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Original research

Contrast and spatial frequency modulation for diagnosis of amblyopia: An electrophysiological approach

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Abstract

Purpose: To evaluate the diagnostic value of visual evoked potentials (VEPs) and to find out which test setting has the most sensitivity and specificity for amblyopia diagnosis.

Methods: Thirty-three adult anisometropic amblyopes were intended in this study and were tested for visual evoked potentials with different stimulus conditions including three spatial frequencies [1, 2, and 4-cycles-per-degree (cpd)] at four contrast levels (100, 50, 25, and 5%). We also tested psychophysical contrast sensitivity and compared the results with electrophysiological ones. We plotted Receiver Operating Characteristic (ROC) curve for each VEP recording and psychophysical contrast sensitivity to evaluate the area under the curve, sensitivity, specificity, and cut-point value of each test stimulus for detecting amblyopic eyes.

Results: Thirty-three amblyopic and 33 non-amblyopic eyes were examined for psychophysical contrast sensitivity and VEPs. Area under the ROC curve (AURC) findings showed that VEP with different stimulus settings can significantly detect amblyopic eyes, as well as psychophysical contrast sensitivity test. We found that P100 amplitudes had the largest AURC in response to stimuli of 2-cpd spatial frequency at 50 ($P < 0.001$) and 25% ($P < 0.001$) contrast levels, respectively. Cut-off amplitudes for these stimuli were 8.65 and 4.50 μV, which had a sensitivity of 0.758 and 0.697 and a specificity of 0.788 and 0.848, respectively. The sensitivity and specificity of VEP P100 amplitude in response to the stimuli with 2 cpd spatial frequency and 50 and 25% contrast were greater than the findings obtained from psychophysical contrast sensitivity test.

Conclusion: According to our findings, assessment of VEP amplitudes in response to stimuli of 2-cpd spatial frequency at 50 and 25% contrast levels can best detect amblyopia with highest sensitivity and specificity and thus, are the protocols of choice for detection of amblyopic eyes.

Keywords: Amblyopia; Visual evoked potentials; Contrast sensitivity

Introduction

Amblyopia is a developmental disorder of central visual pathways and occurs when an amblyogenic factor affects the visual system of a growing child and diminishes the normal development of the visual nervous system.[1–4] Recent studies suggest that the plasticity of the adult sensory nervous system is more than that believed in the past.[3,5] There is clear evidence that substantial plasticity still remains in the visual

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system of an amblyopic individual at the synaptic, cellular, and cortical representation levels even after adolescence.[3,6−12] The improvement of visual function in adult amblyopes motivates us to diagnose and treat amblyopia in adults responsibly.

Reduction of contrast sensitivity is one of the main consequences of amblyopia[9,11,12] and is more prominent in anisometropic amblyopia.[3,13]

Diagnosis of amblyopia based on the patient's responses to stimuli with reduced contrast can be achieved by psychophysical or electrophysiological methods. Visual evoked potential (VEP) has been widely studied in amblyopia and reduction of amplitude and increasing of latency of P100 wave are the most agreed findings between authors who studied VEP in amblyopia.[14−20] Thus, amplitude and latency of visually evoked responses to stimuli with different contrast levels as well as psychophysical measurements of contrast sensitivity could be noticeable clinical findings for diagnosis of amblyopia. Levi and Harwerth[17] suggested that VEPs can be applicable clinically in detecting amblyopia in those who cannot be tested for psychophysical contrast sensitivity since he found that the deficit in psychophysical contrast sensitivity is also present in VEP results. Furthermore, they stated that VEP can differentiate amblyopia from optical blur by comparing the slope of VEP contrast functions (variation of P100 amplitudes with decrease of stimulus contrast).[17] However, there is no standardized protocol for diagnosis of amblyopia by electrophysiological methods. Additionally, there is no evaluation of diagnostic values for VEPs with stimuli of different contrasts and spatial frequencies. In this study, we evaluated the diagnostic value of VEP and compared it with psychophysical contrast sensitivity measurements to introduce an electrophysiological protocol for diagnosis of amblyopia and to find out which test setting has the most sensitivity and specificity for amblyopia diagnosis.

Methods

Subjects

Thirty-three anisometropic amblyopes aged from 16 to 35 years were intended in this study. Three of them had myopic and the others had hyperopic anisometropia. Individuals with amblyopia who did not have any types of strabismus and with the minimum difference of 1.5 diopters refractive error (either sphere or astigmatism) were assumed as anisometropic amblyopes.[21] Thirty-three amblyopic and 33 non-amblyopic eyes were examined for psychophysical contrast sensitivity and VEPs. Each subject was examined for any other ophthalmic conditions including media opacity, retinal disease, motility disorder, and abnormal response of pupil to light. Each patient was asked for general health and any drug use. Patients with any central nervous system disease or those who had been using drugs that affect central nervous system were excluded from the study. Visual acuity was measured with Nidek system Chart SC-1600 (Nidek Co., Aichi, Japan). Minimum and maximum acceptable visual acuity (logMAR) of the amblyopic eyes for inclusion were respectively 0.4 and 0.1 (0.4 and 0.8 Snellen equivalent). Each patient was examined monocularly, with an undilated pupil and with best refractive correction. All the measurements were performed by a single examiner (who was masked in terms of the eyes) and under the same room conditions.

