Recommendations on Electroretinogram Testing in Retinal Disorders

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Received: 08-16-2014
Accepted: 08-18-2014
Published: 08-26-2014

The authors have no proprietary interest in any materials or methods described within this article. This submission has not been published anywhere previously and it is not simultaneously being considered for any other publication.

Keywords: Electrophysiologic Testing; Electroretinogram; Multifocal Electroretinogram; Pattern Electroretinogram; Retinal Diseases.

Introduction

Two organs are crucial to the vision and understanding of what is around us, and the eye the brain as well as their interactions. The retina receives the incoming light and transmits to the brain the information obtained, by sending small ‘signals’ through the visual pathways.

The brain compares the new image with the stored images in his memory. Thanks to this process we find ourselves and to orient in the visual environment that surrounds us. The retina and the brain are two complex systems of highly specialized cells. The reciprocal interactions are essential to ensure the various functions of vision, in particular the identification characters during the reading, the recognition of faces of the people, the perception of different colors, differences in brightness, movement, the distinction between day and night. The visual disturbances may reside in the eye, the optic nerve, or brain. For identify the reasons for the ophthalmologist visual disturbances proceeds primarily to an in-depth examination clinical and functional.

The measurement acuity visual will be used to determine the correction of refractive errors with glasses or contact lenses. The ocular electrophysiology is a diagnostic discipline that uses non-invasive tests to study electrical phenomena associated with physiological processes such as vision and brain activity [1,2]. Exploring the functionality of the visual structures is possible identify defects in the retina, optic nerve, and brain. It becomes imperative to monitor the development of the visual pathways in premature infants, in patients with brain disorders and to assess the residual visual function in low vision patients in order to design and set a course of rehabilitation [1,2]. Other useful applications concern to the graphic recording of the activity of the extrinsic muscles during eye movements horizontal and vertical, not those of the anterior-posterior axis torsion [3]. In order to establish a certain diagnosis, the specialist stimulates eyes with bright flashes precisely defined and it records the potential differences by standardized techniques. To properly assess the results of electrophysiologic testing should be always a conversation on the antecedents and symptoms, measurement of visual acuity, eye examination with the slit lamp and, rule, a fundus examination with the pupils dilated.

The main tests carried out in eye examination are:

- visual evoked potentials (VEP),
- pattern electroretinogram (PERG),
- full-field electroretinogram (ERG),
- multifocal electroretinogram (mfERG),
- multifocal visual evoked potentials (mfVEP),
- dynamic and sensorial electroculogram (EOG).

The purpose of this communication is that to compare and to evaluate the use of several electroretinograms so that the reader can better understand when to refer a patient for this specialized testing.

Full-field electroretinogram (ERG)

The lens focuses light on the retina, which penetrates in the eye from the outside environment. Cells photosensitive highly specialized of the retina, photoreceptors, react to the arrival of light with changes of action potentials. These
variations are transmitted and modulated by other cells of the retina (among other things, the bipolar cells) until, passing by the cells ganglion, the optic nerve and finally the visual center of the brain. The sum of potential changes action products in the various groups of cells retinal can be measured by ERG, since the retina works as a sophisticated computer and it processes the light information. In fact, ERG is an electrophysiological examination with which we measure the activity of the retina after stimulation by flashes of various intensity from light to bright at 33 cm distance [1, 2, 4]. It is performed after pharmacological dilation of the pupils, in dark adaptation for 30 minutes, with reference to the International Society for Clinical Electrophysiology of Vision (ISCEV) guidelines, and it has duration of about 60 minutes [1, 2]. The electrodes record the electrical activity of the retina due to the perception of flashes of varying frequency and intensity, using ERG-Jet electrode lens placed on the surface of the cornea after application of local anesthetic eye drops. The test allows whether the defect is in the cones, rods, Müller cells (which have nutritive functions to the retina), and in bipolar cells, that connect the rods and cones with the ganglion cells [1, 2]. There are a number of conditions, mostly ocular in nature, in which the ERG may provide useful information [4-8]. The diagnoses most commonly suspected when ordering an ERG are predominantly conditions of the retina, including:

- Diffuse macular photoreceptor dystrophies;
- Stationary cone dysfunction disorders;
- Choriretinal dystrophies and albinism;
- Hereditary vitreoretinal disorders;
- Inflammatory choriretinal conditions;
- Circulatory deficient and metabolic retinopathy;
- Intraocular foreign bodies;
- Toxic conditions;
- Retinal detachment;
- Vitamin A deficiency and retinoids.

