7-2014

Electroretinogram evaluation of equine eyes with extensive 'bullet-hole' fundic lesions

Rachel A. Allbaugh
Iowa State University, allbaugh@iastate.edu

Gil Ben-Shlomo
Iowa State University, gil@iastate.edu

R. David Whitley
Iowa State University, dwhitley@iastate.edu

Electroretinogram evaluation of equine eyes with extensive 'bullet-hole' fundic lesions

Abstract

Objective To evaluate the impact of extensive bullet-hole nontapetal fundic lesions in horses on retinal function as measured by full field electroretinography (ERG).

Materials and Methods Full field ERG was performed on two horses with numerous bullet-hole lesions in the nontapetal fundus of both eyes. The ERG was first recorded from the eye with the more extensive lesions in response to a low intensity light stimulus (0.03 cd·s/m^2) that was given at times (T) T = 5, 10, 15, 20 minutes of dark adaptation. Consecutively, combined rod-cone response was evaluated bilaterally in response to high intensity light stimulus (3 cd·s/m^2), followed by cone function evaluation by flicker stimulus (3 cd·s/m^2 at 30Hz). Off-line analysis of the ERG recordings was then performed.

Results Despite extensive bullet-hole lesions in the nontapetal fundus bilaterally in both horses retinal function as measured by ERG did not show any observable deficits. The b-wave amplitude of the full-field ERG increased continuously from 5 to 20 minutes of dark adaptation peaking at 446μv and 377μv for horse number 1 and 2 respectively. The b-wave amplitudes of the combined rod-cone response were OS- 459μv and OD- 392μv for horse number 1 and OS- 491μv and OD- 608μv for horse number 2. The amplitude of the flicker ERG for horse number 1 was OS- 86 μv and OD- 110 μv and for horse number 2 OS- 80 μv and OD- 74 μv.

Conclusions Extensive bullet-hole chorioretinal lesions do not appear to compromise outer retinal function in these horses.

Keywords

horse, retina, bullet-hole, focal chorioretinopathy, electroretinogram, nontapetal fundus

Disciplines

Large or Food Animal and Equine Medicine | Veterinary Anatomy

Comments

This is the accepted version of the following article: Allbaugh RA, Ben-Shlomo, G, Whitley RD. Eletroretinogram evaluation of equine eyes with extensive 'bullet-hole' fundic lesions. *Veterinary Ophthalmology* 2014; 17, 129–133, which has been published in final form at http://dx.doi.org/10.1111/vop.12169

Electroretinogram evaluation of equine eyes with extensive 'bullet-hole' fundic lesions

Rachel A. Allbaugh,† Gil Ben-Shlomo† and R. David Whitley
Iowa State University College of Veterinary Medicine, Department of Veterinary Clinical Sciences, 1526 Lloyd Veterinary Medical Center, 1600 S. 16th St, Ames, IA 50011, USA
† These authors contributed equally to this work

Address communications to:
Rachel A. Allbaugh, Iowa State University, College of Veterinary Medicine, 1526 Lloyd Veterinary Medical Center, 1600 S. 16th St., Ames, IA 50011-1250, USA
Tel: (515) 294-4900, Fax: (515) 294-7520, e-mail: rachelallbaugh@yahoo.com

Abstract
Objective To evaluate the impact of extensive bullet-hole nontapetal fundic lesions in horses on retinal function as measured by full field electroretinography (ERG).
Materials and Methods Full field ERG was performed on two horses with numerous bullet-hole lesions in the nontapetal fundus of both eyes. The ERG was first recorded from the eye with the more extensive lesions in response to a low intensity light stimulus (0.03 cd·s/m^2) that was given at times (*T*) *T* = 5, 10, 15, 20 minutes of dark adaptation. Consecutively, combined rod-cone response was evaluated bilaterally in response to high intensity light stimulus (3 cd·s/m^2), followed by cone function evaluation by flicker stimulus (3 cd·s/m^2 at 30Hz). Off-line analysis of the ERG recordings was then performed.
Results Despite extensive bullet-hole lesions in the nontapetal fundus bilaterally in both horses retinal function as measured by ERG did not show any observable deficits. The b-wave amplitude of the full-field ERG increased continuously from 5 to 20 minutes of dark adaptation peaking at 446µv and 377µv for horse number 1 and 2 respectively. The b-wave amplitudes of the combined rod-cone response were OS- 459µv and OD- 392µv for horse number 1 and OS- 491µv and OD- 608µv for horse number 2. The amplitude of the flicker ERG for horse number 1 was OS- 86 µv and OD- 110 µv and for horse number 2 OS- 80 µv and OD- 74 µv.
Conclusions Extensive bullet-hole chorioretinal lesions do not appear to compromise outer retinal function in these horses.

