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ORIGINAL RESEARCH ARTICLE

Short-duration transient visual evoked potential for objective measurement of refractive errors

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Abstract This study examined effects of uncorrected refractive errors (RE) in a short-duration transient visual evoked potential (SD t-VEP) system and investigated their role for objective measurement of RE. Refractive errors were induced by means of trial lenses in 35 emmetropic subjects. A synchronized single-channel EEG was recorded for emmetropia, and each simulated refractive state to generate 21 VEP responses for each subject. P100 amplitude (N75 trough to P100 peak) and latency were identified by an automated post-signal processing algorithm. Induced hypermetropia and myopia correlated strongly with both P100 amplitude and latency. To minimize the effect of baseline shift and waveform fluctuations, a VEP scoring system, based on software-derived P100 latency, amplitude and waveform quality, was used to estimate the RE. Using the VEP scores, a single VEP response had a high sensitivity and specificity for discerning emmetropia, small RE (<2 diopter) within a 2 diopter range and large RE (2–14 diopter) within a 4 diopter range. The VEP scoring system has a potential for objective screening of RE and for a more accurate 3-step objective refraction.

Keywords Visual evoked potential · Electrophysiology · Refractive error

Introduction

The macula is the region of greatest visual resolution and makes the strongest contribution to the visual evoked potential (VEP) response [1]. Blurred vision from uncorrected refractive error (RE) has been reported to decrease the VEP amplitude [2–4] and alter the latency (implicit time) of the VEP response [5, 6]. An evoked potential measured using a checkerboard or other test field containing sharp contours and a lower check size is particularly sensitive to defocusing by uncorrected RE [7, 8].

It has been speculated that the strong correlation of VEP amplitude with the refractive status might be used as an objective method for refraction [3, 4]. However, with a few exceptions [9, 10], a precise technique for using a VEP response to measure RE

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objectively has not been investigated and little effort has been made to explore the utility of VEP for the assessment of RE.

The short-duration transient VEP (SD t-VEP) system is a modified pattern reversal VEP, designed to improve VEP clinical applicability using a more efficient signal acquisition technique that decreases the test duration and using a post-processing algorithm that provides less subjectivity in the waveform assessment. The automated statistical analysis of the waveforms allows objective determination of the VEP waveform with minimal manual input, and the test can be performed and interpreted without extensive training. The device has been shown to have high test–retest repeatability [11]. The purpose of this study was to evaluate the effects of RE in VEP responses generated with the SD t-VEP system and to investigate their potential role in objective measurement of spherical RE.

Methods

Subject selection

We prospectively enrolled 35 healthy volunteers after approval from the Institutional Review Board of New York Eye and Ear Infirmary. The median age of the 35 study subjects was 25.0 (interquartile range: 22.0–28.0) years. There were 14 (40%) men and 21 (60%) women. All subjects were emmetropic ($\leq$0.25 diopters in any axis) on retinoscopy and had an uncorrected visual acuity of 20/20 or better and a normal ophthalmic examination. Exclusion criteria included a history of ocular trauma or disease, dyschromatopsia, neurological disorders, diabetes, family history of retinal disease and anticipated poor attention span from current or recent use of medications with psychotropic effects.

Device

VEP responses were generated using the Enfant™ NOVA System (Diopsys Inc., Pine Brook, NJ) with software modifications. The device and technique have been described in detail previously [11]. A black and white checkerboard stimulus was presented in a 22-cm circular field. The viewing distance was set to 1 meter, yielding a total display viewing angle of 12.54 degrees. A large stimulus field of 22 cm diameter minimized VEP changes caused by minor alterations in the direction of gaze. A red circular outline with a diameter of 1 cm and a thickness of 0.1 cm was used as fixation target. A check size of 28.87 min of arc was chosen after testing the device parameters in a pilot sample of 4 subjects. A smaller check size could detect smaller changes in refraction, but with larger confidence intervals, and a higher risk of intentional defocusing errors. A larger check size produced smaller confidence intervals but was less sensitive to changes in RE. The checkerboard pattern had white checks of 122.9 cd/m^2 and black checks of 9.59 cd/m^2, resulting in a Michelson contrast of 85% and mean luminance of 66 cd/m^2. The luminance of each stimulus check was temporally modulated in counter phase at 1 Hz (2 reversals per second). Synchronized single-channel SD-tVEP waves were recorded and generated a time series of 240 data points per analysis window.