Pattern electroretinogram (PERG)

The transient PERG is performed at 33 cm distance, with an alternated program on the optoelectronic stimulator. If necessary, an appropriate optical correction is placed for the test distance. Electrodes are positioned on the skin or on the surface of the eye after an anesthetic eye drops instilled; they record the activity of the central retina induced by visual stimuli [1,2,9]. The PERG is evoked by alternating contrast reversal of a black and white square checkerboard pattern of constant mean luminance with stimulus field size 78.8 arc degree (deg) centered on the fovea, check size of 47.3 min arc, contrast 100%, mean luminance 45cd/m2, and 4.5 reversals/s [1,2,9]. The waveform of the transient examination is obtained at low temporal frequencies of the stimuli. The ISCEV standard PERG protocols is coded for monocular or binocular recording and identified by a series of N35, P50, and N95 peaks, each characterized by an amplitude and latency (or time-to-peak). The PERG can directly demonstrate both an objective evaluation of retinal ganglion cells and macular function, because the stimulus is customarily viewed with central fixation. Moreover, clinically this exam can be used in a patient with an abnormal VEP to establish whether a retinal macular dysfunction is present, and thus differentiate between macular and optic nerve dysfunction as a cause for the VEP abnormality [1,9]. The PERG should be considered in conjunction with the ERG. In fact, the ERG is unaffected by disease confined to the macula and a patient with generalized retinal dysfunction sparing the macula will have an abnormal ERG but a normal PERG [1,2].

Multifocal electroretinogram (mfERG)

An important and innovative development of the traditional ERG is the mfERG that was introduced by Sutter and Tran in 1992 as an objective measure of focal retinal function. Sutter adapted the mathematical sequences called binary m-sequences enabling the isolation from a single electrical signal an electroretinogram representing less than each square millimeter of retina in response to a visual stimulus (Fig. 1). Results that are generated by mfERG appears similar to those generated by ERG [10-12]. This test helps us discriminate between optic nerve and retinal disease, detect early drug toxicity, diagnose and distinguish between the various syndromes of choriretinits and follow patients with inherited retinal dystrophies (Fig. 2) [11-14]. Because the mfERG shows good repeat reliability, it can be used to follow the progression of retinal diseases. In fact, diseases such age macular degeneration or Stargardt dystrophy produce focal regions in the macula where the mfERG is nondetectable [11,12].

Figure 1. Normal multifocal electroretinogram (mfERG) of a control.

Figure 2. Multifocal electroretinogram (mfERG) of a patient affected from cone-rod dystrophy.
It uses the same electrodes and amplifiers as conventional ERG recording under light-adapted conditions, and provides a topographical measure of retinal activity that can be compared with the patient's visual fields. The mfERG simultaneously light stimulates and measures bioelectrical signals generated from more than a hundred retinal areas per eye, in a few minutes and therefore stable fixation is essential. The retina is stimulated with an array of hexagonal elements, each of which has a 50% chance of being illuminated every time the frame changes. They are not direct electrical potentials from local regions of retina, but rather a mathematical extraction of the signal [11,12]. The enhanced spatial resolution enables scotomas and retinal dysfunction to be mapped and quantified. The mfERG has helped neuro-ophthalmologists distinguish between diseases of the outer retina (affecting photoreceptors and/or bipolar cells) and diseases of the inner retina (ganglion cells) and optic nerve. When combined with automated perimetry, the mfERG is a valuable tool for localization and differential diagnosis [1,11,12]. When combined with mfVEP, mfERG can differentiate between organic and non-organic causes of visual loss.

The most commonly used display is a topographic map of local ERG activity, in which the responses from the elements in each ring are summed and then divided by the area of the elements of the ring. The waveform of the basic mfERG response, called the first-order kernel, is a biphasic wave. There are usually three peaks: a negative deflection, called N1, followed by a positive peak, called P1, and by a second negative deflection, called N2. The N1 response amplitude is measured from the starting baseline to the base of the N1 trough and the P1 response amplitude is measured from the N1 trough to the P1 peak. The peak implicit times of N1 and P1 are measured from the stimulus onset. Studies in humans have emphasized that N1 response includes contributions from the same cells as the a-wave of the full-field cone ERG [15]. Similarly, the P1 response includes contributions from the components of the cone b-wave and oscillatory potentials of the ERG (amacrines and interplexiform cells). Thus the mfERG appears to be a more sensitive assay for early changes when compared with the ERG. In summary, the mfERG provides an objective equivalent to the visual field by simultaneously assessing approximately multiple retinal locations and the ultimate power of the procedure, however, lies in the fact that the local responses contain components from all levels of the retina [15].

References