Key Words: horse, retina, bullet-hole, focal chorioretinopathy, electroretinogram, nontapetal fundus

INTRODUCTION

Bullet-hole chorioretinal lesions, also termed focal chorioretinopathy,(1) are occasionally observed in equine eyes in the nontapetal fundus horizontally adjacent to or below the optic nerve head.(2-6) One report suggested that bullet-hole scars may be observed in 10 to 20% of horses in the northeastern United States.(4) The classic appearance is pinpoint focal nontapetal depigmentation with possible central hyperpigmentation and may be described as a birdshot pattern.(7) Lesions may be few in number, extensive with a ventral linear distribution, or more diffusely affect the nontapetal fundus causing a dramatic change in appearance. It has been noted that they rarely may extend into the tapetal fundus.(1)

This is the accepted version of the following article: Allbaugh RA, Ben-Shlomo, G, Whitley RD. Eletroretinogram evaluation of equine eyes with extensive 'bullet-hole' fundic lesions. *Veterinary Ophthalmology* 2014; 17, 129–133, which has been published in final form at http://dx.doi.org/10.1111/vop.12169

The exact cause or possible causes of bullet-hole lesions is not known though choroidal vasculitis, infarction and ischemia is the proposed pathogenesis.(1) An association with respiratory disease and viral chorioretinitis has previously been suggested.(4, 8) Studies in foals and ponies experimentally infected with EHV-1 demonstrated development of similar appearing lesions, which supports viral infection as an etiology.(9, 10) An association with equine leptospirosis or a different causative agent of equine recurrent uveitis has also been discussed and bullet-hole chorioretinal lesions may occur in association with peripapillary chorioretinitis, or "butterfly" lesions.(11, 12)

These lesions show histologic loss of normal retinal architecture with retinal pigment epithelium (RPE) hyperplasia and RPE cell migration into the degenerate neurosensory retina but have an uncertain effect on retinal function or vision.(1, 13) Authors of articles detailing bullet-hole lesions in clinical surveys speculate varying impact on vision but no objective assessment of retinal function has been performed. The purpose of this report is to document electroretinogram (ERG) study of two horses affected with numerous bullet-hole lesions in the nontapetal fundus of both eyes.

MATERIALS AND METHODS

Two horses with similar bilateral extensive bullet-hole chorioretinal lesions (Fig. 1) were evaluated at the Iowa State University Lloyd Veterinary Medical Center (ISU LVMC). Both horses were intact female Arabians of similar age, 11 and 12 years old, weighing 430 and 446 kg respectively. Complete ophthalmic examinations were performed including fluorescein staining, tonometry with a rebound tonometer (TonoVet®, Tiolat Ltd, Helsinki, Finland), slit-lamp biomicroscopy (SL-14 Biomicroscope, Kowa Company, Ltd, Tokyo, Japan), and both direct (Welch Allyn, Inc., Skaneateles Falls, NY, USA) and indirect ophthalmoscopy (HEINE Omega 180® Ophthalmoscope, HEINE Optotechnik, Herrsching, Germany) following pupil dilation with tropicamide (1% tropicamide ophthalmic solution, Bausch and Lomb Inc., Tampa, FL, USA). Both horses had undergone complete examinations by the same ophthalmologist (RAA) between 18 and 24 months previously at the times of first fundus pathology recognition with no change in the clinical findings over time.

