Chapter 16

Visual Evoked Potential Recording in Rodents

Yuyi You, Alexander Klistorner, and Stuart L. Graham

Abstract

The visual evoked potential (VEP) is an electronic potential recorded from the visual cortex in response to a visual stimulus. It provides a means to examine the function of the visual pathway from the retina to the occipital cortex. The most common animals employed in VEP laboratory studies are rats. In this chapter, we describe the basic 'flash VEP' recording protocol in rodents and discuss the practical aspects of the preparation including anaesthesia methods, electrode configuration, stimulus design, dark adaptation, filter settings and signal sampling with the authors' personal experience. We also review the recent use of the VEP in laboratory researches in several optic nerve disease models, including glaucoma, ischemic optic neuropathy and optic neuritis.

Key words: Visual evoked potential, Electrophysiology, Visual cortex, Optic nerve, Optic neuritis, Glaucoma, Rodent

1. Introduction

The visual evoked potential (VEP) is an electronic potential recorded from the visual cortex in response to a visual stimulus (e.g. flash stimulus, pattern reversal stimulus, pattern onset/offset stimulus). It reflects the post-retinal function from the retina to the primary visual cortex (1). Optic nerve diseases such as optic neuritis (2) and glaucoma (3) will affect the VEP signal. The VEP provides an objective means for measuring the function of the visual pathway and is widely used to assess the visual performance in laboratory animals, including rats, mice, guinea pigs, rabbits, cats, dogs and primates (4). Rats and mice have become key animal models for ophthalmic research. They are the most common species employed in VEP studies because of their accessibility with a short growth cycle, which is important for genetic studies in mutant strains. Additionally, the visual pathway from the retina to the visual cortex of both species shares many similarities with that of

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humans, such as cell types and structure features (5). Because of the low spatial resolution of the rodent visual system and the high refractive index of the rodent cornea, the flash VEPs are predominantly used.

Since Creel et al. (6, 7) described the VEP waveform in rats and designated the P1, N1, P2, N2, P3 and N3 components (Fig. 1), the rodent VEP has been widely used to study ocular diseases and the effects of drugs on the visual system. However, it is important to note that in the literature the rat (6–20), as well as mouse (21–27), VEP waveforms were variable between different labs. This can be attributed, at least in part, to different strains used in these experiments. Furthermore, length of dark adaptation, anaesthesia, electrode configuration, stimulus design and filter settings also have a significant impact on the latency and amplitude of the VEP waveform (see Notes below (Sect. 4)). For example, the rat VEP amplitude we have reported (28, 29) was smaller than that from Heiduschka et al. (8), which is very likely due to the short adaptation, the albino rat strain and the monocular flash stimulation. Therefore, a standardised recording protocol needs to be determined before the rodent VEP can be compared between different labs. It is also important to understand that the early VEP components (P1–N1–P2 complex, Fig. 1) following the flash illumination are more stable and principally affected by the excitation of the primary visual cortex via retino-geniculate fibres, whereas the later components may have significant contribution from higher visual areas and therefore are affected by behavioural state or level of consciousness (7, 16).

Here, we focus on the rodent VEP recording protocol, summarise the practical procedures and discuss the use of rodent VEP in some rodent eye disease models.

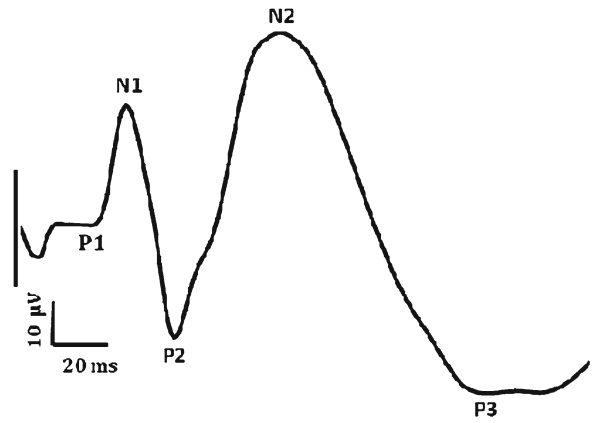

Fig. 1. An averaged flash VEP waveform from SD rats. The components are designated into positive (P1, P2, P3) and negative (N1, N2) peaks.