Procedure

All subjects were tested between 10 am and 2 pm. Electrodes were placed at Oz (active point) and Fpz (reference point), according to the International 10–20 System for electrode placement. An electrode at F7 served as ground. Electrode impedance was maintained below 5 K ohms. All subjects adapted to the field illumination in an otherwise dim room for at least 5 min before the test was run. One eye was randomly selected for the test, and the fellow eye was covered with a dark patch.

Refractive errors were induced by means of frameless trial lenses (±20, ±16, ±14, ±12, ±10, ±8, ±6, ±4, ±2 and ±1 diopters) placed at a vertex distance of 10 mm. The plus lenses were used to simulate corresponding myopic refractive errors, while the minus lenses were used to simulate corresponding hypermetropic refractive errors. The lenses were used in order of highest plus to highest minus lens. A SD t-VEP was recorded in the emmetropic state, with and without use of plano lens, and for each induced refractive state. For emmetropia, VEP recorded with plano lens was used for analysis. A short rest was given after each test. Three additional VEPs were obtained, without using any defocusing lens, at random intervals in order to verify that the test eye remained in its natural emmetropic state during the entire test period.

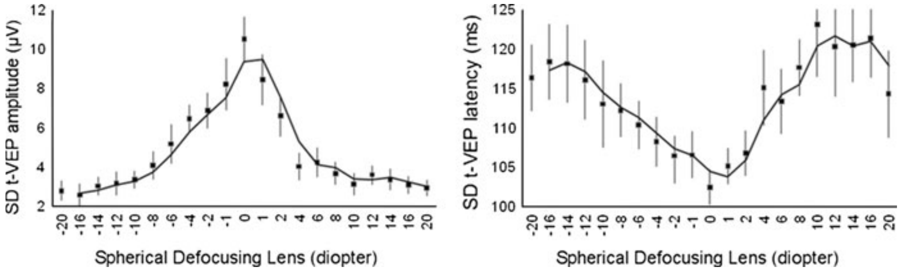

Fig. 1 P100 amplitude and latency as a function of dioptric lens power in a SD t-VEP device. *Error bars* show 95% confidence intervals of the mean VEP amplitude and latency at various dioptric powers. The *trend lines* depict moving averages

Data processing

P100 latency, amplitude measured from baseline to P100 peak and that from N75 trough to P100 peak were obtained for each VEP recording using an automated method, which uses a post-signal processing algorithm and has been previously described [11]. The data processing requires a single manual step of identifying N75 trough and P100 peak, and all VEP records were coded for the refractive errors in order to eliminate observer bias during this step.

Results

Twenty-one SD t-VEP responses, representing emmetropia and all tested refractive errors, were analyzed for each subject to generate a cumulative pool of 735 VEP recordings.

Effects of refractive error on VEP

P100 amplitude progressively decreased and P100 latency progressively increased with an increase in both induced myopia and hypermetropia. P100 amplitude plot as a function of sequential defocusing lenses resulted in U-shaped waves with a peak at emmetropia, while P100 latency plot resulted in an inverted U-shaped wave (Fig. 1). Although an overall similar effect of defocusing lenses on amplitude and latency was seen in all subjects, the absolute values and change in amplitude and latency were variable. Figure 1 shows an overlap in the 95% confidence intervals of mean amplitudes and latencies at both low and high refractive errors. Mean P100 amplitude (induced myopia, r: -0.79, $P = 0.01$; induced hypermetropia, r: -0.90, $P = 0.001$) correlated negatively, while mean P100 latency (induced myopia, r: 0.71, $P = 0.03$; induced hypermetropia, r: 0.95, $P < 0.001$) correlated positively with induced myopia and hypermetropia (Fig. 2).

While 34 (97.1%) emmetropic VEP responses had a sharp (<1 grid square/20 ms) P100 peak and N75 trough, a variable degradation of P100 peak and N75 trough was seen with increasing power of the defocusing lens (Fig. 3). A loss of identifiable waveform was seen in 39/385 (10.1%) VEP responses with ≥±10 diopter lenses.