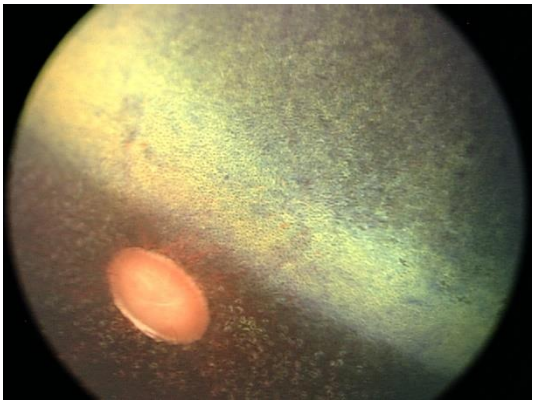

Figure 1. Fundic image of the right eye in a 12 year old female Arabian (Horse 2) showing normal tapetal fundus, healthy optic disc and retinal vasculature yet numerous bullet-hole lesions in the nontapetal fundus.

For ERG evaluation horses were initially sedated with 5 mg of detomidine hydrochloride (Dormosedan®, Pfizer Animal Health, New York, NY, USA) intravenously and additional 3 mg of detomidine was given IV to maintain adequate sedation for the duration of the ERG protocol. Auriculopalpebral nerve blocks were performed bilaterally with 1-2 ml of 2% lidocaine (Xylocaine®, APP Pharmaceuticals, LLC, Schaumburg, IL, USA). To prevent drying of the cornea manual blinking was performed during the recording period. In order to allow for optimal ERG results no examination light illumination or photography was performed within 1 hour of testing and horses were kept in ambient barn lighting.

A mini-Ganzfeld electroretinographic unit (Handheld Multispecies ERG [HMsERG] Model 1000, Xenotec, Inc., Rolla, MO, USA) and gold foil contact lens electrode (ERG-jet™, Fabrinal, La Chaux-de-

.

Fonds, Switzerland) were used to perform testing on both eyes of each horse as has been previously reported.(14, 15) Topical anesthesia (0.5% Tetracaine hydrochloride ophthalmic solution, Bausch and Lomb Inc., Tampa, FL, USA) was applied to each eye prior to corneal electrode placement. The contact lens recording electrode was placed on the cornea with 2.5% hypromellose (Goniovisc™, Sigma Pharmaceuticals, LLC, Monticello, IA, USA) while stainless steel reference and ground electrodes (GVM geliMED, Bad Segeberg, Germany) were placed subcutaneously 3cm posterior to the lateral canthus and midway down the neck, respectively. All electrodes and the first stage amplifier were secured to the halter with tape to facilitate maintaining electrode positioning, as previously described.(14) The examination room was darkened so that testing of the dark adaption curve could commence and illumination was confirmed to be 0 Lux (LX1330B Digital Photometer, Dongguan Huayi Mastech Co., Ltd. Guangdong, China). The ERG was first recorded from the eye with the more extensive lesions in response to four low intensity light stimuli (0.03 cd·s/m^2) given at a frequency of 0.1 Hz at each time (*T*) point: *T* = 5, 10, 15, 20 minutes of dark adaptation. Consecutively, the combined rod-cone response was evaluated bilaterally in response to four high intensity light stimuli (3 cd·s/m^2 at 0.1 Hz) followed by cone function evaluation by flicker stimulus (3 cd·s/m^2 at 30Hz). The four light stimuli were averaged for each time point. The low band-pass limit was 0.3 Hz and the upper was 300 Hz.

Following data acquisition off-line analysis of the ERGs was performed using the HMsERG software. The a- and b-wave amplitudes and implicit times were measured for each horse.

