

Application of visual electrophysiology for the diagnosis and treatment of cataracts

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Abstract: Visual electrophysiology is widely used in clinical ophthalmology. It is also of significant value in the objective assessment of visual function in adult and pediatric cataract patients and for the diagnosis of and research on retinal and visual pathway diseases. This article systematically reviews visual electrophysiology techniques, their applications in the diagnosis and treatment of adult and pediatric cataracts, and factors influencing the application of visual electrophysiology during surgical treatment for cataracts.

Keywords: Visual electrophysiology; cataract; electroretinogram (ERG); visual evoked potential (VEP)

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In both developed and developing countries, cataracts are the leading cause of blindness and poor vision in humans (1). Currently, surgery is the only effective treatment for cataracts (2). Because of the opacity of the lens, the assessment of retinal and visual function in the posterior chamber of the eye in patients with cataracts (especially dense cataract), as well as the prediction of the recovery of the visual acuity of patients after cataract surgery, is relatively difficult. However, with the advent of new measuring methods including light projection testing, color vision testing, laser retinal metering, and visual electrophysiology, many problems related to the assessment of preoperative visual acuity and prediction of postoperative visual function in cataract patients have been solved. In recent years, objective visual electrophysiological techniques have received a great deal of attention from cataract specialists (3). The unique light stimulation used in visual electrophysiological techniques can penetrate the clouded lens and reach the retinas of cataract patients, causing photoelectric conversion that generates biological potentials that reflect the structure and function of the retina and the visual pathway. For pediatric cataract patients, whose visual

function is still in the developmental stage and who often provide poor cooperation on subjective examination, the available visual electrophysiological technology can well meet the requirements for the assessment and prediction of visual function (4). In addition, during the diagnosis and treatment of cataracts, anesthesia, surgical procedures, and intraocular lens (IOL) implantation (5) may all have some impact on visual function, and these changes in visual function can also be assessed and monitored using visual electrophysiological techniques. This article will systematically review the currently available visual electrophysiological techniques, their application in the diagnosis and treatment of adult and pediatric cataracts, and the factors that influence the use of visual electrophysiology during surgical treatment for cataracts.

Overview of visual electrophysiology

Visual electrophysiological examination is widely used in clinical ophthalmology as an objective examination technique for visual function. The electrophysiological techniques commonly used in clinical practice primarily

include the electroretinogram (ERG) and the measurement of visual evoked potential (VEP) (6). Other special visual electrophysiological examination techniques such as multifocal ERG and multifocal VEP are also included (7,8). ERG and VEP can be divided into the 'flash' type and the 'pattern' type based on the type of stimulus used. The flash or pattern stimulus can evoke the generation of potential responses in the retina or in the visual pathway; these can be captured, processed, and recorded by a computer, and the parameters of the waveform, amplitude, and implicit time can be analyzed to provide information on the structure and function of the retina and the visual pathway (9).

The ERG represents the potential response of the retina to stimuli and mainly reflects the functional status of the retina and the optic nerve (10). A standard flash ERG curve consists of three waves: the negative a-wave reflecting outer retinal photoreceptor function, the positive b-wave, which reflects the functions of the inner retinal bipolar cells and Müller cells, and the negative c-wave, which depends on the mutual relationship of the photoreceptor and the pigment epithelial cells. Of these, the b-wave is the most commonly used indicator in the clinical assessment of retinal function. The rising part of the b-wave can be resolved into an oscillatory potential consisting of 4-6 high-frequency wavelets that originate in the inner retina and can reflect the status of the blood circulation. The flash ERG technique is widely used in the diagnosis of retinal diseases such as retinitis pigmentosa, cone-rod dystrophy, toxic retinitis, congenital stationary night blindness, and ocular tumor. The main waves of pattern ERG include P50 and N95; these reflect the functions of the outer retina and the ganglion cells, respectively. Pattern ERG is primarily used for the diagnosis of optic nerve diseases and multiple sclerosis and for the identification of optic nerve and macular degeneration (11).