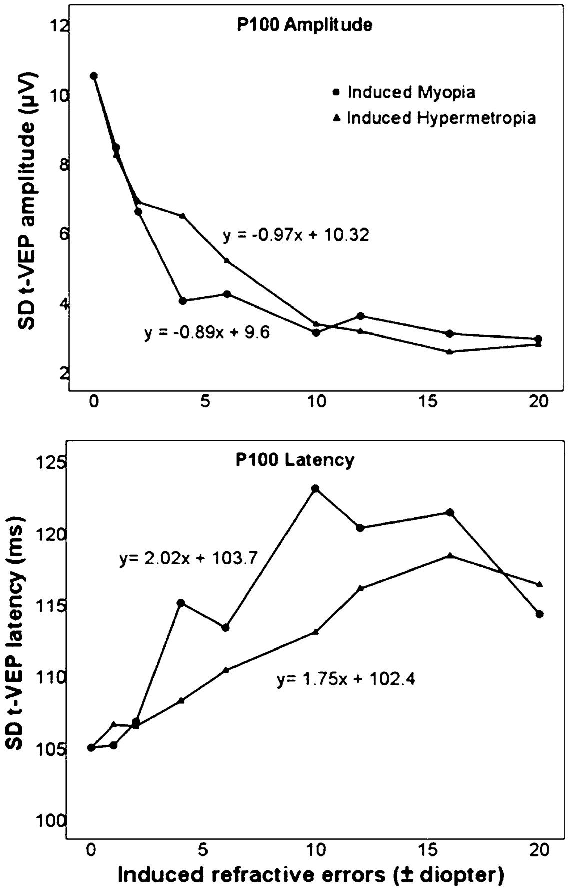

Fig. 2 Correlation of the mean P100 amplitude and latency with induced myopia and hypermetropia

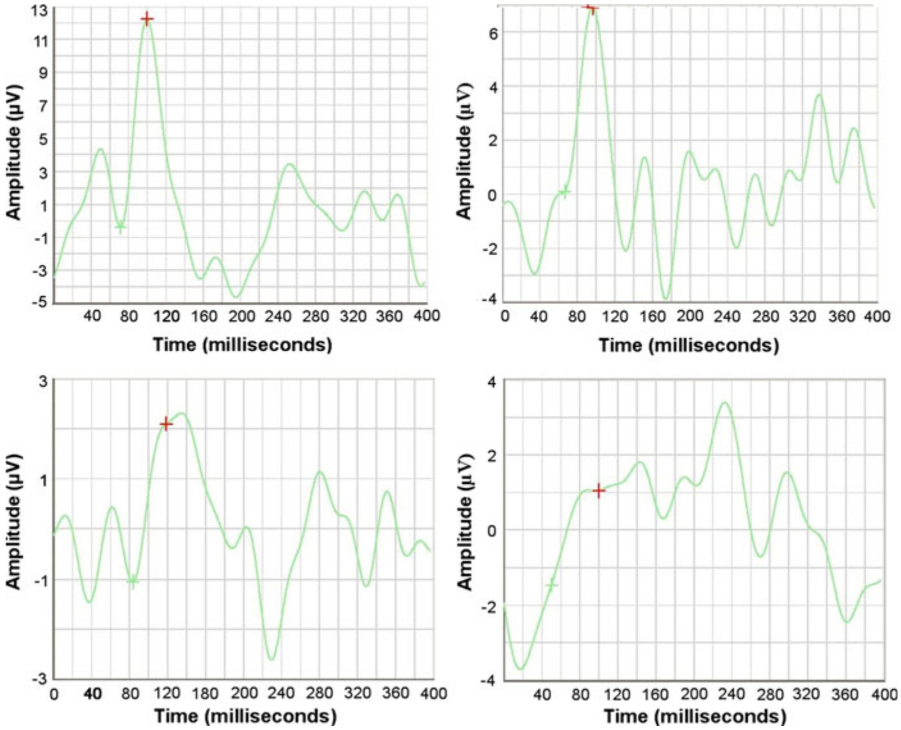

Fig. 3 SD t-VEP recordings showing a sharp (<1 square/20 ms) P100 peak and N75 trough in emmetropia (*top left*), flattening of N75 trough with a −4.0 diopter lens (*top right*), flattening of P100 peak with +10.0 diopter lens (*bottom left*) and a loss of identifiable waveform with a +16 diopter lens (*bottom right*)

Objective refraction using refractive error effects on VEP

Despite a strong correlation of the SD t-VEP amplitude and latency with induced refractive state, there was an overlap in amplitude and latency values for adjacent RE. Intra and inter-individual variations were seen in the type of refractive error artifacts and the amount of change with each successive refractive state. Absolute values for amplitude and latency and regression equations derived from amplitude and latency were found unsuitable for predicting refractive state of the eye.