RESULTS

Clinical evaluation of both horses revealed hundreds of bullet-hole lesions in the nontapetal fundus medial, lateral and ventral to the optic nerve head in OU with OS lesions subjectively more numerous in both horses. (Fig. 2) The tapetal fundus, retinal blood vessels and optic nerve heads appeared normal bilaterally in both horses with no evidence of retinal vascular attenuation over affected nontapetal regions. Incidental findings in Horse 1 (11 year old Arabian mare) included very mildly cystic corpora nigra and very mild vitreal degeneration in OU. Though no vision deficits were observed based on cranial nerve examination and navigation in ambient and dim light, moderate mydriasis was present in OU during clinical examination with positive but incomplete pupil light reflexes. The intraocular pressures were normal (OS- 26 mm Hg and OD- 28 mm Hg). Repeat evaluation of the pupils outside the clinical setting in sunlight revealed normal complete pupil constriction OU. Horse 2 (12 year old Arabian mare) also had mild vitreal degeneration (OD<OS), present and complete PLRs, and no detectable vision deficits based on cranial nerve examination and navigation in ambient and dim light. Intraocular pressures were OS- 17 mm Hg and OD- 16 mm Hg. Both horses initially exhibited occasional nervous excitement in the hospital setting, similar to other equine outpatients, but settled in quickly with no continued or consistent behavior issues.

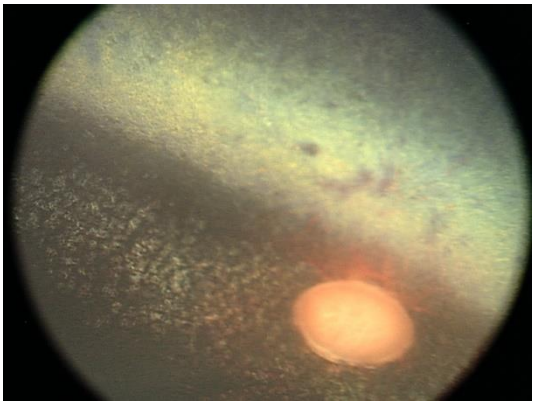

Figure 2. Appearance of the left fundus in the same patient showing subjectively denser bullet-hole lesions.

.

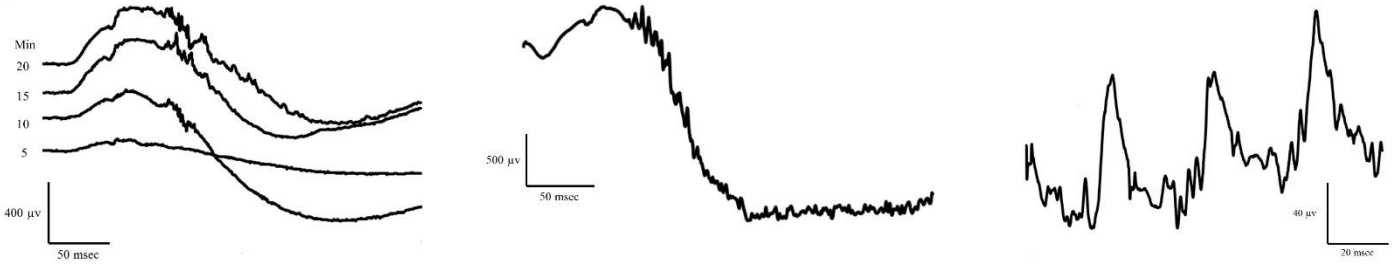

Figure 3. Representative traces of the different responses, recorded from the left eye of Horse 2. (a) Individual traces demonstrating the increased b-wave amplitude of the rod response during dark adaptation. (b) Combines rod-cone response. (c) Flicker cone response.

The scotopic b-wave amplitude increased continuously from 5 to 20 minutes of dark adaptation peaking at 446µv and 377µv for Horses 1 and 2 respectively. The b-wave amplitudes of the combined rod-cone response were OS- 459µv and OD- 392µv for Horse 1 and OS- 491µv and OD- 608µv for Horse 2. The full data of the a- and b-waves amplitudes and implicit times are presented in Tables 1 and 2. The amplitude of the flicker ERG for Horse 1 was OS- 86µv and OD- 110µv and for Horse 2 OS- 80µv and OD- 74µv. (Table 3) Representative traces of the ERG recordings are shown in Figure 3.