VEP, which is mainly used for assessment of the functional integrity of the retina and the visual pathway, originates in the deep layers of the visual cortex and is extracted from the brain waves by repeated superposition averaging (9). In the description of the VEP waveform, "N" refers to the negative wave and "P" refers to the positive wave. In the waveform of flash VEP, only P2 is relatively stable; the other components are highly variable, and its clinical application is therefore limited (12). The VEP pattern, which has been widely used in clinical practice, includes the typical "positive-negative-positive" three-phase composite waves (N75, P100 and N135) in which P100 and N135 show small individual differences (13).

VEP is affected by any disease that affects the visual cortex and the visual pathway, including glaucoma, optic neuritis, ischemic optic neuropathy, traumatic optic neuropathy, neurofibroma, pressure on the optic nerve caused by a tumor, demyelination, multiple sclerosis, and hydroxychloroquine toxic maculopathy (9,14-18). VEP can also be used in the examination of visual function in patients with refractive media opacity (19). The signals obtained using the multifocal visual electrophysiological technique originate from multiple small regions of the retina (20); they can thus be used not only to evaluate the function of the retina and the visual pathway in a local area (7) but also to determine the location and severity of the lesion. The technique is also very sensitive to early abnormalities of the retina and optic nerve (21).

Application of visual electrophysiological techniques in the diagnosis and treatment of adult cataracts

Visual electrophysiological techniques are widely used in the diagnosis and treatment of adult cataracts. The blockage of lens opacity caused by this condition could impede preoperative ophthalmological examination of the structure and function of the posterior eye chamber in patients with cataracts alone or complicated with other diseases; thus, postoperative recovery of visual function can often not be well predicted for cataract patients, and it is not possible to determine their surgical risk. With visual electrophysiological techniques, the impact of lens opacity is minimal, and preoperative and postoperative test results for visual acuity are therefore comparable; also, prediction of visual acuity in cataract patients, when made using these techniques, is consistent with the results obtained via laser retinal meter, displaying an accuracy of approximately 70-80% (22,23). As early as 1951, researchers used visual electrophysiological techniques to predict the postoperative vision of cataract patients and claimed that the opacity of the refractive medium does not significantly affect the ERG (24). Subsequent studies have shown that visual electrophysiological techniques can be successfully used to predict visual prognosis for cataract patients (25). According to the preoperative parameters of the visual electrophysiological waveform (such as amplitude and implicit time), the visual prognosis can be preliminarily evaluated (26). Normal amplitude of this waveform predicts better recovery of visual acuity in the patient, and reduced amplitude indicates the possibility of poor prognosis of

vision and visual function.

Despite the foregoing, not all researchers agree that the lens opacity that exists in cataract patients has no impact on visual electrophysiological examination. Some researchers believe that the defocusing and light absorption effect of the lens opacity can affect the test results of VEP and other visual electrophysiological tests (27). The defocus effect caused by the increased density of the opacified lens can reduce the sharpness of the contour in the stimulus pattern or the contrast of the stimulus, thereby reducing the visual electrophysiological parameters (19). The lens of elderly patients contains a component, GSH-3-OHKG, that can yellow the lens. This component can increase the absorption of short-wavelength light by the lens (28), leading to prolonged implicit time of blue-yellow VEP (19). Furthermore, the scattering effect of lens opacity will also affect the results of visual electrophysiological examination. Under conditions of light scattering, the multifocal ERG showed a decreased response in the central retinal zone, and the amplitude of the peripheral area was increased (29).

