The obvious and the more hidden components of the electroretinogram

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SUMMARY

If recorded in a precise and meticulous way the a-and b-waves of the ERG are very obvious deviations from the baseline, the standing potential of the eye. The c-wave, the oscillary potentials, the d- and the i-wave, and not to mention the photopic negative response, are considered more of the hidden ERG components in this publication. Elucidating these responses can be challenging but surely very exiting.

Keywords: ERG, electroretinography, dog, retina, retinal function

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Introduction

Electroretinography (ERG) has proven to be an objective and a useful tool to assess retinal function in animals. The technique is most commonly used for a pre-operative evaluation of retinal function in association with cataract surgery. It is also used for diagnostics in association with various forms of retinal degenerations such as progressive retinal atrophies (PRA), sudden acquired retinal degenerations (SARD) and toxic retinal degenerations. In recent years ERGs have been invaluable in assessing the effect of treatment trials for retinal degenerative disease, such as gene therapy, stem cell therapy and subretinal implants [1, 2]. It is important to keep in mind the possibility of recording a perfectly normal ERG from a completely blind patient and that the only information obtained by the ERG is whether the retina is functional or not.

In order to investigate the visual pathway and/or cortical function other diagnostic tests such as recording of visual evoked potentials (VEP) are needed. The flash ERG and flash visual evoked potentials (VEPs) are the most commonly used electrophysiological techniques in veterinary ophthalmology. Other electrophysiological methods such as the electrooculogram (EOG), pattern and multifocal ERG are important but less frequently used diagnostic tools.

The flash electroretinogram

Numerous excellent papers and books have been published on topics of technical and practical issues concerning ERG examination in various animal species. Some of these will be briefly mentioned but the main emphasis of the present paper is to describe various contributions to the ERG from the cells and structures of the retina.

The full field ERG is a summation of electrical impulses obtained after stimulation of the entire retina with light [3]. By altering the conditions under which the ERG is recorded as to the intensity, frequency, wavelength and duration of the light stimulus, in addition to the state of light adaptation of the patient, the function of the different retinal cells can be evaluated individually. A stimulation system with a blue-white xenon flash of light has often been used to stimulate the retina,

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Figure 1 Photograph showing the recording session in a sedated dog with a portable ERG unit.

but newer recording equipments with Light Emitting Diodes (LED) is becoming more common (Fig. 1) [4]. Visual stimulation of the retina with light induces membrane potential changes over time in a large number of excitable cells [5]. Thus, electrical currents are produced and recorded by means of electrodes. The electrical activity picked up by the electrodes is processed by a computer and electroretinograms are obtained. Several technical and biological factors may influence the outcome of these electrophysiological recordings.