Table 1. Rod response of the left eye: b-wave amplitude and implicit time during dark adaptation

Dark adaptation	Horse 1 - b-wave		Horse 2 - b-wave	
(Min)	Amplitude (µv)	Implicit time (msec)	Amplitude (µv)	Implicit time (msec)
5	269	78	91	59
10	354	79	221	66
15	432	90	368	78
20	446	85	377	79

Table 2. Combined rod-cone response: amplitude and implicit time

		Horse 1		Horse 2	
		Amplitude (µv)	Implicit time (msec)	Amplitude (µv)	Implicit time (msec)
a-wave	Left eye	160	13	140	14
	Right eye	159	13	93	14
b-wave	Left eye	459	77	491	62
	Right eye	392	69	608	61

Table 3. Amplitudes of the cone flicker responses.

	Horse 1	Horse 2
	Amplitude (µv)	Amplitude (µv)
Left eye	86	80
Right eye	110	74

.

DISCUSSION

Extensive bullet-hole, or focal, chorioretinal lesions were found in both of the horses in this report as an incidental finding during ocular exams for other reasons. Horse 1 was noted to have numerous chorioretinal scars during prepurchase examination and was referred for evaluation. Horse 2 was noted to have bullet-hole lesions during a general physical, including a complete ocular examination. No evidence of lesion progression was noted in either horse up to two years following initial examination, however the lesions were too numerous to accurately count during either examination. Visual deficits were not noted at any time by the current or previous owners and attempted maze testing performed in the ISU LVMC did not reveal any subjective visual impediments. Furthermore, both horses are used for trail riding and no vision deficits have been observed when riding at any time of day, including night time.

Determining the effect of fundic or other ocular lesions on vision is extremely challenging due to lack of studies evaluating this correlation and the inability to use verbal communication with the veterinary patient, unlike with human patients. Subjective tests, such as maze testing and observation of the horse in unfamiliar environments can provide a crude estimate of visual function. Retinal function tests such as the full field ERG can help provide objective information to complete the assessment. Since the full field ERG evaluates cumulative retinal function, results within normal values do not guarantee normal function of all photoreceptors. Topographic evaluation of retinal function can be performed utilizing the multifocal ERG and may add to our understanding of the effect of bullet-hole lesions on retinal function. Moreover, post retinal lesions may affect vision but not the full field ERG. Nonetheless, when ERG deficits are present, it is likely that visual deficits are also present.

For both horses, ERG recordings were consistent with retinal function measured in horses free of ocular disease as recorded in our laboratory (data not published) and as previously reported.(14) The horses in this study are older than the horses in our previous report for which the average age was 6.2 years.(14) Comparison of ERG values should be ideally performed between breed- and age-matched groups. To date, there are no studies evaluating the effect of age on equine ERG. Nevertheless, the amplitudes in these two studies seem comparable. Ben-Shlomo *et al* have demonstrated that multifocal outer retinal lesions spread throughout half of the retina lead to significant reduction of b-wave amplitude in the rat.(16) While direct comparison between the equine and rat retina is suboptimal, we hypothesized that extensive bullet-hole lesions, as seen in these two horses, would affect the full field ERG amplitude if these lesions involved the outer retina. Such an effect was not documented in this study; however, further anatomical study would help determine the effect of bullet-hole lesions on these horses' outer retinas.