The responses of cataract patients to various types of visual electrophysiological examination techniques are not always uniform. The waveform of flash ERG depends on the intensity of the light reaching the retina. With flash stimulation at high intensity, the results of flash ERG examination for patients with simple cataract are consistent with those of subjects with a transparent refractive medium. Pattern ERG, which is only slightly affected by the opacity of the lens or other refractive media (22), is also relatively stable, especially for high-intensity pattern stimulation. However, multifocal ERG or VEP of cataract patients often produces abnormal results, showing a lower or abnormal response in the central retinal region compared to normal values (30). The blurred vision caused by cataracts can act as a high-frequency filter to selectively eliminate high spatial frequencies, especially in the central region of the retina, with relative retention in the peripheral area (31). In addition, blue-yellow VEP can detect visual anomalies in cataract patients that are undetectable using standard-pattern VEP (19). Some scholars also found that the temporal frequency characteristics (TFC) of the visual system measured using VEP are hardly affected by the opacity of the refractive medium; this technique thus provides high sensitivity and specificity and can better reflect the function of the retina and optic nerve in patients with cataract, and it can be used as an indicator of clinical reference (3).

For patients with simple age-related cataracts, the

results of visual electrophysiological examination are usually normal, suggesting a good prognosis. For cataract patients whose conditions are complicated by diseases of the retina or the visual pathway, the results of the visual electrophysiological examination are often abnormal, suggesting the possibility of a poor prognosis. If the preoperative flash ERG examination for a cataract patient with Behcet disease showed anomalies in a-wave and b-wave patterns, the postoperative recovery in visual acuity was poor (32). Cataract patients with abnormal preoperative TFC results were usually found after surgery to be suffering from complications associated with damage to the retina or the optic nerve (3). ERG can also be used to record the progression of posterior capsular opacification in the lens and can contribute to assessing the timing of surgery for cataract patients with retinal pigment degeneration (32). High-frequency (40 Hz) flash ERG examination can also help determine the prognosis of visual function in cataract patients complicated with full-thickness tapetoretinal abiotrophy (33). If the macula was evoked with central ERG red light at 18-20 degrees, the biological potential of cataract patients with macular dystrophy was significantly different from the normal value. The results of preoperative visual electrophysiological examination of cataract patients complicated with various types of glaucoma, macular degeneration, or optic nerve dysfunction were abnormal. In addition, visual electrophysiological techniques can also be used in various studies such as the pathogenesis of endophthalmitis during cataract surgery and the impact of the injection of high doses of cefuroxime into the anterior chamber on the retina (34,35).

Overall, although the opacity of the lens was shown to have a significant influence on some visual electrophysiological examinations, the degree of opacification and the electrophysiological changes showed no correlation (30). We believe that for patients with mild-to-moderate cataracts and relatively good vision, a pattern stimulus should be used to improve the accuracy of assessment. For patients with severe cataracts and poor vision, the use of a strong flash stimulus is recommended to reduce the impact of the dense opacity of the lens on the light intensity reaching the retina. To assess the function of local areas within the retina, use of the multifocal visual electrophysiological technique is recommended. In summary, visual electrophysiological techniques are usually only minimally affected by the opacity of the lens and can be used as an objective examination for the prediction of the prognosis of visual function in patients with cataract,

thereby providing a reference for clinical diagnosis and treatment.

Application of visual electrophysiological techniques for the diagnosis and treatment of pediatric cataracts