2. Materials

1. Animals: Rat (e.g. Sprague-Dawley, Long-Evans), mouse (e.g. C57BL/6J)
2. Anaesthetics: Ketamine (80 mg/kg) and medetomidine (0.5 mg/kg)
3. Mydriatic eye drops: 1.0% tropicamide (Alcon Laboratories)
4. Warming pad: Homoeothermic blanket system (Harvard Apparatus)
5. Impedance Meter: F-EZM5 (Grass)
6. Electrodes Screw electrodes: M1.0 × 3 mm Csk Slot M/T 304 S/S (Micro Fasteners, Australia)

   Subdermal needle electrodes: F-E3M-72 (Grass)
7. Dental cement: Rapid Repair (DeguDent GmbH)
8. Visual stimuli: Strobe photostimulator PS33-PLUS (Grass) or a Ganzfeld stimulator
9. Band-pass filter and amplifier: BMA-400 Bioamplifier (CWE, Inc.)
10. Computer-based signal analysing system: CED Power1401 and Spike 2 (Cambridge Electronic Design, Ltd.)

3. Methods

3.1. Anaesthesia

Animals are anaesthetised with an intraperitoneal injection of ketamine (80 mg/kg) and medetomidine (0.5 mg/kg) for both surgery and VEP recording (see Note (Sect. 4.1) for the choice of anaesthetics).

3.2. Screw Electrode Implantation

After anaesthesia, the skin on the head is disinfected with 75% ethanol and a longitudinal incision is made. Small burr holes are drilled manually using a micro hand drill at 7 mm behind the bregma and 3 mm lateral of the midline. Screw electrodes are implanted through the skull just into the cortex (area 17), penetrating the cortex to approximately 0.5 mm. A reference screw electrode is also implanted on the midline 3 mm rostral to the bregma. Dental cement is used to encase and fix the screws. The wound is sutured and antibiotics administrated (Fig. 2 below with photograph and diagram showing landmarks and electrode positions). At least 1 week is allowed for the rats to recover from the surgery.

3.3. Recording Procedures

The animals are anaesthetised, placed in a dark room and allowed to adapt to darkness for 5 min. Body temperature is maintained at

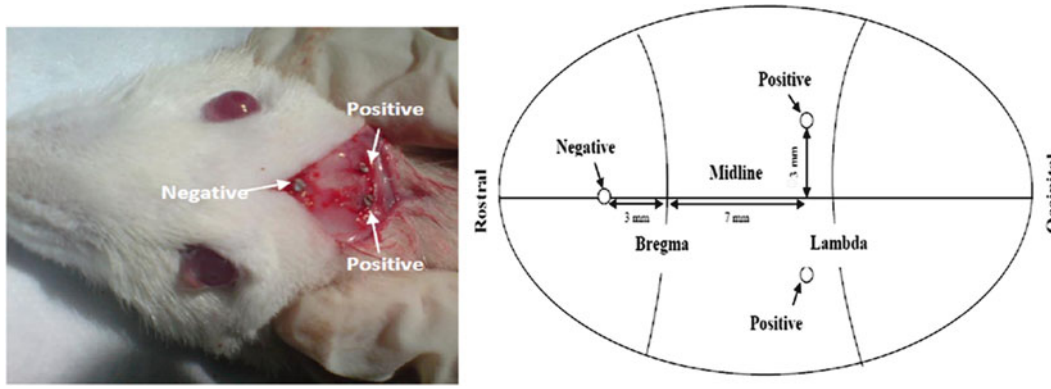

Fig. 2. Positive electrodes are implanted in area 17 of the primary visual cortex (7 mm behind the bregma and 3 mm lateral of the midline). A negative electrode is implanted on the midline 3 mm rostral to the bregma (You et al. ARVO 2011 E-Abstract 6100).