A VEP scoring system, based on P100 latency, amplitude and waveform quality, was used to estimate spherical RE from SD t-VEP recordings (Table 1). The scoring system gave equal importance to P100 amplitude and latency. Points were awarded for higher amplitudes and proximity of P100 occurrence to 100 ms. Points were deducted for degradation of P100 peaks and N75 troughs.

The VEP scoring system was tested within the study sample using ROC curves, and sensitivity and specificity of VEP responses in predicting various RE were calculated (Table 2). The sensitivity measured the proportion of cases where the refractive error predicted by a VEP score would be the actual refractive error (true positives). The specificity measured the proportion of cases where the refractive error not predicted by a VEP score will actually not be the refractive error (true negatives). Scores > 14 had 94.1% sensitivity for emmetropia, thereby implying that 94% of emmetropic VEP scored more than 14 on the VEP scoring system. Similarly, scores > 17 had 97.3% specificity for emmetropia, thereby implying that 97% of ametropic VEP scored less than 17 on the VEP scoring system. Scores > 11 predicted ametropia of $\leq\pm2$ diopters with a sensitivity and specificity of 85%. For RE between ±2 and ±14 diopters, scores from a single VEP could estimate a RE within a 4 diopter range with a sensitivity and specificity between 75 and 85%. The sensitivities and specificities fell to below 70% for RE > 14 diopters.

Discussion

The degradation of VEP response with uncorrected RE is well established. It has been shown that the VEP

Table 1 A VEP scoring system for objective measurement of spherical refractive error using a SD t-VEP

P100 Amplitude		P100 Latency	
μV	Points awarded	ms	Points awarded
>8	9	100	9
7–8	8	100 ± ≤2.5	8
6–7	7	100 ± ≤5.0	7
5–6	6	100 ± ≤7.5	6
4–5	5	100 ± ≤10.0	5
3–4	4	100 + >10, ≤15	4
2–3	3	100 + >15, ≤20	3
1–2	2	100 + >20, ≤25	2
0–1	1	100 + >25, ≤30	1
<0 or no identifiable wave form	0	100 + >30 or no identifiable wave form	0

P100 Peak		N75 Trough	
Quality	Point deducted	Quality	Point deducted
<1square/20 ms	0	<1square/20 ms	0
>1square/20 ms	−1	>1square/20 ms	−1
Bifid or notched but identifiable peak	−2	Bifid or notched but identifiable peak	−2
No identifiable waveform	−3	No identifiable waveform	−3

Table 2 Sensitivities and specificities of the VEP scoring system for SD t-VEP in predicting emmetropia and spherical refractive errors

Waveform score	Refractive state	Sensitivity (95% CI)	Specificity (95%CI)
>17	Emmetropia	55.9% (37.9–72.8%)	97.3% (95.7–98.4%)
>14	Emmetropia	94.1% (80.3–99.3%)	84.4% (81.0–86.8%)
>11	0 to ±2D	85.8% (79.6–90.9%)	84.5% (81.1–87.5%)
8–11	> ±2D to <±6D	83% (75.5–88.9%)	81.1% (77.7–84.3%)
5–8	>±6D to <±10D	81.5% (73.8–87.8%)	80.1% (76.5–83.3%)
2–5	>±10D to ≤14D	78.6% (70.6–85.3%)	75.2% (71.4–78.7%)
<2	>14D	68.0% (61.0–74.5%)	63.2% (58.8–67.5%)

amplitude decreases and the implicit time prolongs as lenses of increasing plus or minus dioptric power are placed in front of the test eye [2–6]. Our study confirms these findings in a SD t-VEP device. We found a strong negative correlation of P100 amplitude and a strong positive correlation of P100 latency with induced refractive errors. In addition to these two parameters, our results show that there is also a qualitative degradation of the VEP waveform with degradation of P100 peaks and N75 troughs with increasing refractive errors.

Previous studies speculating on the use of VEP in objective refraction were based on the assumption that the sharpest retinal image gives the largest VEP amplitude. The VEP scoring system for measuring RE in our study with a SD t-VEP system, however, is based on the assumption that the sharpest retinal image gives the best quality VEP, which may or may not be the largest evoked potential. Millodot and Riggs studied the effect of RE on VEP amplitude using an analogue signal averaging method and found that amplitude was sensitive to a change in ±0.25 D in their two study subjects, provided that no effort at accommodation was made [4]. Regan described a fast method of detecting RE based on VEP amplitude using an analogue Fourier analysis method and reported that best lens power could be found within an error margin of ±0.5 D in 10–20 s in 8 study subjects [9]. Bostrom et al. using the same technique in 5 subjects reported that even though the spherical refractive state could be measured within ±0.5 D, large slow-wave fluctuations limited the clinical usefulness of the technique [10].