Because of their weak dependence on the cooperation of the subjects, visual electrophysiological techniques are also widely applied for the diagnosis and treatment of pediatric cataracts. Congenital cataracts (CC), with an incidence of 1/10,000-15/10,000 in children worldwide, are the most common type of pediatric cataract (36). Currently, surgery is an important treatment for CC (2), but the postoperative results are uncertain; therefore, ophthalmologists should preoperatively perform an objective assessment of the postoperative visual acuity and recovery of visual function in pediatric CC patients. Clinically, many efficient and simple methods are available for the assessment of visual function in adults and older children. However, for younger pediatric CC patients with poor cooperative ability, the objective assessment methods for visual acuity include preferential looking and optokinetic nystagmus as well as visual electrophysiological techniques. The traditional visual electrophysiological examination requires ocular fixation of the subject for a long period of time; this is obviously difficult for infants and very young children, and therefore, its application in examination for pediatric cataract is limited. In recent years, the emergence of the handheld portable flash stimulator has reduced the dependence on long visual fixation in pediatric patients, and the technique can even be applied to the examination of sleeping children or in children after sedation by drugs (37). The pattern stimulus is no longer simply a boring black and white checkerboard; instead, ever-changing cartoon graphics in the center of the checkerboard attract the child's attention, allowing the physician to achieve the goals of examination and improving the success rate. Thus, modern visual electrophysiological techniques can be used to supplement methods involving preferential looking and optokinetic nystagmus in the diagnosis and treatment of cataracts in children as well as to monitor the effectiveness of treatment for pediatric amblyopia (4).

In general, it is believed that visual deprivation in adults does not lead to amblyopia. However, the short-delay implicit time of VEP observed after surgery in patients with prolonged monocular dense cataracts suggests that the central visual system in adults still has some sensitivity to

the visual deprivation caused by long-term dense cataracts. These patients often achieve good recovery in visual acuity if early surgical treatment is provided. Pediatric patients with CC causing visual deprivation are in the critical period of visual development, and their visual prognosis is generally poor, especially for pediatric patients who undergo surgery at late stages of the disease. For pediatric patients with amblyopia, although clear image perception can be restored after surgery, VEP of the affected eye still showed decreased amplitude and implicit time, indicating poor visual function; thus, auxiliary treatment for amblyopia is needed after surgery in such cases. For pediatric patients with monocular CC, visual acuity and visual function can be substantially increased after postoperative training involving covering the healthy eye, and the VEP result can be rapidly normalized after 1 year. However, the VEP amplitude of pediatric CC patients complicated with nystagmus is usually low because their ocular fixation cannot be maintained for a long period (4). Some studies showed that the variability of the VEP amplitude is high, with no corresponding relationship to visual acuity, so the evaluation of amblyopia in pediatric CC patients using amplitude only is insufficient. McCulloch *et al.* recommended the use of the "threshold check size" of VEP as an assessment indicator; this value is relatively stable and displays low variability, and it is the only indicator of VEP corresponding to the visual acuity test in which single letters are presented (4).

Visual electrophysiological techniques can also be used in the diagnosis and treatment of other types of cataracts, besides CC, in children. For example, in pediatric patients with IOL implantation after surgery for traumatic cataracts, macular edema may easily occur due to the presence of abnormal ganglion cells in the central retinal area; this condition is reflected as the extended first negative peak in the pattern VEP (38). In pediatric cataract patients with insulin-dependent diabetes mellitus, each wave of the ERG showed different manifestations under different conditions, and the high-frequency ERG displayed amplitude repression (39). In addition, the diagnosis of newborn patients with complicated suspected CC and visual dysfunction can be confirmed by ERG examination after sedation.

Factors influencing the use of visual electrophysiology in surgical treatment for cataracts

To better apply visual electrophysiological techniques,

a number of important factors related to the process of diagnosis and treatment for cataracts must be understood. In addition to the above-mentioned opacity of the lens, other factors such as anesthesia, surgical operation, and IOL implantation can also cause abnormalities in the results of the visual electrophysiological examination.