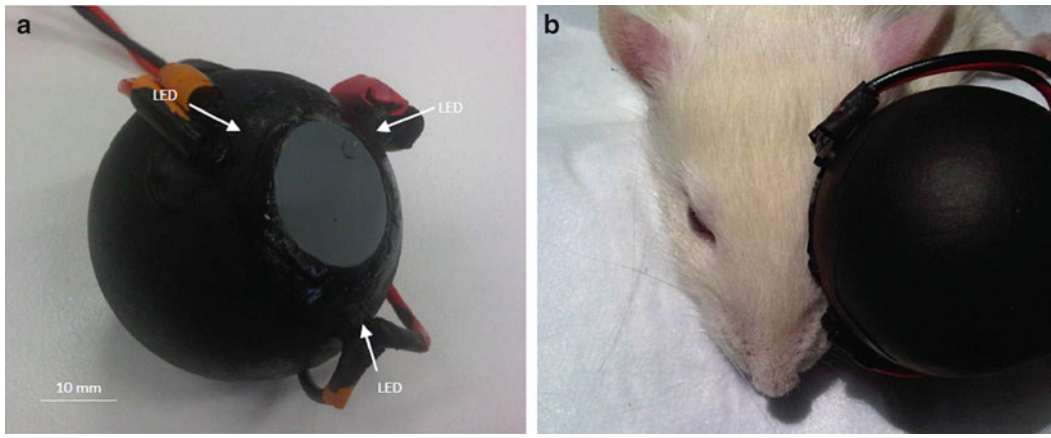

Fig. 3. (**a**) A mini-Ganzfeld stimulator; (**b**) mini-Ganzfeld with a positioned rat (You et al. (29)).

37 ± 0.5°C by the homoeothermic blanket system with a rectal thermometer probe. The pupils are dilated using 1.0% tropicamide eye drops. The skin over the skull is opened to access the preplaced in situ screws. The screw over the contralateral visual cortex of the stimulated eye and the reference screw are connected to the amplifier. A needle electrode is inserted into the tail as the ground. The electrode impedance is measured and maintained below 5 kΩ. The strobe photostimulator is fixed 15 cm from the eye. Alternatively, a mini-Ganzfeld stimulator (Fig. 3) can be used which should be placed directly on the skin around the eyelids to provide superior eye isolation. The illuminations of all stimuli need to be calibrated by a photometer. Photic stimulation is delivered 100 times at a frequency of 1 Hz. Responses are amplified 20,000 times with low and high band-pass filter settings of 1 and 100 Hz. The signal is sampled at 5 kHz.

3.4. VEP Follow-Up in an Individual Animal

After the recording, the wound is closed and antibiotics administrated. The animals are allowed to recover on a warming pad. The VEP can be repeatedly recorded on individual animals to study the time course of diseases or to assess the effects of therapeutic agents.

4. Notes

4.1. Anaesthesia and Body Temperature Maintenance

Different types of anaesthetics and the depth of anaesthesia can affect the VEP waveforms (4, 27). The VEP latency with pentobarbital anaesthesia was longer than that with ketamine in rabbits (30). Meeren et al. (16) compared the rat VEP recorded during various sleep–wake states, and they found state-dependent alterations of the N2–P3 components. In our lab, we routinely use ketamine (31) in combination with an alpha-adrenoceptor agonist such as xylazine (15 mg/kg) or medetomidine diluted in saline and injected intraperitoneally. Combination ketamine/medetomidine anaesthesia provides stable anaesthesia (60–90 min) that can quickly be reversed by administration of an alpha-receptor antagonist such as atipamezole (2.5 mg/kg). Medetomidine is a more selective agent than xylazine (32) and is therefore used in preference. Top-up doses should contain ketamine only (10% of initial dose). Pentobarbital sodium (Nembutal®) also has been widely used for VEP recording in rodents. However, it is important to note that pentobarbital is not permitted for use in rodent recovery experiments in some countries according to the local animal ethics legislations. Corneal clouding and cataracts in rodents can reduce the light available to the retina and affect the reliability of the VEP signal. The cataracts mainly result from the dehydration of the cornea in anaesthetised animals (33, 34). The authors recommend that moisture eye drops (e.g. Optive®) be used regularly during the recording procedures.

Body temperature can also have a significant impact on the speed of nerve conduction, especially in demyelinated nerves (Uhthoff phenomena) (35). Temperature-dependent changes in visual evoked potentials were observed in rats (36, 37)—both flash and pattern VEP latencies were significantly longer as body temperature was lowered (37). In our lab, the body temperature of the rodents is maintained at 37 ± 0.5°C during the experiments by a homoeothermic blanket system with a rectal thermometer probe.

