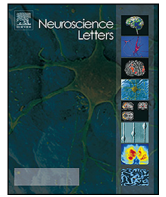
Neuroscience Letters 589 (2015) 7–12

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet



Research article

The electroretinogram of Mongolian gerbil (*Meriones unguiculatus*): Comparison to mouse

Shengyan Yang[a,1], Xiaopeng Luo[a,c,1], Guoyin Xiong[a], Kwok-Fai So[a], Hui Yang[b,**], Ying Xu[a,d,*]

[a] GHM Institute of CNS Regeneration, Jinan University, 601 West Huangpu Ave, Guangzhou, China
[b] State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, No. 54 Xianlie Road S., Guangzhou, China
[c] Department of Pathophysiology, Jinan University School of Medicine, 601 West Huangpu Ave, Guangzhou, China
[d] Co-Innovation Center of Neuroregeneration, Nantong University, Jiangsu, PR China

HIGHLIGHTS

- Mongolian gerbil has a slightly smaller scotopic response than mouse.
- Gerbil has a larger photopic response than mouse.
- Gerbil has a higher photopic flicker fusion frequency than mouse.
- Gerbil, but not mouse, has an *i*-wave and *d*-wave as humans.

ARTICLE INFO

Article history:
Received 17 September 2014
Received in revised form
18 November 2014
Accepted 7 January 2015
Available online 8 January 2015

Keywords:
Mongolian gerbil
Electroretinogram
Mouse
Cone

ABSTRACT

The Mongolian gerbil (*Meriones unguiculatus*) is a diurnal rodent whose retinal photoreceptors comprise 13% cones in contrast to 1–3% in nocturnal mice and rats. Moreover, it displays a retinal structure more analogous to that of human than of mouse. However, the electroretinogram (ERG) recordings of gerbils have not yet been well studied. Thus, here we compared the ERGs of gerbils and C57 mice. We recorded responses to full-field flashes of increasing intensities under both dark and light adaptation. We also investigated responses to flickers of increasing frequencies and to long-duration flashes under photopic conditions. In scotopic, the amplitudes of the gerbil *a*- and *b*-waves are slightly smaller than those of the mouse waves. However, in photopic, the gerbil wave amplitudes are 2-fold larger than those of mice. Gerbils also exhibit larger flicker responses and higher flicker fusion frequencies than mice. Furthermore, unlike mice, gerbils show a positive OFF response (*d*-wave) and a post *b*-wave positive potential (*i*-wave), features commonly observed in human photopic ERGs. Our results suggest that gerbils may complement rod-dominant mice as models for studying retinal cone function and pathologies.

© 2015 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Most rodents are nocturnal, but the Mongolian gerbil (*Meriones unguiculatus*) is primarily diurnal. In accordance, compared to rats and mice, gerbils have better visual acuity about 2 cycles/degree [1], and better photopic vision. Correspondingly, unlike mouse and rat retina where photoreceptors are 1–3% cones [2], gerbil retina comprise 13% cones. In addition, the gerbil retina displays the same layers as the human retina [3], and has a cone-dominated avascular macula-like region called visual streak [4] akin to the human fovea. As vision for human activities is due in large part to foveal cones, we explored if the gerbil, whose retinal structure is more analogous to that of human than of mouse, could complement the rod-dominated mouse as a model for studying cone function and pathologies.

Indeed gerbil has been used to study damages to the visual system, to evaluate the therapeutic effect of drugs [5], and to test the effects of virally delivered genes to the retina [6]. However, these studies tested primarily the morphological and behavioral changes with little emphasis on the functional changes. The reports

* Corresponding author at: GHM Institute of CNS Regeneration, Jinan University, 601 West Huangpu Ave, Guangzhou, China. Tel.: +86 20 85227086; fax: +86 20 85223563.
** Corresponding author. Tel.: +86 20 87331549;
fax: +86 20 87333271.
E-mail addresses: 13710584767@163.com (H. Yang), xuying@jnu.edu.cn (Y. Xu).
[1] Both contributed equally to this work.

http://dx.doi.org/10.1016/j.neulet.2015.01.018
0304-3940/© 2015 Elsevier Ireland Ltd. All rights reserved.

investigating electroretinograms (ERGs) are quite limited. Over two decades ago, a few reports applied simple flashes at specific light intensities [2,5,7], while other studies mainly focused on cone spectral sensitivity [8]. More recently multifocal ERG studies were performed to measure local cone responses [6,9]. However, it is still not known how the ERG responses of the diurnal gerbil differ from those of nocturnal rodents like mouse, and if gerbil ERGs share the characteristics of human ERGs.

Thus, here we examined gerbil ERG responses to full-field flashes of increasing intensities/frequencies and to long-duration flashes, and then compared these to ERG responses of C57 mice.

2. Methods

All animal procedures were performed according to the statement of the Association for the Use of Animals in Ophthalmic and Visual Research and approved by competent ethics committees at Jinan University. All efforts were done to minimize the number of animals used and their suffering.

2.1. Animals

The study was performed on 24 adult Mongolian gerbils (*Meriones unguiculatus*, 3–5 months old, 12 females and 12 males) and 23 adult C57 mice (6–8 weeks old, 16 females and 7 males). All animals were kept under standard laboratory conditions with 12 h/12 h light/dark cycles supplied with regular food and water.