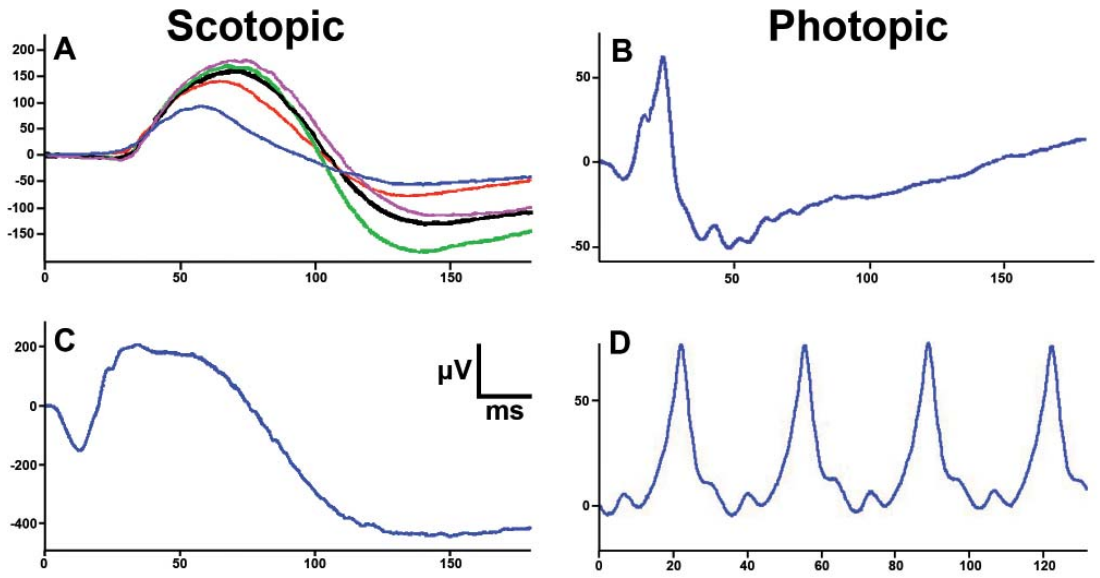
Biological factors

Biological aspects which may influence the results of the ERG recordings are: age of the patient, breed, time of day, prior exposure to bright light, pupil dilation, position of the eye, position of the patient, distance between patient and stimulator, choice and depth of sedation/anaesthesia, drugs, body temperature and oxygenation [6-11]. It is important to use standardized conditions when performing ERGs in order to be able to evaluate the recordings in a correct manner. ERGs should preferably be performed at the same time of day due to diurnal variations in the "shedding" of the photoreceptors [9]. Pupil dilation, position and exposure of the eye should be assessed by means of dim red light prior to and during the ERG-procedure. In order not to light adapt the rod photoreceptors' exposure to bright light, such as when performing fundus photography and indirect ophthalmoscopy, should be avoided at least one hour prior to ERG examination [12]. Downward rotation of the eye can be avoided by the use of conjunctival stay sutures, muscle relaxant drugs or retro bulbar saline injections. Further, eyelid speculae ensure good separation of the eyelids.

Electrodes

In order to record an ERG an active (positive) corneal electrode is used, a reference electrode (negative), positioned 2-5 cm temporal to the lateral canthus of the eye, and a ground electrode,

Figure 2 A) Dark adaptation series showing the rod-derived b-waves in a normal dog using 10 mCds/m² light intensities stimulation under scotopic conditions. Bottom curve (blue) is the b-wave recorded after 4 minutes of dark adaptation. Uppermost recording (red line) reflects recording after 20 minutes of dark adaptation. C) Scotopic combined rod-cone response obtained by the use of a standard single flash (3.0 Cds/m² intensity). B) Photopic single flash cone response D) Photopic 30Hz flicker cone response. The latter two recordings (B,D) performed using 3.0 Cds/m² after 10 minutes of light adaptation (30 Cd/m²).



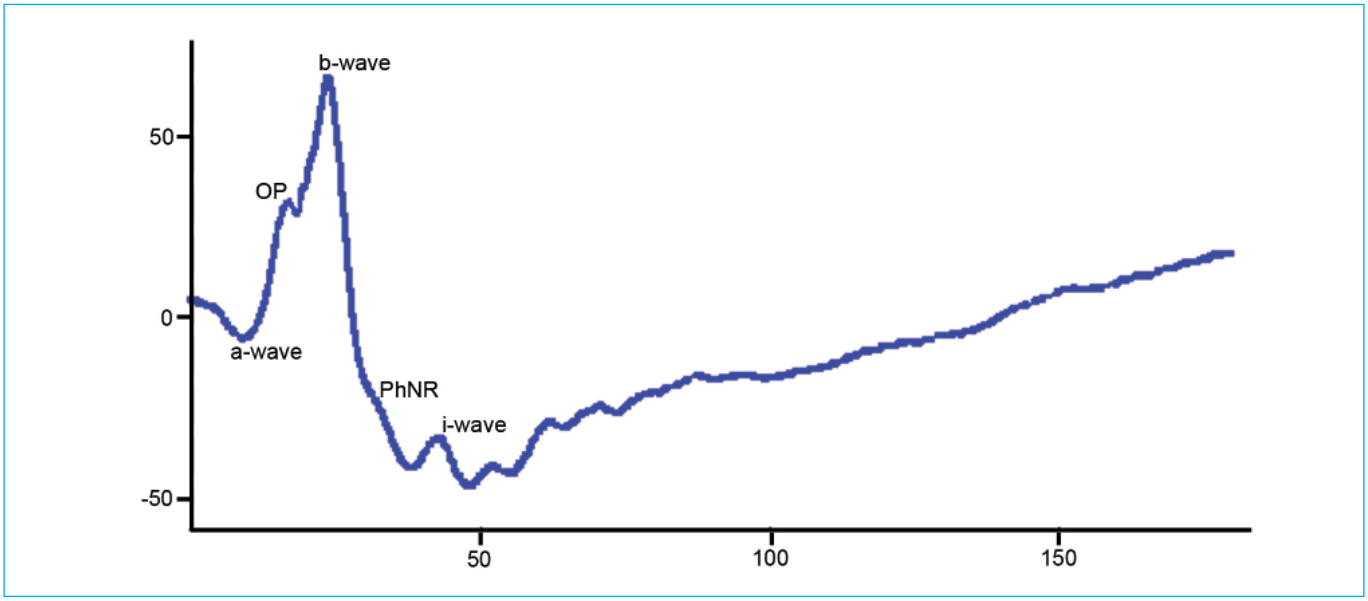


Figure 3 A photopic single flash cone response from a normal dog after stimulation using the standard flash (3 Cds/m²) and averaging 32 flashes. The timing of the a-, b- and i-wave is shown, in addition to oscillary potentials (OPs) and the photopic negative response (PhNR).