4.2. Electrode Configuration

Electrode positioning requires consideration of the anatomy of the rodent visual cortex. The recorded VEPs are the net postsynaptic potentials in large pyramidal cells oriented perpendicular to the visual cortical surface (38). Unlike humans, the primary visual cortex of rodents is relatively flat and exposed on the surface of the brain. Cytoarchitectonic area 17 occupies an area of 2–3 mm^2 and is the

Table 1
Intersession reproducibility analysis of the rat VEP latency with subdermal needle and implanted screw electrodes (both with 3 cd/m^2 strobe flash) (29)

	Sw (ms)	CoV (%)	ICC
Needle ($n=6$)	7.95	11.14	0.02
Screw ($n=5$)	3.83	6.74	0.73
P value	0.024*	0.013	0.001*

Sw within-subject standard deviations; *CoV* coefficient of variation; *ICC* intraclass correlation coefficient
*$P<0.05$

only cortical area that receives its principle input from the dorsal lateral geniculate nucleus (4, 39). We routinely implant the screw electrodes through the skull into area 17 (7 mm behind the bregma and 3 mm lateral of the midline) to serve as the active electrodes (Fig. 2). A variety of the negative electrode positions are described in the literature for rodent VEP recording (6–27). We have found that a screw electrode on the midline 3 mm rostral to the bregma provided superior signal with high signal-to-noise ratios. For the ground lead, it is convenient to use a stainless needle electrode and insert into the animal's tail, two-thirds from its base.

Some laboratories also use subdermal needles as the active electrodes to measure the VEP in rodents non-invasively (26). However, it has been reported that the electrode positioning significantly affected the latency and amplitude of the VEP waveform (15) and the position of the needle electrode is relatively more variable. We found that the intersession reproducibility of the VEP parameters was significantly higher with screw electrodes than with subdermal needle electrodes (Table 1) (29). Therefore, the choice of the electrodes is dependent on the objective of the research. If the project aims at quantifying the nerve conduction by the VEP or monitoring the visual system function over time, we suggest that only screw electrodes be used. Furthermore, the amplitude of the VEP with subdermal electrodes is significantly smaller than that with screws.

4.3. Dark Adaptation

Both rod and cone pathways contribute to the VEP (5). The purpose of dark adaptation is to ensure higher photoreceptor sensitivity, and the amplitude of the VEP significantly increased in dark-adapted rats. In our lab, the animals are placed in a dark room and allowed to adapt to dark for 5 min before the actual recording (28, 29). We found overnight dark adaptation is not necessary for the VEP, which is a routine procedure for electroretinogram (ERG) recording (34).

First, the amplitude of the VEP after 5-min adaptation is already quite acceptable and repeatable for analysis. Secondly, it is not convenient to perform VEP recording in fully dark-adapted animals with a standard flash (3 cd s/m^2), as VEP recording needs about 100 repeated flashes to minimise the noise from the cortical activity (electroencephalogram, EEG)—the flashes rapidly light-adapt the animals. Thirdly, the VEP is designed to investigate post-retinal function; therefore, it is not important to separate the rods and cones in most cases. However, to obtain more reliable VEP signals, we highly recommend the recording be performed under dim background lighting with constant luminance.

4.4. Visual Stimuli

The flash VEP in rodents is well described using various visual stimuli, including a strobe photostimulator (7, 11, 15) and the full-field (Ganzfeld) system (8, 9, 12, 24). These conventional visual stimuli work well for rodents. As the flash illumination can significantly affect the latency and amplitude of the VEP, it is important to always calibrate the stimulus before recording. The stimulus intensity can be measured in cd s/m^2. 3.0 cd s/m^2 is the International Society for Clinical Electrophysiology of Vision (ISCEV) standard flash (40). In many eye disease models, one eye is treated, leaving the other to serve as an internal control. Using the conventional visual stimuli, we found it difficult to entirely isolate the treated eye and the control eye even when well covered, especially in some albino species. This may be due to light penetration through the surrounding scalp and tissue. We designed a mini-Ganzfeld stimulator for the rodents, which consists of a 40-mm diameter ball, three LEDs and an intensity controller (Fig. 3), and it provided superior repeatability in both latency and amplitude.

