Introduction

Multifocal electroretinograms (mfERGs)\textsuperscript{1,2} have been used clinically to diagnose and follow the progression of various eye diseases. The results of experimental studies suggest that mfERGs reflect not only the activity of cells in the outer layers of the retina but also those in the inner retinal layers, such as ganglion cells and amacrine cells.\textsuperscript{3–8} We recently found a positive wavelet, designated the “s-wave,” in the first-order kernel of human mfERGs.\textsuperscript{9} This wave appears on the descending limb of P1 when the base period\textsuperscript{10} (bpd) of the stimulus is long.\textsuperscript{9} The amplitude of the s-wave elicited by stimulation of regions close to the optic disc is larger than that recorded for stimulation far from the optic disc, and the implicit time is shorter for the former than for the latter.\textsuperscript{9} In patients with optic neuritis, the s-waves are markedly reduced or lost, and reappear when the optic neuritis is resolved.\textsuperscript{9} In human glaucomatous eyes, the amplitude of the s-wave is significantly smaller than that recorded from normal eyes.\textsuperscript{11} The s-wave amplitudes in glaucomatous eyes decrease as the visual field loss of those eyes increases.\textsuperscript{12} In addition, the s-wave amplitude is correlated with the retinal nerve fiber layer thickness in glaucomatous eyes.\textsuperscript{13}

From these findings, we infer that the s-wave most likely originates from the neural activity of retinal ganglion cells (RGCs) and their axons. Confirmatory evidence supporting this view, however, has not been obtained.

The purpose of the present paper was to clarify whether the s-wave was present in the first-order kernel of the

LABORATORY INVESTIGATION

The s-Wave of the Multifocal Electroretinogram in Cats

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Abstract

Purpose: To characterize the s-wave of the multifocal electroretinogram (mfERG) in cats, and to determine the contribution of the inner retina to the s-wave by examining the effects of tetrodotoxin (TTX) and N-methyl d-aspartate (NMDA) injected into the vitreous cavity.

Methods: mfERGs were recorded from 15 eyes of 15 male cats under general anesthesia. The stimulus consisted of 37 elements, and the luminance of the bright and the black elements were 200 and 4 cd/m\textsuperscript{2}, respectively. The stimuli were presented in a pseudorandom binary m-sequence at six different base periods (bpds) from 13.3 to 426.7 ms. Fifty microliters of 7.0 \textmu M TTX followed by 50 \textmu l of 4.0 mM NMDA were injected into the vitreous cavity.

Results: The shape of the mfERGs in the cats resembled that in humans. The s-wave appeared on the descending limb of P1, as seen in human mfERGs, in 11 eyes, and the s-wave amplitude increased significantly as the bpd was increased. TTX and NMDA resulted in the disappearance of the s-wave at all bpds, while the amplitude of P1 remained unchanged.

Conclusions: The s-wave is present in the mfERG in the cat, and its loss following injections of TTX and NMDA supports the view that the s-wave reflects the function of the ganglion cells and their axons.


Key Words: cat, ganglion cell, multifocal ERG, s-wave

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mfERGs of cats, and whether properties of the s-wave in cats were similar to those in humans. If the s-wave is present, then conventional neurotoxic agents such as tetrodotoxin (TTX), a drug known to block the sodium channels of RGCs and amacrine cells, leading to suppression of their function and the onset of action potentials, and N-methyl-D-aspartate (NMDA), a glutamate agonist blocking NMDA receptors and suppressing the function of RGCs and amacrine cells, can be used to determine which cells contribute to the s-wave.

Materials and Methods

Animal Preparation

The cats were treated in accordance with the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Vision Research.

The left eyes of 15 mature male cats (approximate body weight, 3.0 kg), free of abnormalities of the ocular fundus as determined by indirect ophthalmoscopy, were used. To obtain ocular stability, general anesthesia was induced by intramuscular injection of ketamine hydrochloride (10 mg/kg) and xylazine (1 mg/kg). The body temperature was maintained at 36.5°–38°C with a heating pad. Mydriasis was induced by topical 0.5% tropicamide and 0.5% phenylephrine hydrochloride (Mydri-P; Santen Pharmaceutical, Osaka, Japan).

mfERG Recordings

After light adaptation for about 15 min in a 252-lux room, the refractive error was measured with a refractometer (Retinomax K-plus 2; Nikon, Tokyo, Japan), and a lens with the spherical equivalent of a refractive error plus 3.0 diopters was placed in front of the examined eyes. A bipolar Burian-Allen contact lens-type electrode was placed on the anesthetized cornea. A silver disc electrode was attached to the right earlobe as the ground electrode. The other eye was covered with black tape.

A Visual Evoked Response Imaging System (VERIS; Tomey, Nagoya, Japan) was used to record the mfERGs. The optic axis of the cat eye was confirmed by searching the location of the optic disc and the area centralis of the fundus by indirect ophthalmoscopy. The area centralis is located approximately three optic disc diameters temporal to the disc, is darker in color than the surrounding retina, and is avascular. The body and head positions of the cat were adjusted so that the optic axis was directed to the center of the stimulus monitor screen.

Initially, mfERGs were recorded by stimulation with a bpd of 13.3 ms, and the eye position was adjusted until the amplitude of the response recorded from the area corresponding to the optic disc was smaller than that recorded from the surrounding areas (Fig. 1, arrow). This technique confirmed that the position of the cat’s eye and the distance between the eye and the monitor were optimal.

The method used for stimulation was the same as that employed in our studies of the s-wave in humans. Briefly, the stimulus consisted of 37 hexagonal bright (200 cd/m²) and black (4 cd/m²) elements, arranged in a concentric pattern at a visual angle of 20° × 30° on a 17-inch (about 43-cm) cathode ray tube (CRT) monitor. The stimulus elements were smallest at the center and increased in size toward the periphery. The bright or black elements were presented in a pseudorandom binary m-sequence at six different frequencies, namely, 75, 37.5, 18.75, 9.4, 4.7, and 2.34 Hz (i.e., at bpd of 13.3, 26.7, 53.3, 106.7, 213.3, and 426.7 ms, respectively). Dim elements (66.6 cd/m²) were interposed between bright and black (or bright) elements at a fre-