Optical coherence tomography (OCT) could be performed to assess retinal structural changes in the region of these lesions as has been recently described.(17, 18) A single horse with bullet-holes had spectral domain (SD)-OCT performed and images showed hyperechoic lesions suggesting cellular proliferation or migration within the outer retina.(18) It is unknown whether the changes represent primary retinal cells, migrating pigment cells, or other changes. As previously mentioned, histologically-studied lesions show loss of normal retinal architecture with pigment cell alterations but effect on retinal function or vision is still uncertain.(1) Fluorescein angiography could also be performed to further characterize the lesions in these two horses and compared to normal horse findings.(19) Slater *et al* noted hyperfluorescence to focal depigmented lesions in the nontapetal fundus which occurred in three ponies six to eight weeks following experimental intranasal EHV-1 infection and speculated choroidal infarction

.

as a cause but did not note retinal vascular phase deficits or leakage to suggest peripapillary retinal compromise.(10) A more recent publication points out that infarction of the choroidal vasculature would be expected to appear as nonfluorescing, dark areas on fluorescein angiography which is inconsistent with the previous description.(11)

Critical review of the two cases in our study does reveal some indicators of possible retinal compromise. The first is the relative mydriasis and incomplete PLRs noted for Horse 1 at the time of both clinical examinations 2 years apart; however, when pupil size was later evaluated outside on a sunny day complete pupil constriction was present OU. This finding suggests sympathetic stimulation affecting pupil dilation due to anxiety at the time of in-hospital examinations.(20) The second was initial nervous behaviors to unfamiliar objects and circumstances in the hospital as noted during the ophthalmic examinations and intermittently observed by owners of both horses. Behaviors like this are not uncommon in horses and are especially notable in Arabians with an apparent higher grade of reactivity than horses of some other breeds; hence we did not attribute it to visual deficits.

As is consistent with a claim in the literature(6) and personal experience, no evidence of active chorioretinal disease or bullet-hole lesion progression was noted in either of these patients. Nell and Walde(11) do state that widespread occurrence of bullet-hole lesions may lead to progressive fundus degeneration accompanied by subtle to obvious visual impairment, but that did not occur in these two horses with extensive lesions. Both horses were reexamined 16 months following ERG assessment for a total of 34-40 months follow-up with no changes noted. It is possible that respiratory disease or viral infection earlier in these horses' lives could have caused the chorioretinal scars. The lesion extent in both horses is more severe than those pictured in other reports, yet still did not affect ERG results or cause any observable visual deficits.

In one study of 204 racing Thoroughbreds 50% of horses had peripapillary focal inactive bullet-hole lesions that numbered less than 20 and were presumed to have little impact on equine vision. Five horses in the study had greater than 20 lesions with one of the horses noted to have greater than 50 appearing in a linear band.(3) The horses with more than 20 lesions were categorized with potential vision-threatening eye disease in that report. In these two horses with extensive bullet-hole chorioretinal lesions no outer retinal function deficits were observed on electroretinographic evaluation. Further studies could be performed to evaluate in vivo structural changes to the retina and inner retinal function. Histologic examination could also be performed to look for microscopic structural changes if ocular tissues become available in these horses for other reasons.

In conclusion, even extensive bullet-hole chorioretinal lesions may not cause observable visual or ERG deficits in horses. This is consistent with the previous claim that equine bullet-holes may be considered nonprogressive incidental findings.(6) Horses with lesions may still be good companion horses and this should be considered when performing equine prepurchase examinations.

REFERENCES

1. Matthews AG. Fundus. In: Barnett KC, Crispin SM, Lavach JD, Matthews AG, editors. Equine Ophthalmology: An Atlas and Text. 2nd ed. London: Saunders Elsevier; 2004. p. 211-46.

.

