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Research Article

# Induced Myopia and Hyperopia Effect on a Normal Electroretinogram

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## Abstract

**Significance:** To determine if uncorrected refractive error influences the results of an electroretinogram (ERG).

**Purpose:** To investigate how induced myopia and hyperopia alter electroretinogram (ERG) results in a rabbit model.

**Methods:** The ERG's were measured in New Zealand white rabbits (n = 10) after dark adaptation. The ERG's were then repeated using a high-plus contact lens to simulate myopia (-10D and -20D) and high-minus contact lenses to simulate hyperopia (+10D and +20D).

**Results:** Induced refractive error with contact lenses showed a significant reduction in scotopic ERG amplitudes in myopia -10D (P = .0479), and hyperopia +10D (P = .0206) and +20D (P = .0487). There was no significant statistical difference in the implicate time or a/b wave ratios between plano and induced myopia or hyperopia.

**Conclusions:** There was a significant decrease in ERG amplitudes after induced refractive error in our animal study. Corrective refraction may need to be given to patients prior to ERG or a corrective calculation could be developed to provide a more accurate interpretation of ERG's performed in patients with significant myopia or hyperopia. ERGs performed on highly myopic and hyperopic patients should be interpreted with caution and our study provides credence to disparities seen in this patient population.

**Keywords:** Myopia; Amplitudes; Electroretinogram

## Introduction

Retinal electrophysiology, and specifically electroretinograms (ERGs), are a diagnostic test that measure electrical activity of the retinal tissue [1]. It measures electrical potential response to light as it is conducted from the rods and cones through the retinal components to the optic nerve fibers. Since its development, normative data for electroretinograms have been compiled to distinguish normal versus abnormal responses to light [2]. Both retina specialists and pediatric ophthalmologists use electroretinograms in the clinical setting for a multitude of disease processes. At the discretion of the pediatric ophthalmologist, electroretinograms are often ordered in preverbal patients with concern for decreased vision or unexplained nystagmus. Based on neuronal and non-neuronal response to light, an ophthalmologist may speculate on possible visual potential and the possible etiologies of the decreased visual function.

Electroretinograms have been shown to be affected by refractive error and axial lengths [3-5]. The underlying cause of a decrease in amplitude can be explained by underlying retinal pathology or an optical defocus of light [6-8]. Additionally, several of the more common forms of retinal degeneration are associated with pathognomonic high refractive error [9-12].

Multiple prior studies have been performed to investigate the effect of refractive error on electroretinogram recordings. Increasing axial length has been shown to have a reduction in amplitudes with no effect on implicit times [3]. In addition, there has been reported decrease in retinal function with increasing myopia [4]. Current theory for decreased electroretinogram amplitudes involve the observed fundus changes in progressive myopia, often prominent retinal thinning, with instances of electroretinogram changes even preceding visible macular pathology [4,13,14].

Alternatively, the optical defocus of light as demonstrated in Figure 1 shows the changed focal point will affect the intensity by scattering the light field across a larger surface area which will change the overall electroretinogram amplitude. With increasing high myopia, the light entering the eye from optical infinity will be focused farther in front of the retina. With increasing high hyperopia, light entering the eye from infinity will be focused farther behind the retina. Previous research by Chan et al showed refractive blur reduced central amplitudes [8]. Our study involved the performance of electroretinograms with induced refractive error to remove any potential retinal changes to isolate the full effect of optical defocus. We hypothesized light that does not focus optimally on the surface of the retina, as seen in large refractive errors, will adversely affect the recorded electroretinogram output.

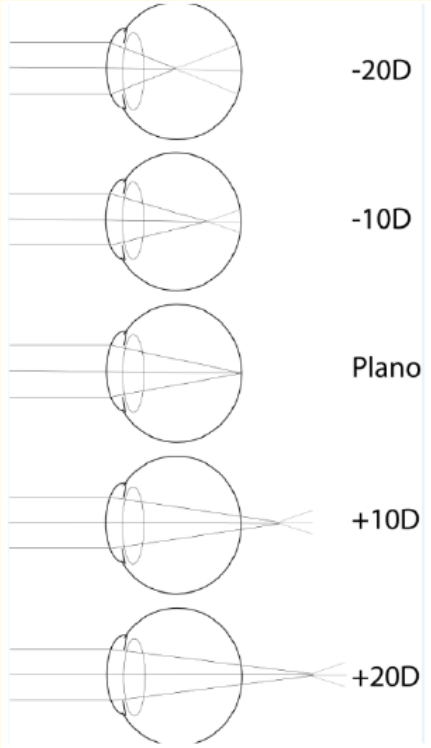


**Figure 1:** Effect of refractive error on optical defocus.

## Methods

Electroretinograms were performed on rabbits as approved by the Institutional Animal Committee for Use and Care at the University of Colorado. All procedures were performed in accordance with the ARVO statement for Use of Animals in Ophthalmic and Vision Research.

