The effects of cataract stage, lens-induced uveitis and cataract removal on the ERG in dogs with cataract

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Abstract

Objective The purpose of this study was to determine the effects of cataract stage, lens-induced uveitis and cataract removal on the ERG in dogs with cataract.

Animals Studied Fiftyseven dogs diagnosed with unilateral or bilateral cataract in which ERG was recorded at Rakuno Gakuen University Teaching Animal Hospital from 2001 to 2004.

Procedures In the ERG, four responses were recorded; rod ERG, standard combined ERG, single-flash cone ERG and 30 Hz flicker ERG. Cataracts were divided into four stages; incipient, immature, mature and hyper-mature, and with or without lens induced uveitis (LIU). Non-cataractous eyes in dogs with unilateral cataract were used as the control. We compared ERG amplitude, implicit time and the ratio of the b-wave to the a-wave amplitude of cataractous versus non-cataractous eyes, preoperative versus postoperative cataractous eyes, and cataractous eyes with and without LIU.

Results In incipient, immature and hyper-mature cataractous eyes, no significant difference was confirmed in ERG amplitude, while in mature cataractous eyes, decreased amplitude was confirmed in all responses compared with control eyes. However, no significant difference in b/a ratio was found in any stage of cataract. In postoperative eyes, increased amplitude was recorded in all responses compared to preoperative values. In eyes with LIU, a decreased amplitude in the rod ERG and b-wave of

standard combined ERG was recorded, and furthermore, a significant decline was confirmed in b/a ratio.

Conclusion ERG values were influenced by cataract stage and LIU. LIU was associated with a reduction in the b/a ratio .

Key Words: cataract, dog, electroretinogram, lens-induced uveitis

INTRODUCTION

Electroretinographic (ERG) recording is a valuable non-invasive tool in the evaluation of retinal function.[1-3] Evaluation of retinal function by ERG in the presence of an opaque medium when the fundus is not visible is valuable in clinical practice. ERG recording is an essential examination before cataract extraction.[4, 5] However, the effects of cataract stage, lens-induced uveitis and cataract removal on the ERG in dogs have not been reported.

The ERG is influenced by dark adaptation time, pupil size, stimulus intensity and other factors.[6-9] The ERG measures an electrical potential which arises in the retina after light stimulation from the front of the eye. Light passes through the optic media; cornea, anterior chamber, lens and vitreous, and reaches the retina. Opacity of the media acts as a filter that reduces stimulus strength. It was reported that the ERG was slightly reduced in amplitude in a dog with cataract with a normal retina,[9, 10] but concrete differences in the ERG amplitude, implicit time and b/a ratio, the ratio of b-wave amplitude to a-wave amplitude in standard combined ERG according to the stage of cataract have not been reported. The present study examined the differences in ERG in various cataract stages, and compared the ERG before and after cataract surgery.

The development of juvenile cataract in dogs is rapid, and resorption of cataract and leakage of lens protein from the lens capsule frequently occur.[11, 12] As a result, lens protein enters the aqueous and is exposed to

the immune system of the uvea. This causes lens-induced uveitis (LIU).[12, 13] LIU is a major cause of complications in cataract surgery.[4, 14] The influence of LIU on retinal electrophysiological function has not previously been reported. So we herein discuss the effects of cataract and LIU on the ERG.