usually placed at the occipital process [13, 14]. A variety of corneal electrodes are available, including mono-and bipolar contact lens electrodes, fibers and gold plates. The monopolar contact lens, such as the Jet lens, is the most commonly used in canine ERGs. An ionic conductive solution, such as methylcellulose or a carbomer gel, is used for proper contact with the cornea. It is important to avoid air bubbles between the contact lens and the cornea in order to obtain reliable results. Fibre electrodes may also be used, such as the Dawson, Trick, and Litzkow (DTL) electrode. Reference and ground electrodes can be epidermal (surface electrodes) or intra dermal (needle electrodes) made of metal, such as platinum, silver-silver chloride, nickel chromium, stainless steel, silver and gold alloys and plating. To allow comparison between ERG recordings in and between patients, the electrodes and their positions have to be standardized as variations in these parameters significantly influence the results obtained [14].

ERG protocol

The choice of ERG protocol is dependent upon the objective for the examination. If the main goal is to evaluate whether a patient is suitable for cataract surgery or not, or if it is suffering from SARD, a short ERG protocol can be sufficient, while if the aim of the examination is to characterize or differentiate a generalized retinal degeneration, a more meticulous procedure should be considered. Detailed information on recommended protocols for the dog is given in "Guidelines for clinical electroretinography in the dog" by Narfström et al. [13]. Based on these protocols it is possible to add additional tests if needed, although care must be taken, especially under scotopic conditions, not to light adapt the retina. Rod function is investigated following dark adaptation using low intensity stimuli. The mixed rod-cone function is also investigated under scotopic conditions using higher stimuli. Pure cone derived recordings can be achieved by light adapting the retina for ten minutes with bright light (30-40 cd/m²), due to desensitization of the rod system. Cone function is thereafter studied using multiple flashes of bright light (Fig. 2). The critical flicker fusion frequency (CFFF) is the frequency of light stimulation using a specific intensity of light where the eye can no longer discern flickering light as single flashes, but perceives a steady light [15]. The CFFF varies between species and with background light intensity. High light intensity flicker stimulation can be used to separate cones from rods since the CFFF is much lower for rods (10-20 Hz) than for cones (60-90 Hz) for the canine specifically [16].

The "standard" full field ERG using bright light in scotopic conditions is composed of a leading negative a-wave followed by a positive b-wave. A positive c-wave can be observed under very stable recording conditions when longer duration flashes are used (>300 ms) [17]. The a-wave originates mainly from the photoreceptors, the b-wave from the ON-bipolar cells and the c-wave from the retinal pigment epithelium (RPE). In addition, several other wavelets such as the i-wave and d-wave can be observed under certain conditions (Figure 3). Amplitudes, implicit times, wave forms and whether specific wavelets are present or not in the recording, vary between species [18, 19]. Oscillary potentials (OPs) can be seen on the rising phase of the scotopic and photopic b-wave under certain circumstances and are considered to mainly represent amacrine cell contributions. Rod- and cone photoreceptors contribute to the ERG to varying degrees, depending on light adaptational status of the retina and the intensity of the stimulus used. In general, rod photoreceptors dominate in the dark adapted retina (scotopic conditions) using low intensity stimuli, while the cone photoreceptors contribute significantly in the light adapted retina (photopic conditions) using stimuli of higher intensity. Mixed rod-cone activity can be investigated using higher intensity stimulus under scotopic conditions. The ERG recordings obtained under photopic conditions using high intensity flickering light is mainly cone photoreceptor mediated, although other retinal cells, such as