The Ethics Committee of Iran University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Declaration of Helsinki. All participants signed a written informed consent.

The psychophysical contrast sensitivity test

Monpack One® (Metrovision, Pérenchies, France) is originally an electrophysiological testing device, but it has benefits for testing some psychophysical measurements, too. It employs vertical sine-wave gratings for measurement of psychophysical contrast sensitivity at various spatial frequencies. The device displays stimuli with increasing contrast, and patient commands to stop the process when first recognized the gratings from a plain screen. At the end of the procedure, the device gives us a plot of contrast sensitivity function (CSF). Since VEPs were recorded at 1, 2, and 4-cycles-per-degree (cpd) spatial frequencies, measurements for these spatial frequencies were derived from the CSF plot obtained from psychophysical test.

The VEPs were recorded by Metrovision Monpack One® electrophysiological testing device with monopolar electrodes which gold-plated cupula electrodes were placed on the scalp according to international 10/20 system. The skin was cleaned with an abrasive gel and then with alcohol before applying electrodes. Electrodes were filled with Ten 20® (Weaver and Company, Aurora, CO, USA) adhesive conductive paste to maintain electrical connection properly. We used an electrode on the ear lobe as ground electrode. The impedance of electrodes was maintained below 5 kΩ according to International Society for Clinical Electrophysiology of Vision (ISCEV) standards for clinical VEPs.[22] Signals were amplified by 20000 times and band passed (1−100 Hz). Sixty events were averaged for every trial, and analysis time was 250 ms post-stimulus.[23]

Patients sat at 1 m from the stimulus display monitor so that the stimulus field subtended 23.6° of the arc horizontally. Transient pattern-reversal VEPs were elicited by a checkerboard stimulus, which reversed its contrast every 200 ms (2.5 Hz). The component sizes of stimuli (check sizes) were selected at 30, 15, and 7 min of arc (min arc), which represents 1, 2, and 4-cpd spatial frequencies. VEPs were recorded for each spatial frequency at four contrast levels of 100, 50, 25, and 5%. For each VEP recording, P100 amplitude and latency were noted down. VEP recordings have been performed for both amblyopic and non-amblyopic eyes separately.

Statistical analysis

Statistical analyses were conducted using SPSS version 22.0 (IBM SPSS, Armonk, NY, USA). Due to non-normal

Table 1
Area under the ROC curve (AURC) data for visual evoked potential (VEP) P100 amplitude.

	SF = 1				SF = 2				SF = 4			
Contrast (%)	100	50	25	5	100	50	25	5	100	50	25	5
AURC	0.677	0.602	0.621	0.670	0.690	0.825	0.806	0.526	0.686	0.613	0.551	0.657
Significance	0.013	0.155	0.090	0.018	0.008	0.000	0.000	0.715	0.009	0.115	0.481	0.028
95% CI	0.548 to 0.807	0.465 to 0.739	0.485 to 0.785	0.536 to 0.804	0.562 to 0.817	0.722 to 0.928	0.697 to 0.916	0.385 to 0.667	0.557 to 0.815	0.475 to 0.750	0.411 to 0.690	0.525 to 0.789

AURC: Area under the ROC curve; CI: Confidence interval; SF: Spatial frequency.

distribution of the data, we used non-parametric Spearman's Rho test for evaluation of correlation between psychophysical and VEP measurements. In order to assess diagnostic value of VEP, we plotted Receiver Operating Characteristic (ROC) curve and computed area under the curve. We used Youden index to determine the sensitivity, specificity, and cut-point values of each stimulus setting in diagnosis of amblyopia. Amplitude measurements were plotted as a function of spatial frequency, which are called "Spatial Frequency Tuning Functions (STF)" at each contrast level.[19,24] We considered *P*-value less than 0.05 to be statistically significant.

Results

Thirty-three adult anisometropic amblyopes aged 16−35 years old (25.21 ± 6.23 [Mean ± SD (Standard deviation)]) were intended in this study. Thirty-three amblyopic eyes and 33 non-amblyopic eyes were evaluated. Mean visual acuity was 0.2 ± 0.1 in amblyopic eyes and 0.0 ± 0.0 in non-amblyopic eyes in logMAR unit. Spherical equivalent refractive error was +1.79 ± 2.93 (Mean ± SD) in amblyopic eyes and +0.73 ± 1.45 in non-amblyopic eyes.