MATERIALS AND METHODS

Animals

Fifty-seven dogs diagnosed with unilateral or bilateral cataract in which ERG was recorded at Rakuno Gakuen University Teaching Animal Hospital from 2001 to 2004 were used. Eighteen dogs had unilateral cataract, and 39 had bilateral cataract. Eighteen dogs (18 eyes) had non-cataractous eyes, and their median age was 3.1 years old. Eleven dogs (12 eyes) had incipient cataract, and their median age was 3.4 years old. Eight dogs (9 eyes) had immature cataract, and their median age was 3.4 years old. Thirty-one dogs (39 eyes) had mature cataract, and their median age was 4.2 years old. Nineteen dogs (22 eyes) had hypermature cataract, and their median age was 3.3 years old. Thirteen dogs (14 eyes; 7 mature cataract and 7 hypermature cataract) developed LIU, and their median age was 3.6 years old. In this study, the eyes that developed mature or hypermature cataract, conjunctival hyperemia, aqueous flare, or iris thichening, and did not have other causes of inflammation were diagnosed as having LIU. Seven dogs (8 eyes) underwent ERG recording again 4 to 18 months after cataract surgery (median 10.9 months). Five dogs (5 eyes) diagnosed with LIU underwent ERG recording again after treatment of LIU before cataract surgery.

Electroretinography

The method of ERG recording was according to a previous study using a

contact lens electrode with a built-in light source.[15] The ERG instrument used was a portable ERG LE-3000 (TOMEY Corporation, Nagoya, Japan), which incorporates a stimulator, amplifier and recorder. The frequency band was 0.3 – 300 kHz. We used an ERG contact lens electrode with a built-in light source (LED electrode H2000, Kyoto Contact Lens, Kyoto, Japan). Before ERG recording, the pupils were dilated with 0.5% tropicamide and 0.5% phenylephrine hydrochloride (Mydrin-P, Santen, Osaka, Japan). ERG was recorded under sedation with a combination of 0.01 mg/kg medetomidine (Domitor, Meiji, Tokyo, Japan), 0.15 mg/kg midazolam (Dormicam, Yamanouchi, Tokyo, Japan), and 0.025 mg/kg butorphanol (Stadol, Bristol-Meyers, Tokyo, Japan). Four responses were recorded in the ERG: rod ERG, standard combined ERG, single-flash cone ERG, and 30 Hz flicker ERG. The intensity of light of rod ERG was 0.0096 cd/m^2/sec, and that of the other responses was 3.0 cd/m^2/sec. Rod ERG and combined ERG were recorded after 30 minutes of dark adaptation, and cone ERG and flicker ERG were performed after 10 minutes of light adaptation.

Statistical analysis

ERGs of 18 non-cataractous eyes were used as the control. Age and ERGs of incipient, immature, mature and hypermature cataractous eyes were compared to control using Student's *t*-test. ERGs of postoperative eyes were compared to preoperative eyes and control using paired *t*-test or Student's *t*-test, respectively. ERGs of LIU eyes were compared to ERGs of mature and hypermature cataractous eyes that were not inflamed using

Student's *t*-test. ERGs of LIU eyes were compared to ERGs of the eyes that were treated for LIU using a paired *t*-test. Differences with $P < 0.05$ were considered to be statistically significant.

RESULTS

There was no significant difference of age in cataractous dogs of each stage compared to control. ERG amplitude, b/a ratio and implicit time in each stage of cataract are shown in Tables 1 and 2. In incipient and immature cataractous eyes, no significant differences were observed in ERG amplitude, b/a ratio and implicit time compared to control. In mature cataractous eyes, a significant decrease in ERG amplitude was observed in all responses ($P < 0.05$), but no significant difference was observed in b/a ratio compared to control. In mature cataractous eyes, there was significant prolongation of the a-wave implicit time in the standard combined ERG ($P < 0.05$). In hypermature cataractous eyes, no significant differences were observed in ERG amplitude and b/a ratio compared to control. In hypermature cataractous eyes, there was significant prolongation of the a-wave implicit time in the standard combined ERG ($P < 0.05$).

ERG amplitude, b/a ratio and implicit time before and after cataract surgery for all cataract groups were combined and averaged and are shown in Tables 3 and 4. After cataract surgery, a significant increase in ERG amplitude was observed ($P < 0.05$), but no significant change was observed in b/a ratio compared to before surgery. Significant shortening was observed in the a-wave implicit time compared to before surgery ($P < 0.05$). There was no significant difference in amplitude, b/a ratio and implicit time of postoperative eyes compared to those of control eyes.