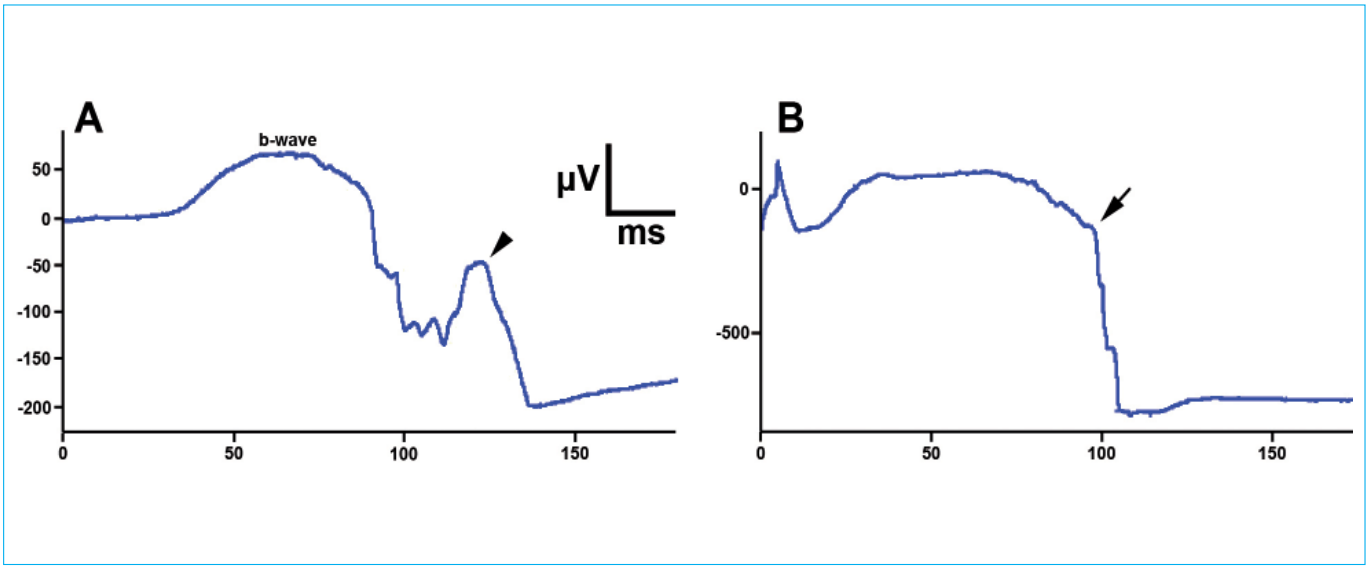


Figure 4 A) An eye blink and movement following the flash onset distorts the waveform of this scotopic rod response. The lens falls out towards the end of the recording (arrowhead). B) An eye blink occurs after the light stimulation, obscuring the a- and b-wave complex. The lens is displaced (arrow) and falls out.

bipolar cells, contribute to a varying degree depending on the frequency and duration of the light flashes [5].

Separating the components of the ERG

Cone and rod responses can thus be grossly separated by altering the intensity and frequency of the stimulus in addition to changing the background light. As previously stated rod responses are obtained under dark adapted conditions using low intensity of light stimulation. Averaging can be used if necessary, but sufficient time must be allowed between flashes in order not to light adapt the rods. The patient can either be dark adapted prior to ERG-examination or examination can be performed during the process of dark adaptation. The amount of time required to dark adapt varies between species. Nocturnal animals (i.e. rod dominated retinas) require longer time to dark adapt compared to diurnal animals (i.e. more cone dominated retinas) [16]. Cats require longer time to completely dark adapt than dogs. In order to completely dark adapt, a dog has to be in a absolutely dark room for 40-60 minutes [20]. Dark adapting the patient during the ERG examination is commonly used in dogs and cats to evaluate the rods' ability to dark adapt (Figure 2). In cases of progressive rod-cone degeneration (PRA), the rods fail to dark adapt in a normal manner, showing lower amplitudes than those obtained in unaffected dogs.

Cone derived responses are best recorded under photopic conditions using brighter flashes and/or flashes of higher frequencies than for rods. The time to light adapt from a dark adapted state is shorter than the dark adaptation time. It is recommended that the patients are allowed to light adapt for 10 minutes [13, 21].

Color filters can be used to produce light of a specific wavelength in order to isolate separate elements of the ERG response [22]. In most cases similar results can be achieved, however, by altering the white light settings of the photostimulator. Color filters are either built into the equipment or can be added in front of the photostimulator. Color filters need to be matched so they allow the same light intensity to pass through for comparison of recordings [23]. The most commonly used filters are blue (440 nm) and red (600nm), for isolation of rod and cone responses, respectively [22, 24]. Neutral density filters can also be used in log units to reduce or increase the level of light stimulation in steps.

Various drugs can be used for research purposes in order to block transmission at defined levels in the retina. For example, aspartate or a combination of DL-2-amino-4-phosphobutyric acid (APB) and a combination of cis-2,3-piperidinedicarboxylic acid (PDA) can be used to block transmission to the second order neurons post synaptic to the cone photoreceptors [25].