We compared VEP signals from this full-field stimulus with a focal flash (light-emitting diode, LED) and found the full-field flash showed significantly better repeatability than the LED (Fig. 4 and Table 2) (29). Considering that rat photoreceptors distribute more peripherally than human (41), we suggest that only a full-field stimulus should be used for rodent flash VEP recording and the pupils should always be fully dilated. Rodent VEP responses may also be obtained using patterned stimuli (25). A pattern stimulus is used to assess several aspects of the visual system, such as visual acuity, cortical magnification factor and contrast threshold. However, it is important to consider the low spatial resolution and high corneal refraction of rodents when designing the pattern stimuli (26).

4.5. Filter Settings and Signal Averaging

The VEP is an EEG-based signal; however, it is small compared to the EEG. Therefore, the stimulation usually has to be repeated ~100 times to obtain an adequate signal-to-noise ratio from the EEG. It is estimated that after 100 repetitions, noise is reduced tenfold (38). The settings of low and high band-pass filter also have effects on the rat flash VEP (42). According to the literature,

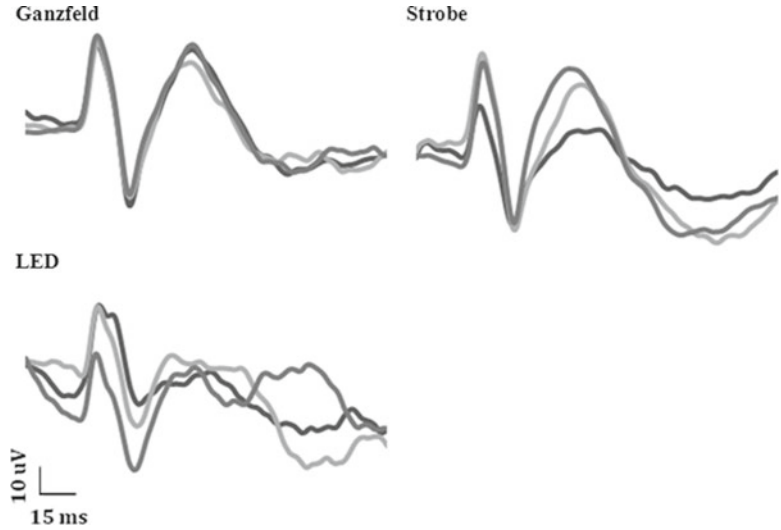

Fig. 4. Overlays of the VEP traces recorded from an individual rat using different flash stimulators.

Table 2
Intraclass correlation coefficient of the rat VEP using different visual stimuli ($n = 10$) (29)

		Ganzfeld	Strobe	LED
Intrasession	Latency	0.85	0.72	0.59
	Amplitude	0.96	0.83*	0.70*
Intersession	Latency	0.70	0.62	0.42*
	Amplitude	0.81	0.70	0.44*

*$P < 0.05$ compared to Ganzfeld

the low band-pass setting is usually 0.1–1 Hz and the high band-pass is 100–200 Hz. We routinely sample VEP waveforms using filter settings of 1–100 Hz, with which the signal should be sampled at least about 250–300 Hz to ensure that more than two samples are collected by the computer during each cycle of the highest frequency (f_{MAX}) (Nyquist rate $= 2 \times f_{MAX} = 200$ Hz; $2.3 \times f_{MAX} = 230$ Hz is for practical use) (38). We usually set the sampling rate at 5 kHz, as we also use this system to record the ERG, the f_{MAX} of which is 1,000–2,000 Hz.

4.6. Examples of VEPs in Eye Disease Models

The VEP is used extensively in pharmacological and toxicological experiments, as it provides a non-invasive means of monitoring neural activity and sensory processing in vivo.