2. Rushton J, Tichy A, Brem G, Druml T, Nell B. Ophthalmological findings in a closed herd of Lipizzaners. Equine veterinary journal. 2013 Mar;45(2):209-13. PubMed PMID: 23009263. Epub 2012/09/27. eng.
3. Hurn SD, Turner AG. Ophthalmic examination findings of Thoroughbred racehorses in Australia. Vet Ophthalmol. 2006 Mar-Apr;9(2):95-100. PubMed PMID: 16497233.
4. Rebhun WC. Retinal and optic nerve diseases. The Veterinary clinics of North America Equine practice. 1992;8(3):587-608.
5. Matthews AG, Crispin SM, Parker J. The equine fundus. III: Pathological variants. Equine veterinary journal Supplement. 1990 Sep(10):55-61. PubMed PMID: 9079119. Epub 1990/09/01. eng.
6. Wilkie DA. Diseases of the ocular posterior segment. In: Gilger BC, editor. Equine Ophthalmology. 2nd ed. Maryland Heights, Missouri: Elsevier Saunders; 2011. p. 367-96.
7. Cutler TJ, Brooks DE, Andrew SE, Denis HM, Biros DJ, Gelatt KN, et al. Disease of the equine posterior segment. Vet Ophthalmol. 2000;3(2-3):73-82.
8. Roberts SR. Chorioretinitis in a band of horses. Journal of the American Veterinary Medical Association. 1971 Jun 15;158(12):2043-6. PubMed PMID: 5104477. Epub 1971/06/15. eng.
9. Slater JD, Gibson JS, Barnett KC, Field HJ. Chorioretinopathy associated with neuropathology following infection with equine herpesvirus-1. The Veterinary record. 1992 Sep 12;131(11):237-9. PubMed PMID: 1332242. Epub 1992/09/12. eng.
10. Slater JD, Arnold JA, Taylor KM, Baxi S, Field HJ. Fluorescein angiographic appearance of the normal fundus and of focal chorioretinal lesions in the horse (Abstract). Investigative Ophthalmology and Visual Science. 1995;36(4):S779.
11. Nell B, Walde I. Posterior segment diseases. Equine veterinary journal Supplement. 2010 Mar(37):69-79. PubMed PMID: 20939170. Epub 2010/10/14. eng.
12. Williams RD, Morter RL, Freeman MJ, Lavignette AM. Experimental chronic uveitis. Ophthalmic signs following equine leptospirosis. Investigative ophthalmology. 1971 Dec;10(12):948-54. PubMed PMID: 5128770. Epub 1971/12/01. eng.
13. Gilger BC. Equine ophthalmology. In: Gelatt KN, Gilger BC, Kern TJ, editors. Veterinary Ophthalmology. II. 5th ed. Ames, Iowa: Wiley-Blackwell; 2013. p. 1560-609.
14. Ben-Shlomo G, Plummer C, Barrie K, Brooks D. Characterization of the normal dark adaptation curve of the horse. Vet Ophthalmol. 2012 Jan;15(1):42-5. PubMed PMID: 22051221. Epub 2011/11/05. eng.
15. Church ML, Norman JC. Electroretinogram responses of the normal thoroughbred horse sedated with detomidine hydrochloride. Vet Ophthalmol. 2012 Sep;15 Suppl 2:77-83. PubMed PMID: 22498137. Epub 2012/04/14. eng.
16. Ben-Shlomo G, Belokopytov M, Rosner M, Dubinsky G, Belkin M, Epstein Y, et al. Functional deficits resulting from laser-induced damage in the rat retina. Lasers in surgery and medicine. 2006 Aug;38(7):689-94. PubMed PMID: 16868934. Epub 2006/07/27. eng.
17. Pinto NI, Gilger BC. SD-OCT corneal and retinal measurements on standing horses. Abstracts: 44th Annual Meeting of the American College of Veterinary Ophthalmologists, Puerto Rico, November 4–9, 2013. Veterinary Ophthalmology. 2013;16(6):E26-E50.
18. Gilger BC, Pinto NI, Clode AB. Common equine ocular fundus lesions evaluated by SD-OCT (abstract). IEOC/Acrivet Equine Ophthalmology Symposium. 2013:43.

.

19. Molleda JM, Cervantes I, Galan A, Tardon R, Gallardo JM, Martin-Suarez EM. Fluorangiographic study of the ocular fundus in normal horses. Vet Ophthalmol. 2008 Sep;11 Suppl 1:2-7. PubMed PMID: 19046263. Epub 2008/12/17. eng.
20. Gum GG, Mackay EO. Physiology of the eye. In: Gelatt KN, Gilger BC, Kern TJ, editors. Veterinary Ophthalmology. I. 5th ed. Ames, IA: Wiley-Blackwell; 2013. p. 171-207.

.