Analyzing the electroretinogram

The baseline of the ERG is the standing potential of the eye [17]. The ERG recording obtained from a standard single flash is a marked deviation from the baseline and composed of the leading negative a-wave, followed by the positive b-wave (Fig. 2). The positive c-wave is usually not observed in regular clinical recordings. The amplitudes of the a-and b-wave are measured in microvolt (μV) while the time to peak (implicit time) is measured in milliseconds (ms). The amplitude and timing of the a-wave is measured from the baseline to the a-wave through. Amplitude and implicit time of the b-wave is measured from the peak of the a-wave to the peak of the b-wave. Under scotopic and photopic conditions using high intensity of light stimulation oscillatory potentials (OPs) can be observed on the rising edge and at the peak of the b-wave. OPs can be filtered out to be analyzed separately. Ganglion and amacrine cells have been shown to contribute to the cone driven (photopic) b-wave and OPs in rats [26].

It is especially important to evaluate the timing of the ERG a- and b-waves because disturbances, such as muscle twitching and electrical noise, might be misinterpreted as either a- or b-waves. Muscle artefacts, for instance, are often observed following the a- and b-wave complex (Figure 4).

The ERG recordings are the results of contributions from various retinal cells. Some of the contributors are hyperpolarizing while others are depolarizing. The degree to which they contribute to the recordings is dependent upon several factors such as adaptational state of the eye, background light, flash intensity, duration of the flash(es) and flash frequency. Reduction or drop out of one or several of these bioelectric currents may increase or decrease the amplitudes depending upon the polarity of the current. The scotopic threshold response (STR) is the first recordable negative corneal response to very low intensity stimulus under scotopic conditions in the fully dark adapted retina. The STR is elicited by dim stimuli near the psychophysical absolute threshold [27]. This ERG response peaks 75 to 96 ms after the flash with a maximal amplitude of at least 50 µV in the dog and reflects activation of amacrine and ganglion cells [28, 29]. The STR should not be mistaken for the a-wave which, as mentioned earlier, originates mainly from the photoreceptors and appears at markedly higher light stimulation levels than the STR. In addition, cells post synaptic to the photoreceptors (hyperpolarizing bipolar cells and/or horizontal cells) have been shown to contribute significantly to the photopic a-wave in the low photopic range in primates [19].

The photopic negative response (PhNR) can be observed as a broad through below the baseline following the b-wave (Fig. 3). It is produced in response to a single flash under rod-suppressing (photopic) conditions [30]. It can be seen under standard conditions but is best observed using red flashes presented on a blue background. The retinal ganglion cells and/or glial cells provide a major contribution to the PhNR, which can be useful in assessing ganglion cells and optic nerve integrity [31]. The amplitude of the cone b-wave is a result of the combined interaction between the activation of the ON-depolarizing bipolar cells, which contributes to push the baseline of the ERG to the peak of the b-wave and the OFF-hyperpolarizing bipolar cells that acts to pull the baseline to bring it back to its pre-stimulus value (the "push-pull" concept) [32]. The ON- and OFF- effect is also considered the reason for the phenomenon " photopic hill", in which the photopic b-wave gradually increases in amplitude in response to progressively brighter stimuli, reaches a plateau and then rapidly decreases, even though the intensity of the flash continues to increase [33]. Affection of the ON-pathway has been suggested for humans with X-linked retinoschisis, Congenital Stationary Night Blindness (CSNB), acquired night blindness, melanoma associated retinopathy and cone or cone-rod dystrophy [34, 35]. OFF-responses seem to be affected in cone- and cone-rod dystrophies in man and in cone-rod dystrophy in dog [35, 36].

Flicker can be performed under scotopic or photopic conditions. The rod-mediated flicker is recorded under scotopic conditions using low intensity light in order not to light adapt the retina. The cone flicker is traditionally considered to reflect the cone photoreceptors, although by altering the intensity and frequency of the flashes, cells proximal to the photoreceptors have been shown to contribute substantially. Postreceptoral ON-and OFF-components contribute to the sine-wave flicker ERG, especially at higher stimulus frequencies as shown in primates by Kondo & Sieving (2001). The cone photoreceptors contribute substantially to the ERG responses at 4 Hz and are dominating at frequencies equal to or less than 10Hz. At frequencies 16 Hz and above post synaptic neurons are increasingly contributing to the b-wave. The OFF-components have a maximum amplitude around 10Hz to 30 Hz, while ON-component rise steadily up to 48 Hz [25].