Ten New Zealand white rabbits (Charles River Laboratories), 5 females and 5 males, were anesthetized with an intramuscular injection of ketamine HCL (30 mg/kg) and xylazine (5 mg/kg) followed with 1-2% isoflurane maintenance inhaled with 3 L/min oxygen prior to all studies. The animals were dark adapted for a minimum of 20 minutes again prior to performing the electroretinogram and dilated with 0.2% tropicamide and 1% phenylephrine. Electroretinograms were performed using a mini Ganzfeld stimulator (LKC technologies, Gaithersburg, MD) using ERGjet electrodes (La Chaux de Fonds, Switzerland) placed directly on the cornea.

Two electroretinograms were performed on each animal, one without refractive correction and one with a contact lens to induce high refractive error. The order of no refractive correction and induced refractive error was randomized to avoid bias and the animals were dark adapted a second 20 minutes between the two electroretinograms.

We used Proclear Cooper Vision contact lens (Hamble, UK) which was placed directly onto the cornea and the ERGjet electrode was placed over the contact lens. Rabbits were randomly selected for differing powers of -10D (n = 6), +10D (n = 6), -20D (n = 4) and +20D (n = 4) contact lenses.

Statistics of the scotopic b-wave amplitude, a/b wave amplitude ratio and implicit time in step 1 were calculated on Graphpad Prism 5.03 (La Jolla, CA) by two tailed paired t-test. The scotopic electroretinograms were selected to be analyzed as rods predominate in a rabbit retina [3]. Amplitudes were considered significantly different if P < .05.

## Results

In our study, we induced high myopic and high hyperopic refractive error with contact lenses in a rabbit model. Recorded amplitude and implicit time of the scotopic b-wave was compared with and without contact lens installation. Induced myopia with +20D contact lens, (P = .0479) and induced hyperopia with -10D and -20D contact lens, (P = .0206 and P = .0487 respectively) gave significantly reduced recorded amplitudes in 10 rabbits. Further, larger studies and human models are needed, but the defocus of light does impact electroretinogram results.

Cumulative scotopic amplitudes are shown in Figure 2 and the associated statistics are given in Table 1. No significant change in implicit times or a/b wave ratios were noted (data not shown). Significant differences in recorded scotopic amplitudes in simulated hyperopia with -10D and -20D contact lenses, (p = .0206 and p = .0487 respectively) and simulated myopia with +20D contact lenses, (p = .0479) were found.

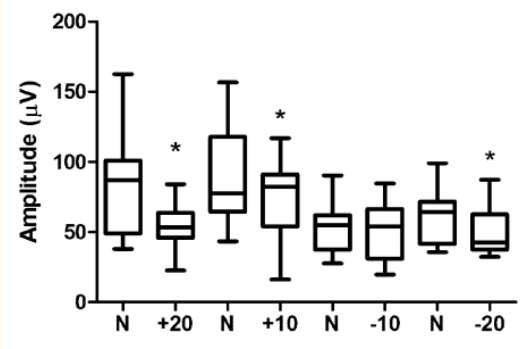


**Figure 2:** Control amplitudes compared to amplitudes after induced refractive error.

Table 1. Mean control amplitudes versus induced refractive error amplitudes,

NoCL = No Contact Lens.

| | NoCL | +20D | NoCL | +10D | NoCL | -10D | NoCL | -20D |
|---|---|---|---|---|---|---|---|---|
| Mean Amplitude (µV) | 83.7 | 53.63 | 88.04 | 70.96 | 51.76 | 50.79 | 61.27 | 51.23 |
| Lower 95% CI (µV) | 59.95 | 43.9 | 71.03 | 56.08 | 43.88 | 40.87 | 48.96 | 39.52 |
| Upper 95% confidence interval (µV) | 107.4 | 63.36 | 105.1 | 85.84 | 59.64 | 60.72 | 73.59 | 62.93 |
| Standard Error of Mean | 10.79 | 4.42 | 8.06 | 7.02 | 3.74 | 4.7 | 5.53 | 5.26 |
| Standard Deviation | 37.38 | 15.31 | 34.21 | 28.94 | 15.85 | 19.95 | 18.33 | 17.43 |
| Number | 4 | 4 | 6 | 6 | 6 | 6 | 4 | 4 |