One of our findings is the intra and inter-individual variability in the absolute values of the VEP parameters and a change in these values in response to each step change in the RE. The topic of variability has not been addressed in the previous studies. Accommodation does not appear to be the only underlying cause since the variability is seen with both plus and minus lenses and at high and low RE. Our scoring system combines degradation of amplitude, latency and waveform quality with RE to generate a single score. The scoring, therefore, should be more resistant to the variability compared to the use of amplitude values alone. In the absence of sensitivity and specificity data for the range of RE tested, it is not possible to estimate false positives, false negatives and variability in the previous studies. We used a check size of 28.87 min of arc instead of 20 min of arc or smaller used by Regan [9] and 14 min of arc used by Bostrom et al. [10]. It has been reported that when check size exceeds 25–35 min, the VEP amplitude may paradoxically increase when the retinal image is blurred [12]. However, Sokol and Moskowitz did not find this paradoxical effect with VEP latencies [5]. We found that smaller check sizes made the amplitude and latency more sensitive to a change in the RE but at a cost of wider confidence intervals, while establishing device parameters for the SD t-VEP in a pilot study with 4 subjects.

Using the scoring system, a single SD t-VEP response could differentiate emmetropia from ametropia with a sensitivity of 94% and a specificity of 97%. A single SD t-VEP had a good sensitivity and specificity in predicting small RE within a 2 diopter range and large RE (up to 14 diopters) within a 4 diopter range. Since the scoring system has a very high specificity for emmetropia, it can also be used for a more accurate assessment of spherical RE using a 3-step technique—Step 1: A VEP response is scored using VEP scoring system to estimate approximate RE. Step 2: Two additional VEP responses are recorded using a plus and minus lens with dioptric power estimated in Step 1. The VEP yielding a better score identifies myopia/hypermetropia, Step 3: The estimated error is refined using a straddling technique with lenses within the range of estimated RE. VEP responses are obtained in pairs of sequentially narrower dioptric range with the highest emmetropic score as an endpoint.

The scoring method for SD t-VEP refraction has several limitations. It was not investigated for astigmatic errors. Regan described a technique of using a stenopaic slit in measuring astigmatic powers from the VEP amplitude [9]. However, others have found that latency but not amplitude is sensitive to astigmatic errors and significant effects are only seen in the horizontal and vertical meridians [5, 13]. We are investigating the feasibility of using a meridional stimulus pattern and stenopaic slit in measuring astigmatic errors with a SD t-VEP system. It is possible that the scores may deviate in the older persons and cutoff scores may have to be redefined for them [14, 15]. In addition, scores may not be valid in patients in whom a dense media opacity or macular pathology also contributes to the retinal image blur. However, the principle of achieving a best VEP score in an emmetropic state will essentially remain the same. Even in such cases, VEP refraction should be possible using the 3-step refraction technique with an aim to achieve the best possible score.

One of the reasons that VEP refraction has not found a clinical application may be a lack of well-defined clinical indications. VEP is the only objective way to measure the perceptual response of the visual pathway. A VEP refraction appears physiologically more valid than retinoscopy since it measures the perceptual response of the visual pathway to different refractive states [4]. The retinoscopy determined that refraction produces a small but systematic error since the light may be reflected from a different layer than the photoreceptors and may increase the risk of a ‘small eye artifact’ in eyes with a very short axial length [16]. Even though a VEP refraction appears cumbersome and time consuming, it is equivalent to a combined retinoscopy and subjective refraction and may take a similar or less time in patients with difficult refraction. A single SD t-VEP response is generated in 20 s, and the post-signal processing algorithm calculates values for different parameters from the N75-P100 waveform complex within 10 s. Despite these favorable points, VEP refraction offers no particular advantage and is not a practical substitute for classical refraction in routine cases. However, VEP refraction may be used as an alternative or complement to classical refraction under the following conditions: (1) difficult subjective refraction because of ambivalent responses and/or poor cognitive status (2) unexplained spectacle intolerance (3) patients with microphthalmia or normal eyes with very short axial lengths (4) difficult retinoscopy in small fixed pupils. In addition, since automated output from a SD t-VEP device is easy to interpret, it has a good potential for screening RE in various non-ophthalmic settings.

In conclusion, a VEP scoring system that includes the quality of a VEP response can be used to both screen and accurately measure spherical RE with a SD t-VEP device.

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