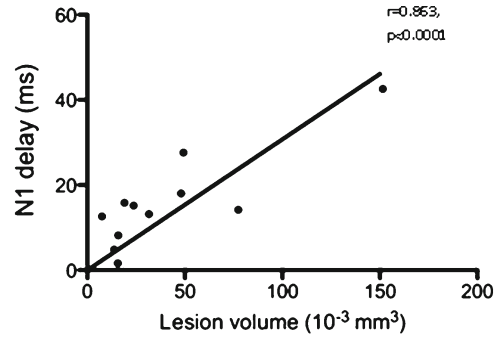

Fig. 5. The VEP is proposed to assess the integrity of the visual pathway in optic neuritis patients by Halliday et al. (2). The amplitude of the VEP is believed to reflect the number of functional optic nerve fibres (46). It was also suggested that the effect of conduction change can be qualitatively measured by the latency delay of the VEP (2, 47, 48). There was an assumption that initial latency prolongation of the VEP corresponds to the size of the demyelinated area of the optic nerve in optic neuritis, while subsequent shortening of latency was thought to represent the process of optic nerve remyelination. The VEP is also used to investigate visual pathway function in some laboratory models of multiple sclerosis (49, 50). In these studies, a correlation between VEPs and histopathologic results was observed. However, it is hard to reproduce and to quantify the demyelination in the visual pathway in a multiple sclerosis model. We recently develop a rat model of focal demyelination in the optic nerve. The figure shows linear regression analysis of the latency delay of N1 peak and the lesion volume in the optic nerve ($r = 0.863$, $p < 0.0001$) (You et al. (28)).

The VEP is also employed in many eye disease models, especially optic nerve disease models to assess the visual function. In a retinal ischemia-reperfusion model of rat, the reduction in VEPs was correlated with the duration of ischemia (12). In another paper, the VEP was used to assess the neuroprotective effect of transcorneal electrical stimulation on optic nerve injury (11). The VEP was also useful in developing a rodent model of anterior ischemic optic neuropathy (19). Recently, we used the VEP to assess the amount of demyelination in a rat model of focal demyelination in the optic nerve and observed a strong correlation between the latency delay and the lesion size (Fig. 5) (28).

ISCEV has published several standards for VEP and ERG recording in humans. A dog electroretinography recording guideline was also proposed (43). As mentioned above, in the literature rodent VEP waveforms were relatively variable. A VEP recording standard is necessary before rodent VEPs can be compared between different labs. A multifocal VEP (44) has not been reported in animals, which may also be useful in assessing the visual function of specific regions of the visual field. The blue-on-yellow VEP may be useful in investigating the koniocellular pathway in primates (45).