**Table 1**: Mean control amplitudes versus induced refractive error amplitudes.

NoCL = No Contact Lens

µV = microvault

D = diopters

In 2 of the rabbits with induced very high hyperopia with a -20 contact lens, there was a significant decrease in amplitude from 94.97 μV to 47.23 μV (P = .0007), and 129.9 μV to 53.7 μV (P = .0007). Induced hyperopia with a -10D contact lens had a decrease in amplitude from 49.6 μV to 23.07 μV (P = .0094). Induced myopia (-20D) had a decrease in amplitude from 49.6 μV to 23.07 μV (P = .0229). In 2 of the rabbits with induced high hyperopia with a -20D contact lens, there was a significant decrease in amplitude (P < .5).

## Discussion

Electroretinograms record the neuronal and non-neuronal activity response to light. For an accurate electroretinogram to be recorded, you need a proper light stimulus and normal retinal cell response [2]. Prior studies have looked at axial length and amount of myopia effect on electroretinogram amplitudes. There has been reproducible data that reveal a correlation between increased myopia and decrease in amplitudes [3-5]. These studies cannot, however, correct for any underlying retinal pathology at a cellular level that may occur prior to visible retinal pathology. Our study focuses on the light stimulus in an induced myopic or hyperopic relative to a normal retina. We hypothesize that light which does not focus at the optimal focal point in the surface of the retina, as seen with large refractive errors, will scatter the optical input and reduce the overall intensity of the recorded amplitude.

With large induced refractive errors (+20D and -20D), there was a significant decrease in amplitudes recorded in the majority of rabbits tested. These rabbits did not undergo a dilated exam pre- electroretinogram refraction, but any limitations to amplitude based on underlying pathology would have been reflected in the control electroretinograms preformed on the same rabbits. In future studies, we could add cycloplegic refractions and dilated fundus exams to our study.

Limitations of this study include the study population, small study population and old technology. Indeed, when presented, several ophthalmologists were critical that the study would be much more "interesting" if it were performed on humans. Additional concerns were that the contact lens material could have contributed to the lower electroretinogram amplitudes, and that large refractive errors of 10D and 20D are not that common in the human population.

Our clinical interest in this research is based on the many electroretinograms that are performed at our institution in infants presenting with nystagmus, with or without clinically decreased visual function. As such, the rabbit model closely resembles infants given their inability to cooperate and necessity for general anesthesia. The concern about the material of contact lenses interfering with the electroretinogram results can certainly be addressed in future studies by performing "baseline" electroretinograms without contacts lenses, and then with a Plano or low power (-0.50 or +0.50) contact lens to unequivocally determine the effect of the contact lens itself on the electroretinogram findings. There are many ophthalmic conditions presenting with nystagmus and poor vision in infants that additionally present with high refractive error, which was the impetus for this study in determining how abnormal refractive error contributes to electroretinogram results.

There may be a correlation between refractive error and recorded amplitude, therefore warranting future studies with improved electroretinogram technology and pattern electroretinogras. As we improve electroretinogram recording, we can improve the strength of the study by increasing the number of animals studied and additionally experimenting with human models [9-12,15-26].

As we continue to research this possible association, we must take into consideration the clinical implications. A proper refraction on all patients undergoing an electroretinogram is warranted. As we better understand if there is an effect on the interface with use of a contact lens, we may be able to correct a patient's refractive error prior to diagnostic testing and at a minimum, this should be taken into consideration during interpretation. If there is a linear correlation, there may be corrective equations or factors to apply to amplitudes based on pretesting refractions.

In our rabbit model, there was a significant decrease in amplitude after induced refractive error. As future studies continue to isolate the defocus of light and its relationship to recorded amplitudes, refractive error should be a consideration in the interpretations of electroretinograms.

## Summary

We performed ERG on animals that had normal vision with and without different diopter to replicate myopic and hyperopic

vision to determine the effect on ERG amplitude. There was an observable difference in scotopic amplitude with induced myopia and hyperopia.

## Ethics Statement

All animal experiments were conducted in accordance with USDA regulations and the ARVO statement for the Use of Animals in Ophthalmic and Vision Research. The animal studies were approved by the University of Colorado Institutional Animal Care and Use Committee.

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