2.2. Preparation

All animals were dark adapted for 12 h before the daytime experiment. Animals were anesthetized with intraperitoneal injection of chloral hydrate (4.5 μg/g body weight) under dim red light. Pupils were dilated by topical application of phenylephrine HCl (0.5%) and tropicamide (0.5%), and eyes were lubricated and hydrated by 1% methylcellulose. Animals were placed on a heated platform that used a circulating water pump bath to maintain a constant temperature (37 °C).

2.3. Electroretinograms (ERGs)

ERG recordings from gerbils and C57 mice were performed at similar times during the day under identical settings and conditions. ERGs were recorded with gold plated wire loop electrodes contacting the corneal surface as the active electrode. Stainless steel needle electrodes were inserted into the skin near the eye and into the tail serving as reference and ground leads, respectively. ERG data was collected through the amplifier of RETI-scan system (Roland Consult, RETI-scan, Germany) at a sampling rate of 2 kHz.

Animals were first tested under dark adaptation. They were exposed to full-field scotopic flashes of 1.3 ms duration presented by a Ganzfeld (Roland Consult, Germany) with intensities ranging from 0.0001 to 100 cd s/m^2 (corresponding to −4.0 to 2.0 log cd s/m^2). The system limited the maximum (100 cd s/m^2) and minimum intensities (0.0001 cd s/m^2). Flash stimuli with intensities above10 cds/m^2 were delivered by Xenon lamp, and those below 10 cd s/m^2 were delivered by green (525 nm) LED.

To study the cone-driven intensity responses, we light adapted rods with a saturating background (green, 20 cd/m^2) for 10 min and then presented flashes of increasing intensities ranging from 0.1 to 100 cd s/m^2.

For each condition (scotopic and photopic), 3–10 responses were averaged to the luminance of flash stimuli, with the stimulus interval varying from 2 to 10 s at low intensities to 1 min at intensities above 3.0 cd s/m^2.

To find the critical flicker fusion frequency under photopic conditions, we applied a background light of 20 cd/m^2 (λ = 525 nm) and presented flashes(3 cds/m^2) at 5, 10, 20, 30, 40, 50 and 55 Hz (maximum allowed by the system). Averages of 50 presentations were used. OFF responses were recorded using a square wave white stimulus of 133 cds/m^2 lasting 500 ms on a 20 cd/m^2 green background.

2.4. Data analysis

ERG waveforms were analyzed with RETIport software (Roland) after applying 50 Hz low-pass filtering. *A*-wave amplitude was measured from baseline to first negative peak, and *b*-wave amplitude was measured from *a*-wave trough to subsequent positive peak. For flicker ERGs, peak-to-trough amplitudes of the middle three wavelets were measured and averaged. For photopic negative responses (PhNRs), amplitude of negative peak following *b*-wave was measured relative to baseline. For OFF response at the offset of light step, peak amplitude was measured from baseline and implicit time was measured from light offset to peak response. For post *b*-wave positive wave (*i*-wave), amplitude was taken as the peak to the trough of the *b*-wave, and the time from *i*-wave peak to *b*-wave peak was measured.

For each animal, values recorded from both eyes were averaged and treated as a single data point. As both genders gave similar results, we combined them for each species. All data in figures are presented as mean ± SEM. Statistical comparisons between gerbil and mouse were performed using two-tailed Student's *t*-test, and comparisons between different test conditions within one species were performed using paired Student's *t*-test. A *p*-value below 0.05 ($p < 0.05$) was considered significant and $p < 0.01$ was considered highly significant.

2.5. Measuring pupil and retina size

Since the eyes of mice and gerbils differ in size, it is important to determine the photon flux falling on the retina for any given intensity. To relate flash intensity experienced at the cornea to that falling on the retina, we used the following equation:

[illuminance at the retina] = [illuminance at the cornea] × [pupil area]/[retina area]([10], and personal communication with Arkady Lyubarsky). We measured the areas of dilated pupils and retinas in 3–4 gerbils and 3–4 mice. Under dark adaptation, we imaged the dilated pupil 5 min and 30 min after exposure to dilating agent using a Leica EZ4HD microscope, and measured its diameter with ImageJ software. Then the animal was sacrificed by overdose anesthesia, and the retina was removed from the eyecup, fixed with 4% paraformaldehyde for 30 min, flattened and mounted on a coverslip and sealed. The whole-mount retina was imaged with a Leica DM6000B microscope and the size measured with ImageJ.

We found that 5 min after applying dilating agent, the pupil diameter for both gerbils and mice reached nearly 99% of the full dilation seen 30 min after application. For gerbil, the diameter of fully dilated pupil was 4.2 ± 0.1 mm, so area was 14.1 ± 0.5 mm^2. For mouse, this diameter was 2.1 ± 0.1 mm, so area was 3.4 ± 0.2 mm^2 (close to 3.2 mm^2 seen in [10]). Retinal area in gerbils was 68.9 ± 1.6 mm^2 and in mice was 16.7 ± 0.8 mm^2. Since the ratios of pupil area to retinal area for gerbils and mice were very similar (0.205 for gerbil and 0.202 for mouse), light intensity units given as cd s/m^2 at cornea will translate to similar values of photons/μm^2 on retina for both animals.

Download English Version:

https://daneshyari.com/en/article/6281047

Download Persian Version:

https://daneshyari.com/article/6281047

Daneshyari.com