ERG amplitude, b/a ratio and implicit time in eyes with LIU are shown in Tables 5 and 6. Significant decreases were observed in the amplitude of rod ERG and b-wave of the standard combined ERG in LIU eyes compared to non-inflamed mature and hypermature cataractous eyes ($P < 0.05$). The b/a ratio in LIU eyes was 1.31 ± 0.28 (median ± S.D.), which was significantly smaller than that in non-inflamed mature and hypermature cataractous eyes ($P < 0.05$). There was significant prolongation of the a-wave implicit time of the standard combined ERG in LIU eyes compared to mature and hypermature cataractous eyes ($P < 0.05$).

ERG amplitude, b/a ratio and implicit time in eyes after treatment of LIU are shown in Tables 7 and 8. After treatment of LIU before cataract surgery, a significant increase in b-wave amplitude was observed compared to before treatment ($P < 0.05$), and a significant increase in b/a ratio was also observed ($P < 0.05$). There was no significant difference in implicit time of eyes after treatment of LIU compared to those of eyes before treatment.

DISCUSSION

In this study, the results showed that ERG a and b wave amplitudes decreased similarly, so that b/a ratio in the combined ERG was unaffected in canine eyes with cataract. In postoperative ERG recordings, increased amplitude was recorded in all responses compared to preoperative recordings. However, in cataractous eyes with LIU, not only ERG amplitude, but also b/a ratio decreased. Therefore when we evaluate the ERG as preoperative examination, it was thought that reduction of amplitude by opacity of lens in mature cataractous eye and reduction of b/a ratio in LIU eyes had to be taken into consideration.

The ERG is influenced by stimulus intensity; ERG amplitude increases and implicit time decreases as light stimulation increases up to a certain strength.[6, 7, 9] The presumed reason for decreased ERG amplitude and prolonged implicit time in eyes with mature cataract is that cataract acts as a filter that reduces stimulus strength. On the other hand, it was reported that larger ERG amplitude was recorded in human eyes with cataract compared to eyes without a cataract.[16] The reason was considered to be that the cataract scattered stimulus light and a larger retinal area was illuminated. In a previous study, an external light source that did not stimulate the full field was used. In our study, full-field stimulation was used, and the ERG amplitude was decreased in cataractous eyes.

After cataract extraction, a significant increase in ERG amplitude was observed in all responses compared to before surgery. We considered that

the stimulus intensity reaching the retina was increased after cataract extraction, so that the ERG amplitude after surgery was increased. In humans, it is reported that ERG amplitude was decreased 2 to 3 weeks after cataract surgery.[16] This was explained by impairment of retinochoroidal circulation. In this study, the ERG was recorded 4 to 18 months after cataract surgery, and no intraocular inflammation was detected at the times the ERG was recorded. It appears that the reduction of amplitude in mature cataractous eyes was caused by lens opacity, because ERGs of postoperative eyes with improved lens clarity increased compared to preoperative values.

A decreased b/a ratio resulting from decreased b-wave amplitude was detected in LIU eyes. ERG mainly evaluates the function of photoreceptor cells.[1-3] The photoreceptor cell layer of the retina is nourished by diffusion from the uveal vessels in the choroid in dogs.[17] It was considered that the reduction of ERG amplitude in LIU eyes was based on the reduction of photoreceptor function. We thought that the reduction of photoreceptor function was due to impairment of outer retinal perfusion by the choroid caused by LIU. The ERG b-wave originates from bipolar cells and Muller's cells present in the inner part of the retina.[3, 9] The inner part of the retina is supplied by retinal vessels.[17] In humans, the decreased ERG b-wave amplitude is caused by impairment of retinal circulation, such as central retinal vein occlusion.[9] With LIU lymphocytic-plasmacytic perivascular cuffing of retinal vessels is reported.[19] So we propose that LIU may also affect choroidal and retinal circulation resulting in a decrease in the ERG

b-wave.