Evaluation of the ERG

The ERG recordings should be evaluated carefully in regards to a- and b- wave implicit times, amplitudes and ERG wave forms.

Biological aspects and technical aspects which can influence the recordings, as described initially, have to be taken into consideration when performing this evaluation. It is important to evaluate all amplitude and implicit time parameters, especially those automatically recorded by the ERG equipment. The reason is that ERG units are usually programmed to measure amplitudes and implicit times within specific periods of time following the onset of the flash stimulus. An artefact that occurs within the time period of the actual a- and b-wave complex can be mistaken for an a- or b-wave and give false results (Fig. 4). In such instances the amplitudes and implicit times may have to be calculated manually or the results be discarded. Prolonged implicit time is often associated with progressive retinal degenerations in several species [17]. Reduced a- wave amplitudes may indicate an affection of the photoreceptors, while reduced b-wave amplitudes may indicate an affection of the inner retina. In most cases of retinal pathology the ERG amplitudes are reduced, such as in progressive retinal degenerations in dogs and cats [17, 36-39]. However, there are reports on conditions in which the amplitudes are supranormal. Some of these are explained by inflammatory reactions of the retina (metal poisoning and drug induced), changes affecting retinal circulation or by modulation of the inner retina (atypical cone dystrophies) [10, 40].

Several mathematical procedures have been developed to facilitate comparison between individuals, such as the b/a ratio, the response/intensity and the Naka-Rushton function. The b/a ratio can be calculated for several responses and can serve as a quantitative index, since the a-wave mainly reflects activity of the photoreceptors, while the b-wave has its origin in the bipolar cells. A reduced b/a ratio may indicate post receptoral damage, while an increased b/a ratio could point towards an affection of the outer retinal layers [39]. The values of the b/a ratio vary depending on the intensity and condition under which it is recorded. The ratio is reduced with increasing light intensity under scotopic conditions. The response-intensity function can be calculated by plotting either amplitude or implicit time versus (logarithmic) stimulus intensity. Both functions follow a sigmoidal curve with saturation observed at 0.6 log unit at attenuation. The Naka-Rushton equation provides a convenient way of summarizing a large amount of data. By recording a whole intensity-response function, instead of single responses,

considerably more information on the condition of the retina can be gathered. Chances of discerning retinal disorders increase, since gain problems and light absorption problems can be differentiated.

ERG results from one individual should always be compared with ERG recordings, obtained under the same conditions, from a normal age matched animal of the same breed. It has been shown that ERG results do not follow strictly a normal (Gaussian) distribution, but are slightly skewed. Percentiles are independent of data distribution and have therefore proven to give a better statistical description than mean and standard deviation. It is therefore recommended that the 5th and 95th percentiles of the median are used as limits of normality [24, 38]. Last, but not least, for publication of results always remember to include the results of an age matched normal control when illustrating a retinal disease process using ERG.

References

[1] NARFSTROM (K.), VAEGAN, KATZ (M.), BRAGADOTTIR (R.), RAKOCZY (E.P.), SEELIGER (M.) - Assessment of structure and function over a 3-year period after gene transfer in RPE65-/- dogs. *Doc Ophthalmol* 2005, Jul;**111(1):**39-48.

[2] MAJJI (A.B.), HUMAYUN (M.S.), WEILAND (J.D.), SUZUKI (S.), D'ANNA (S.A.), DE JUAN (E.) Jr. - Long-term histological and electrophysiological results of an inactive epiretinal electrode array implantation in dogs. *Invest Ophthalmol Vis Sci* 1999, Aug;**40(9):**2073-81.

[3] GOURAS (P.) - Symposium on electrophysiology: electroretinography: Some Basic Principles. *Invest Ophthalmol Vis Sci* 1970, Aug **1;9(8):**557-69.

[4] MANBOK (J.), NARFSTROM (K.), PARK (S), PARK (Y.), SEO (K.), SON (W.) - Comparison of two electroretinography systems used in dogs: the RETIcom and the HMs-ERG. Submitted, The Veterinary Journal 2007.

[5] FRISHMAN (L.J.) - Origins of the electroretinogram. In: Heckenlively JR, Arden GB, editors. Principles and practice of clinical electrophyiology of vision. 2 ed. Massachusets: The MIT press; 2006, p. 139-83.

[6] JONES (R.D.), HAMILTON (B.F.), DASS (P.D.) - The effects of physostigmine on the electroretinogram in the beagle dog. *Vet Res Commun* 1995, **19(2):**135-47.