References

1. Creutzfeldt O, Maekawa K, Hosli L (1969) Forms of spontaneous and evoked postsynaptic potentials of cortical nerve cells. Prog Brain Res 31:265–273
2. Halliday A, McDonald W, Mushin J (1972) Delayed visual evoked response in optic neuritis. Lancet 1:982–985
3. Towle V, Moskowitz A, Sokol S, Schwartz B (1983) The visual evoked potential in glaucoma and ocular hypertension: effects of check size, field size, and stimulation rate. Invest Ophthalmol Vis Sci 24:175–183
4. Ridder W (2006) Visual evoked potentials in animals. In: Heckenlively JR, Arden GB (eds) Principles and practice of clinical electrophysiology of vision. The MIT Press, Cambridge, pp 935–947
5. Ridder W, Nusinowitz S (2006) The visual evoked potential in the mouse—origins and response characteristics. Vision Res 46:902–913
6. Creel D, Dustman R, Beck E (1973) Visually evoked responses in the rat, guinea pig, cat, monkey, and man. Exp Neurol 40:351–366
7. Creel D, Dustman RE, Beck EC (1974) Intensity of flash illumination and the visually evoked potential of rats, guinea pigs and cats. Vision Res 14:725–729
8. Heiduschka P, Schraermeyer U (2008) Comparison of visual function in pigmented and albino rats by electroretinography and visual evoked potentials. Graefes Arch Clin Exp Ophthalmol 246:1559–1573
9. Iwamura Y, Fujii Y, Kamei C (2003) The effects of certain H1-antagonists on visual evoked potential in rats. Brain Res Bull 61:393–398
10. Iwamura Y, Fujii Y, Kamei C (2004) The effects of selective serotonin-reuptake inhibitor on visual evoked potential in rats. J Pharmacol Sci 94:271–276
11. Miyake K-I, Yoshida M, Inoue Y, Hata Y (2007) Neuroprotective effect of transcorneal electrical stimulation on the acute phase of optic nerve injury. Invest Ophthalmol Vis Sci 48:2356–2361
12. Jehle T, Wingert K, Dimitriu C, Meschede W, Lasseck J, Bach M, Lagreze WA (2008) Quantification of ischemic damage in the rat retina: a comparative study using evoked potentials, electroretinography, and histology. Invest Ophthalmol Vis Sci 49:1056–1064
13. Papathanasiou ES, Peachey NS, Goto Y, Neafsey EJ, Castro AJ, Kartje GL (2006) Visual cortical plasticity following unilateral sensorimotor cortical lesions in the neonatal rat. Exp Neurol 199:122–129
14. Tomita H, Sugano E, Yawo H, Ishizuka T, Isago H, Narikawa S, Kugler S, Tamai M (2007) Restoration of visual response in aged dystrophic RCS rats using AAV-mediated channelopsin-2 gene transfer. Invest Ophthalmol Vis Sci 48:3821–3826
15. Onofrj M, Harnois C, Bodis-Wollner I (1985) The hemispheric distribution of the transient rat VEP: a comparison of flash and pattern stimulation. Exp Brain Res 59:427–433
16. Meeren H, Van Luijtelaar E, Coenen A (1998) Cortical and thalamic visual evoked potentials during sleep-wake states and spike-wave discharges in the rat. Electroencephalogr Clin Neurophysiol 108:306–319
17. Goto Y, Furuta A, Tobimatsu S (2001) Magnesium deficiency differentially affects the retina and visual cortex of intact rats. J Nutr 131:2378–2381
18. Yargicoglu P, Yaras N, Agar A, Gumuslu S, Bilmen S, Ozkaya G (2003) The effect of vitamin E on stress-induced changes in visual evoked potentials (VEPs) in rats exposed to different experimental stress models. Acta Ophthalmol Scand 81:181–187
19. Bernstein S, Guo Y, Kelman S, Flower R, Johnson M (2003) Functional and cellular responses in a noval rodent model of anterior ischemic optic neuropathy. Invest Ophthalmol Vis Sci 44:4153–4162
20. Herr D, Kim T, King D, Boyes W (1996) Possible confounding effects of strobe “clicks” on flash evoked potentials in rats. Physiol Behav 59:325–340
21. Green D, Herreros de Tejada P, Glover M (1994) Electrophysiological estimates of visual sensitivity in albino and pigmented mice. Vis Neurosci 11:919–925
22. Lopez L, Brusa A, Fadda A, Loizzo S, Martinangeli A, Sannita WG, Loizzo A (2002) Modulation of flash stimulation intensity and frequency: effects on visual evoked potentials and oscillatory potentials recorded in awake, freely moving mice. Brain Res 131:105–114
23. Mazzucchelli A, Conte S, D’Olimpio F, Ferlazzo F, Loizzo A, Palazzesi S, Renzi P (1995) Ultradian rhythms in the N1-P2 amplitude of the visual evoked potential in two inbred strains of mice: DBA/2J and C57BL/6. Behav Brain Res 67:81–84
24. Peachey NS, Roveri L, Messing A, McCall MA (1997) Functional consequences of oncogene-induced horizontal cell degeneration in the retinas of transgenic mice. Vis Neurosci 14:627–632
25. Porciatti V, Pizzourusso T, Maffei L (1999) The visual physiology of the wild type mouse determined with pattern VEPs. Vision Res 39:3071–3781