In this study the following two things were determined. The effect of lens opacity on ERG was a decrease in all ERG parameters, while the effect of LIU on ERG was only a decreased b-wave amplitude with a subsequent reduction of the b/a ratio. We therefore considered that the b/a ratio may be an indicator of LIU in combination with other findings such as conjunctival hyperemia, episcleral injenction, aqueous flare, iris hyperpigmentation and so on. Therefore, a reduction of the b-wave detected at the time of the preoperative ERG examinationmay indicate the need for more aggressive perioperative anti-inflammatory therapy and raise concern for the greater risk of postoperative inflammation and secondary glaucoma.

At the last conclusion, When the ERG amplitude is decreased, it is important to take into consideration not only the possibility of retinal diseases but also the condition of the anterior segment including the degree of lens opacity or the presence of anterior uveitis.

Table 1. ERG amplitude and b/a ratio in each stage of cataract

Stage of cataract	Rod	Standard combined			Cone	Flicker
		a-wave	b-wave	b/a ratio		
Control (n=18)	135.4±45.6	138.1±27.1	246.2±47.7	1.82±0.34	47.0±9.8	68.7±20.8
Incipient (n=12)	131.5±40.1	141.0±42.1	235.1±44.7	1.74±0.33	45.4±9.0	68.0±17.9
Immature (n=9)	126.4±30.3	154.3±32.6	259.5±38.3	1.72±0.29	54.4±7.6	64.2±17.3
Mature (n=39)	63.5±34.1*	116.6±38.3*	215.6±54.6*	1.90±0.32	38.2±11.0*	52.4±18.2*
Hypermature(n=22)	121.0±44.7	131.8±48.8	243.93±80.62	1.90±0.38	44.8±12.9	58.0±20.4

Data are presented as mean value (in microvolt) ± standard division. The ERG amplitude and b/a ratio of the cataracts of each stage were compared to control eyes. Symbols represent a significant difference ($P<0.05$) evaluated by Student's *t*-test compared to control eyes.

Table 2. ERG implicit time in each stage of cataract

Stage of cataract	Rod	Standard combined		Cone	Flicker
		a-wave	b-wave		
Control (n=18)	67.5±7.3	12.8±1.9	30.1±3.2	24.6±1.3	23.4±2.5
Incipient (n=12)	70.0±8.6	12.7±1.5	28.4±4.9	24.2±0.8	22.1±0.3
Immature (n=9)	68.0±8.5	12.9±1.2	28.4±3.1	27.9±1.1	22.1±0.5
Mature (n=39)	73.4±13.5	15.0±2.0*	29.4±3.8	25.0±1.9	23.3±2.7
Hypermature(n=22)	67.0±10.4	14.4±1.9*	29.6±4.3	25.3±1.4	22.3±0.9

Data are presented as mean value (in millisecond) ± standard division. The ERG implicit time of the cataracts of each stage was compared to control eyes. Symbols represent a significant difference ($P<0.05$) evaluated by Student's *t*-test compared to control eyes.

Table 3. ERG amplitude and b/a ratio before and after cataract surgery

	Rod	Standard combined			Cone	Flicker
		a-wave	b-wave	b/a ratio		
Preoperative(n=8)	56.8±35.8	117.7±22.3	201.1±55.6	1.77±0.16	37.6±12.8	39.4±15.8
Postoperative(n=8)	97.6±37.4	137.5±12.8*	242.8±67.5*	1.77±0.43	42.5±17.7*	53.1±19.2*
Control (n-18)	135.4±45.6	138.1±27.1	246.2±47.7	1.82±0.34	47.0±9.8	68.7±20.8

Data are presented as mean value (in microvolt) ± standard division. The ERG amplitude and b/a ratio of the postoperative eyes were compared to preoperative and control eyes. Symbols represent a significant difference ($P<0.05$) evaluated by paired *t*-test compared to preoperative eyes. There was no significant deference of amplitude of postoperative eyes compared to that of control eyes.