[7] IOHOM (G.), WHYTE (A.), FLYNN (T.), O'CONNOR (G.), SHORTEN (G.) - Postoperative changes in the full-field electroretinogram following sevoflurane anaesthesia. *Eur J Anaesthesiol* 2004, Apr; **21(4):**272-8.

[8] GONZALEZ (P.), PARKS (S.), DOLAN (F.), KEATING (D.) - The effects of pupil size on the multifocal electroretinogram. *Doc Ophthalmol* 2004, Jul;**109(1):**67-72.

[9] ANDERSON (D.H.), FISHER (S.K.), STEINBERG (R.H.) - Mammalian cones: disc shedding, phagocytosis, and renewal. *Invest Ophthalmol Vis Sci* 1978, Feb;**17(2):**117-33.

[10] KOMMONEN (B.), HYVATTI (E.), DAWSON (W.W.) - Propofol modulates inner retina function in Beagles. *Vet Ophthalmol* 2007, Mar;**10(2):**76-80.

[11] REYNAUD (X.), HANSEN (R.M.), FULTON (A.B.) - Effect of prior oxygen exposure on the electroretinographic responses of infant rats. *Invest Ophthalmol Vis Sci* 1995, Sep;**36(10):**2071-9.

[12] TUNTIVANICH (N.), MENTZER (A.L.), EIFLER (D.M.), MONTIANI-FERREIRA (F.), FORCIER (J.Q.), JOHNSON (C.A.), *et al.* Assessment of the dark-adaptation time required for recovery of electroretinographic responses in dogs after fundus photography and indirect ophthalmoscopy. *Am J Vet Res* 2005, Oct;**66(10):**1798-804.

[13] NARFSTROM (K.), EKESTEN (B.), ROSOLEN (S.G.), SPIESS (B.M.), PERCICOT (C.L.), OFRI (R.) - Guidelines for clinical electroretinography in the dog. *Doc Ophthalmol* 2002, Sep;**105(2):**83-92.

[14] MENTZER (A.E.), EIFLER (D.M.), MONTIANI-FERREIRA (F.), TUNTIVANICH (N.), FORCIER (J.Q.), PETERSEN-JONES (S.M.) - Influence of recording electrode type and reference electrode position on the canine electroretinogram. *Doc Ophthalmol* 2005, Sep;**111(2):**95-106.

[15] AGUIRRE (G.D.), RUBIN (L.F.) - The electroretinogram in dogs with inherited cone degeneration. *Invest Ophthalmol* 1975, Nov;**14(11):**840-7.

[16] OFRI (R.) - Optics and physiology of vision. In: Gelatt KN, editor. Veterinary ophthalmology. 4 ed. Iowa: Blackwell synergy; 2007. p. 183-219.

[17] NARFSTROM (K.L.), NILSSON (S.E.), ANDERSSON (B.E.) - Progressive retinal atrophy in the Abyssinian cat: studies of the DC-recorded electroretinogram and the standing potential of the eye. *Br J Ophthalmol* 1985, Aug;**69(8):**618-23.

[18] ROSOLEN (S.G.), RIGAUDIERE (F.), LEGARGASSON (J.F.), CHALIER (C.), RUFIANGE (M.), RACINE (J)., *et al.* - Comparing the photopic ERG i-wave in different species. *Vet Ophthalmol* 2004, May;**7(3):**189-92.

[19] BUSH (R.A.), SIEVING (P.A.) - A proximal retinal component in the primate photopic ERG a-wave. *Invest Ophthalmol Vis Sci* 1994, Feb;**35(2):**635-45.

[20] PETERSEN-JONES (S.M.), TUNTIVANICH (N.), MONTTIANI-FERREIRA (F.), KHAN (N.W.) - Electroretinograms of dog and chicken. In: Heckenlively JR, Arden GB, editors. Principles and practice of clinical electrophysiology of vision. 2 ed. Cambridge: Massachusets institute of technology; 2006. p. 911-21.

[21] MARMOR (M.F.), ZRENNER (E.) - Standard for clinical electroretinography (1999 update). International Society for Clinical Electrophysiology of Vision. *Doc Ophthalmol* 1998, **97(2):**143-56.

[22] YANASE (J.), OGAWA (H.), OHTSUKA (H.) - Rod and cone components in the dog electroretinogram during and after dark adaptation. *J Vet Med Sci* 1995, Oct;**57(5):**877-81.