26. Peachey NS, Ball SL (2003) Electrophysiological analysis of visual function in mutant mice. Doc Ophthalmol 107:13–36
27. Henry K, Rhoades R (1978) Relation of albinism and drugs to the visual evoked potential of the mouse. J Comp Physiol Psychol 92: 271–279
28. You Y, Klistorner A, Thie J, Graham S (2011) Latency delay of visual evoked potential is a real measurement of demyelination in a rat model of optic neuritis. Invest Ophthalmol Vis Sci 52:6911–6918
29. You Y, Klistorner A, Thie J, Graham S (2011) Improving reproducibility of VEP recording in rats: electrodes, stimulus source and peak analysis. Doc Ophthalmol 123:109–119
30. Castro-Junior J, Resende L, Bertotti M, Fonseca R, Zanchetta S, Schelp A (2005) Comparision of the effects of barbiturate, benzodiazepine and ketamine on visual evoked potentials in rabbits. Electromyogr Clin Neurophysiol 45:259–262
31. Anis N, Berry S, Burton N, Lodge D (1983) The dissociative anaesthetics, ketamine and phencyclidine, selectively reduce excitation of central mammalian neurones by N-methyl-aspartate. Br J Pharmacol 79:565–575
32. Virtanen R, Savola J, Saano V, Nyman L (1988) Characterization of the selectivity, specificity and potency of medetomidine as an alpha 2-adrenoceptor agonist. Eur J Pharmacol 150:9–14
33. Ridder W, Nusinowitz S, Heckenlively J (2002) Cause of cataract development in anesthetized mice. Exp Eye Res 75:365–370
34. Weymouth AE, Vingrys AJ (2008) Rodent electroretinography: methods for extraction and interpretation of rod and cone responses. Prog Retin Eye Res 27:1–44
35. Smith KJ, Waxman SG (2005) The conduction properties of demyelinated and remyelinated axons. In: Waxman SG (ed) Multiple sclerosis as a neuronal disease. Elsevier Academic Press, Amsterdam, pp 85–100
36. Boyes W, Padilla S, Dyer R (1985) Body temperature-dependent and independent actions of chlordimeform on visual evoked potentials and axonal transport in optic system of rat. Neuropharmacology 24:743–749
37. Hetzler B, Boyes W, Creason J, Dyer R (1988) Temperature-dependent changes in visual evoked potentials of rats. Electroencephalogr Clin Neurophysiol 70:137–154
38. Fahle M, Bach M (2006) Origin of the visual evoked potentials. In: Heckenlively J, Arden G (eds) Principles and practice of clinical electrophysiology of vision. MIT Press, Cambridge, pp 207–234
39. Leamey CA, Protti DA, Dreher B (2008) Comparative survey of the mammalian visual system with reference to the mouse. In: Chalupa LM, Williams RW (eds) Eye, retina, and visual system of the mouse. MIT Press, Cambridge, pp 35–60
40. Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, Tormene AP, Vaegan (2010) ISCEV standard for clinical visual evoked potentials (2009 update). Doc Ophthalmol 120:111–119
41. McCall M, Robinson S, Dreher B (1987) Differential retinal growth appears to be the primary factor producing the ganglion cell density gradient in the rat. Neurosci Lett 79:78–84
42. Shaw N (1992) The effects of low-pass filtering on the flash visual evoked potential of the albino rat. J Neurosci Methods 44:233–240
43. Narfstrom K, Ekesten B, Rosolen S, Spiess B, Percicot C, Ofri R (2002) Guidelines for clinical electroretinography in the dog. Doc Ophthalmol 105:83–92
44. Klistorner A, Crewther D, Crewther S (1997) Separate magnocellular and parvocellular contributions from temporal analysis of the multifocal VEP. Vision Res 37:2161–2169
45. Klistorner A, Graham S, Martins A, Grigg J, Arvind H, Kumar R, James A, Billson F (2007) Multifocal blue-on-yellow visual evoked potentials in early glaucoma. Ophthalmology 114:1613–1621
46. Klistorner A, Arvind H, Nguyen T, Garrick R, Paine M, Graham S, O'Day J, Grigg J, Billson F, Yiannikas C (2008) Axonal loss and myelin in early ON loss in postacute optic neuritis. Ann Neurol 64:325–331
47. Klistorner A, Graham S, Fraser C, Garrick R, Nguyen T, Paine M, O'Day J, Arvind H, Billson F (2007) Electrophysiological evidence for heterogeneity of lesions in optic neuritis. Invest Ophthalmol Vis Sci 48:4549–4556
48. Youl B, Turano G, Miller D, Towell A, MacManus D, Moore S, Jones S, Barrett G, Kendall B, Moseley I (1991) The pathophysiology of acute optic neuritis: an association of gadolinium leakage with clinical and electrophysiological deficits. Brain 114:2437–2450
49. Meyer R, Weissert R, Diem R, Storch MK, de Graaf KL, Kramer B, Bahr M (2001) Acute neuronal apoptosis in a rat model of multiple sclerosis. J Neurosci 21:6214–6220
50. Diem R, Demmer I, Boretius S, Merkler D, Schmelting B, Williams S, Sattler M, Bahr M, Michaelis T, Frahm J, Bruck W, Fuchs E (2008) Autoimmune optic neuritis in the common marmoset monkey: comparison of visual evoked potentials with MRI and histopathology. Invest Ophthalmol Vis Sci 49:3707–3714