Table 4. ERG implicit time before and after cataract surgery

	Rod	Standard combined		Cone	Flicker
		a-wave	b-wave		
Preoperative(n=8)	71.3±29.6	15.3±1.8	28.9±3.9	25.9±1.5	23.9±3.3
Postoperative(n=8)	72.3±7.0	14.0±1.5*	29.8±3.7	24.7±1.1	23.8±2.4
Control (n=18)	67.5±7.3	12.8±1.9	30.1±3.2	24.6±1.3	23.4±2.5

Data are presented as mean value (in millisecond) ± standard division. The ERG implicit time of the postoperative eyes was compared to preoperative and control eyes. Symbols represent a significant difference ($P<0.05$) evaluated by paired *t*-test compared to preoperative eyes. There was no significant deference of implicit time of postoperative eyes compared to those of control eyes.

Table 5. ERG amplitude and b/a ratio of LIU eyes

	Rod	Standard combined			cone	flicker
		a-wave	b-wave	b/a ratio		
Non-inflamed (n=47)	80.9±45.8	121.6±42.2	224.9±65.0	1.90±0.34	40.4±12.0	54.2±18.9
LIU (n=14)	58.9±32.6*	115.7±34.0	146.5±44.1*	1.31±0.28*	32.1±8.6	49.9±16.6

Data are presented as mean value (in microvolt) ± standard division. The ERG amplitude and b/a ratio of LIU eyes were compared to non-inflamed eyes. Symbols represent a significant difference ($P<0.05$) evaluated by Student's *t*-test compared to non-inflamed eyes.

Table 6. ERG implicit time in LIU eyes

Eyes	Rod	Standard combined		Cone	Flicker
		a-wave	b-wave		
Non-inflamed (n=47)	72.7±12.6	14.8±2.0	29.4±3.9	25.1±1.7	23.0±2.3
LIU (n=14)	70.7±7.3	16.2±2.6*	30.4±3.5	26.3±2.4	25.0±2.7

Data are presented as mean value (in millisecond) ± standard division. The ERG implicit time of LIU eyes was compared to non-inflamed eyes. Symbols represent a significant difference ($P<0.05$) evaluated by Student's *t*-test compared to non-inflamed eyes.

Table 7. ERG amplitude and b/a ratio of eyes after treatment of LIU

	Rod	Standard combined			cone	flicker
		a-wave	b-wave	b/a ratio		
Before treatment of LIU (n=5)	57.1±28.8	104.35±31.9	139.8±40.9	1.36±0.21	37.6±8.53	48.2±16.5
After treatment of LIU (n=5)	72.9±38.1	115.0±30.9	219.7±68.9*	1.92±0.33*	43.2±12.4	53.5±13.0

Data are presented as mean value (in microvolt) ± standard division. The ERG amplitude and b/a ratio of eyes after treatment of LIU were compared to eyes before treatment. Symbols represent a significant difference (P<0.05) evaluated by paired t-test compared to eyes before treatment of LIU.

Table 8. ERG implicit time of eyes after treatment of LIU

Eyes	Rod	Standard combined		Cone	Flicker
		a-wave	b-wave		
Before treatment of LIU (n=5)	72.4±6.5	15.1±3.0	29.4±4.8	27.2±3.5	25.5±3.3
After treatment of LIU (n=5)	72.8±8.0	14.0±1.3	30.1±4.8	25.8±1.7	25.4±3.1

Data are presented as mean value (in millisecond) ± standard division. The ERG implicit time of eyes after treatment of LIU were compared to eyes before treatment. There was no significant deference of implicit time of eyes after treatment of LIU compared to those of eyes before treatment.

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