The first factor is the impact of surgical anesthesia on the visual electrophysiology of cataract patients. Anesthesia is critical in cataract surgery. In many developing countries, peribulbar and retrobulbar anesthesia are still used in extracapsular cataract extraction surgery (40,41). Decreased amplitude and implicit time in VEP could be observed shortly following peribulbar and retrobulbar anesthesia, and the waveform was even undetectable in some cases (42); however, it reverted to normal after 2 hours. This illustrates that block anesthesia of the eye nerve is safe and effective and that it causes no permanent damage to the optic nerve. Some studies even demonstrated that when lidocaine was injected into the anterior chamber for pain relief during cataract surgery, no obvious visual electrophysiological abnormalities were observed shortly after the surgery (43). Second, although cataract lens extraction combined with IOL implantation can improve visual acuity in cataract patients, the surgical procedure itself also has some impact on the patients, and these may be reflected as abnormal results on visual electrophysiological examination. Studies have found that although the recovery of visual acuity after cataract surgery was satisfactory, the surgery changed the way in which light was propagated in the eye and/or caused fibrosis in the posterior capsule of the lens or microscopic changes in the retinal structure; thus, abnormalities in postoperative pattern VEP were still observed in 69% of the patients (44). The intraoperative application of indocyanine green dye can reduce the amplitude of the ERG wave, a finding that is particularly significant in dark adaptation ERG and suggests toxic damage in the retina; for this reason, it should be used with caution. After phacoemulsification, the levels of inflammatory mediators such as intraocular cells and prostaglandins increase, sometimes leading to irreversible damage to inner retinal function or facilitating the development of cystoid macular edema (45), which is reflected as a decreased amplitude of the oscillatory potential in flash ERG and as an extended peak time of N95 in pattern ERG (46). Third, IOL implantation in cataract surgery is another factor that can influence the results of visual electrophysiological examinations. Studies have shown that the amount of light scattering in eyes with IOL is 2 times that which occurs in

normal controls of the same age (47). The light scattering can cause repeated stimulation of the retina, leading to increased amplitude and shortened peak time in ERG or VEP (48). Visual electrophysiological abnormalities related to subsequent retinal light damage after cataract surgery have also been reported. Under normal circumstances, because of protection from the cornea and lens, damage to the sensitive retina from ultraviolet and violet-blue light can be avoided (49). Surgical extraction of the lens, with its protective effect, allows ultraviolet and shortwave visible light with phototoxicity to reach the retina, generate reactive oxygen species, and cause tissue damage (50). Therefore, some researchers believe that the implantation of yellow IOL is more protective than the implantation of transparent IOL for postoperative retinal photodamage, and this has been preliminarily verified by the use of ERG technology and an animal model using newborn mice (51). However, it was also reported that multifocal ERG results did not support a protective effect of the implanted Blu-ray filterable IOL (AcrySof Natural SN 60 AT) against the progression of age-related macular lesions (52).

Summary and prospects

Visual electrophysiological techniques can be used not only in determining retinal and optic nerve function but also for accurate prediction of the prognosis of visual acuity and visual function in cataract patients, and these techniques are widely used in the diagnosis and treatment of adults and children with cataracts. Although some controversy still exists, most researchers believe that the opacity of the lens has minimal impact on the results of visual electrophysiological examinations. As long as an appropriate stimulus is selected, assessment of the prognosis of visual function for cataract patients using visual electrophysiological techniques is relatively reliable. Cataract patients whose condition is complicated by the presence of retinal or optic nerve disease often show abnormal visual electrophysiological findings. Because of their characteristics of weak dependence on the cooperation of the subject and objective assessment of visual function, visual electrophysiological techniques have advantages for the diagnosis and treatment of pediatric cataract. Anesthesia, surgical procedures, and IOL also have specific effects on the visual electrophysiological examination: anesthesia can temporarily affect optic nerve function, surgical operation and intraoperative medication may damage the retina, and IOL can cause light scattering. These factors

will all result in abnormal changes in the results of visual electrophysiological examinations.

In summary, the assessment of visual function in cataract patients using visual electrophysiological techniques is relatively reliable, but its accuracy and stability are affected by many factors. Examination providers need to check the relevant factors and standardize the operations. To optimize strategies for improving the accuracy and validity of visual electrophysiological techniques in assessing the development of the retina and optic nerve in pediatric CC patients, further studies and research by many ophthalmic professionals is needed.

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Footnote

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