[23] NARFSTROM (K.), ANDERSSON (B.E.), ANDREASSON (S.), GOURAS (P.) - Clinical electroretinography in the dog with ganzfeld stimulation: a practical method of examining rod and cone function. *Doc Ophthalmol* 1995, **90(3):**279-90.

[24] JACOBI (P.C.), MILICZEK (K.D.), ZRENNER (E.) - Experiences with the international standard for clinical electroretinography: normative values for clinical practice, interindividual and intraindividual variations and possible extensions. *Doc Ophthalmol* 1993, **85(2):**95-114.

[25] KONDO (M.), SIEVING (P.A). - Primate photopic sine-wave flicker ERG: vector modeling analysis of component origins using glutamate analogs. *Invest Ophthalmol Vis Sci* 2001, Jan;**42(1):**305-12.

[26] BUI (B.V.), FORTUNE (B.) - Ganglion cell contributions to the rat full-field electroretinogram. *J Physiol* 2004, Feb 15;**555(Pt 1):**153-73.

[27] GRAHAM (S.L.), VAEGAN - High correlation between absolute psychophysical threshold and the scotopic threshold response to the same stimulus. *Br J Ophthalmol* 1991, Oct;**75(10):**603-7.

[28] ROBSON (J.G.), FRISHMAN (L.J.) - Dissecting the dark-adapted electroretinogram. *Doc Ophthalmol* 1998, **95(3-4):**187-215.

[29] YANASE (J.), OGAWA (H.), OHTSUKA (H.) - Scotopic threshold response of the electroretinogram of dogs. *Am J Vet Res* 1996, Mar;**57(3):**361-6.

[30] NIEMEYER (G.) ERG - components of negative polarity from the

inner retina and the optic nerve response. *Doc Ophthalmol* 2005, Nov;**111(3):**179-89.

[31] VISWANATHAN (S.), FRISHMAN (L.J.), ROBSON (J.G.), HARWERTH (R.S.), SMITH (E.L.) - III. The photopic negative response of the macaque electroretinogram: reduction by experimental glaucoma. *Invest Ophthalmol Vis Sci* 1999, May;**40(6):**1124-36.

[32] SIEVING (P.A.), MURAYAMA (K.), NAARENDORP (F.) - Push-pull model of the primate photopic electroretinogram: a role for hyperpolarizing neurons in shaping the b-wave. *Vis Neurosci* 1994, May;**11(3):**519-32.

[33] WALI (N.), LEGUIRE (L.E.) - The photopic hill: a new phenomenon of the light adapted electroretinogram. *Doc Ophthalmol* 1992, **80(4):**335-45.

[34] ALEXANDER (K.R.), FISHMAN (G.A.), BARNES (C.S.), GROVER (S.) - ON-Response Deficit in the Electroretinogram of the Cone System in X-Linked Retinoschisis. *Invest Ophthalmol Vis Sci* 2001, Feb 1;**42(2):**453-9.

[35] SIEVING (P.A.) - Photopic ON- and OFF-pathway abnormalities in retinal dystrophies. *Trans Am Ophthalmol Soc* 1993, **91:**701-73.

[36] ROPSTAD (E.O.), BJERKAS (E.), NARFSTROM (K.) - Electroretinographic findings in the Standard Wire Haired Dachshund with inherited early onset cone-rod dystrophy. *Doc Ophthalmol* 2007, Jan;**114(1):**27-36.

[37] NARFSTROM (K.), KATZ (M.L.), BRAGADOTTIR (R.), SEELIGER (M.), BOULANGER (A.), REDMOND (T.M.), *et al.* - Functional and structural recovery of the retina after gene therapy in the RPE65 null mutation dog. *Invest Ophthalmol Vis Sci* 2003, Apr;**44(4):**1663-72.

[38] NARFSTROM (K.), EKESTEN (B.) - Electroretinographic evaluation of Papillons with and without hereditary retinal degeneration. *Am J Vet Res* 1998, Feb;**59(2):**221-6.

[39] HYMAN (J.A.), VAEGAN, LEI (B.), NARFSTROM (K.L.) - Electrophysiologic differentiation of homozygous and heterozygous Abyssinian-crossbred cats with late-onset hereditary retinal degeneration. *Am J Vet Res* 2005, Nov;**66(11):**1914-21.

[40] HECKENLIVELY (J.R.), TANJI (T.), LOGANI (S.) - Retrospective study of hyperabnormal (supranormal) electroretinographic responses in 104 patients. *Trans Am Ophthalmol Soc* 1994, **92:**217-31.