However, the investigator did not speculate as to the physiological origin of these gender differences, and we as well could not find any reasonable explanation for these findings. Additionally, in the same investigations Krogh (1976, 1977) reported a positive correlation between subject age and the dark-adapted CRP. We expected to see an age-related effect in the CRP; however, none was observed. It may be that the current data set, although representative of the ages of patients seen in our balance clinic, were not of a sufficiently broad range to show the age effects reported previously by Krogh (1976, 1977).

As a result of these analyses, gender-specific normative lower limits were established for the dark-adapted CRP that we have used clinically for the detection of patients who may be at risk for ophthalmic disease. It is worth noting that age-related macular degeneration is the most common cause of blindness in the developed world (Silvestri, 1997). Our experience, thus far, suggests that when extreme low CRP values are encountered they are inevitably associated with retinal disease. In the context of our Risk of Falls Assessment Clinic, the identification of occult retinal disease (e.g., retinal degeneration, diabetic retinopathy) is helpful in explaining one source of multisensory deficit unsteadiness. The impairments caused by these diseases can reduce, among other things, visual acuity and contrast sensitivity. Additionally, there is no additional cost associated with the acquisition of this data. The data is a byproduct of calibration activities conducted in the normal course of ENG testing.

The two case studies illustrate the potential usefulness of the indirect estimation of the CRP with EOG techniques. Situations where the CRP is abnormally low (i.e., where electrode recordings are "noisy") are ideally suited to the use of infrared videonystagmography as this technique does not require a CRP. For example, central and peripheral disorders that manifest themselves through subtle changes in the recorded eye movement

(i.e., saccadic pursuit) may be missed by the examiner if the gain of the amplifier is increased to a level where the noise floor is interfering with the tracing.

There are significant limitations for the present investigation. It must be acknowledged that this is a far-field recording of eye function. There are more direct methods of evaluating the electrophysiology of the retina. These techniques include electroretinography (ERG). It is our suggestion that data derived from EOG recordings might act as a screening technique for patients who would benefit from ERG. Additionally, our recordings were made with one of many commercially manufactured computerized ENG systems. However, we have obtained analogous calibration values from our rotary chair system (Neurokinetic Model 1010). Clinicians should be cautioned to obtain their own pool of normative data for systems other than the ICS CHARTR system. Finally, it must be stated that we are using estimates of the CRP to help *detect*, not diagnose, significant ophthalmic disease.

CONCLUSIONS

The CRP exists as a function of metabolic activity in the retina and primarily in the retinal pigment epithelium. It follows that ophthalmic disease, and retinal disease in particular, might be reflected in the magnitude of the CRP. The results of the present investigation have suggested that values of the dark-adapted CRP were significantly larger for women, and no age-related decrement in CRP was observed. CRP normal lower limits were derived from this cohort, and preliminary evidence suggests that these lower limits may be used for the detection of patients who may be considered "at risk" for ophthalmic disease. Future studies will be conducted to determine the diagnostic efficiency of CRP amplitude for the identification of patients with ophthalmic disease. Specifically, we intend to record the ratio of the CRP following light adaptation and dark adaptation during the administration of each ENG. This measurement allows an Arden ratio to be calculated and will afford us the ability to further determine the relationship between ophthalmic disease and abnormally low CRP measures.

REFERENCES

Arden GP, Kelsey JH. (1962) Changes produced by light in the standing potential of the human eye. *J Physiol* 161:189–204.

Carl JR. (1997) Principles and techniques of electrooculography. In: Jacobson GP, Newman CW, Kartush JM, eds. *Handbook of Balance Function Testing.* San Diego: Singular Publishing Group, 69–82.

Krogh E. (1976) Normal values in clinical electrooculography. II. Analysis of potential and time parameters and their relation to other variables. *Acta Ophthalmol* 54:389–400.

Krogh E. (1977) Normal values in clinical electrooculography. IV. Analysis of two dimensionless EOG parameters and their relation to other variables. *Acta Ophthalmol* 55:739–749.

Marmor MF, Zrenner E. (1993) Standard for clinical electro-oculography. International Society for Clinical Electrophysiology of Vision. *Arch Ophthalmol* 111:601–604.

Silvestri G. (1997) Age-related macular degeneration: genetics and implications for detection and treatment. *Mol Med Today* 3:84–91.

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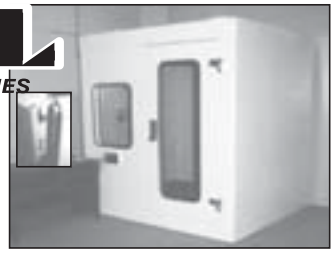

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