ROC curves were plotted to evaluate sensitivity and specificity of electrophysiological and psychophysical tests. Results from evaluating the area under the ROC curves (AURC) indicated that psychophysical contrast sensitivity test using stimuli of 2 and 4-cpd spatial frequencies have significant AURCs in detecting amblyopic eyes from non-amblyopic eyes ($P < 0.001$). In addition, area under logarithm of psychophysical contrast sensitivity curve had significant AURC to detect amblyopic eyes from non-amblyopic eyes ($P < 0.001$). Results from electrophysiological tests indicated that VEP P100 amplitude obtained from stimuli of 1-cpd spatial frequency at 100 and 5% contrast levels, 2-cpd spatial frequency at 100, 50, and 25% contrast levels, and 4-cpd spatial frequency at 100 and 5% contrast levels had significant AURC to detect amblyopic eyes from non-amblyopic eyes ($P < 0.05$) (Table 1). Moreover, AURC obtained from VEP P100 latency using stimuli of 1-cpd spatial frequency at 50 (P = 0.01) and 25% (P = 0.002) contrast levels was significant in detecting amblyopic from non-amblyopic eyes.

Maximum sensitivity and specificity for each stimulus of any spatial frequency and contrast level were calculated according to Youden Index and have been listed in Table 2,

Table 2
Sensitivity and specificity of psychophysical contrast sensitivity test.

	SF = 1	SF = 2	SF = 4	AULCSF
Sensitivity	0.879	0.667	0.727	0.758
Specificity	0.242	0.818	0.758	0.758
Youden Index	0.121	0.485	0.485	0.515
Cut-off value (Log CS)	2.15	2.075	1.930	8.275
LR+	1.16	3.667	3.00	3.125
LR−	0.50	0.407	0.36	0.320

Log CS: Logarithm of contrast sensitivity; LR: Likelihood ratio; SF: Spatial frequency; AULCSF: Area under the logarithm of contrast sensitivity function.

Table 3
Sensitivity and specificity of visual evoked potential (VEP) P100 amplitude.

	SF = 1				SF = 2				SF = 4			
Contrast (%)	100	50	25	5	100	50	25	5	100	50	25	5
Sensitivity	0.545	0.758	0.727	0.667	0.667	0.758	0.697	0.788	0.939	0.515	0.485	0.485
Specificity	0.788	0.455	0.515	0.758	0.667	0.788	0.848	0.333	0.424	0.758	0.636	0.818
Youden index	0.333	0.212	0.242	0.424	0.333	0.545	0.545	0.121	0.364	0.273	0.121	0.303
Cut-off Amplitude	9.150	10.650	8.250	3.750	10.350	8.650	4.500	3.850	8.400	2.600	2.100	0.850
LR+	2.571	1.389	1.500	2.750	2.000	3.571	4.600	1.182	1.632	2.125	1.333	2.667
LR−	0.577	0.533	0.529	0.440	0.500	0.308	0.357	0.636	0.142	0.640	0.809	0.630

LR: Likelihood ratio; SF: Spatial frequency.

Table 4
Sensitivity and specificity of visual evoked potential (VEP) P100 latency.

	SF = 1				SF = 2				SF = 3			
Contrast (%)	100	50	25	5	100	50	25	5	100	50	25	5
Sensitivity	0.333	0.455	0.576	0.303	0.576	0.303	0.364	0.394	0.576	0.515	0.545	0.970
Specificity	0.788	0.939	0.848	0.970	0.636	0.909	0.848	0.848	0.606	0.727	0.636	0.182
Youden index	0.121	0.394	0.424	0.273	0.212	0.212	0.212	0.242	0.182	0.242	0.182	0.152
Cut-off Latency	114.5	114.5	116.0	137.0	116.0	124.0	125.0	142.0	126.5	127.5	132.5	111.5
LR+	1.571	7.500	3.800	10.00	1.583	3.333	2.400	2.600	1.461	1.889	1.500	1.185
LR−	0.846	0.581	0.500	0.719	0.667	0.767	0.750	0.714	0.700	0.667	0.714	0.167

LR: Likelihood ratio; SF: Spatial frequency.

Table 5
Area under the ROC curve (AURC) data for psychophysical contrast sensitivity test.

	SF = 1	SF = 2	SF = 4	AULCSF
AURC	0.544	0.778	0.806	0.758
P-value	0.538	0.000	0.000	0.000
95% CI	0.403 to 0.685	0.665 to 0.892	0.701 to 0.911	0.639 to 0.877

AURC: Area under the ROC curve; CI: Confidence interval; SF: Spatial frequency; AULCSF: Area under the logarithm of contrast sensitivity function.

Table 3, and Table 4 along with the Cut-Point values. As well, AURC data have been listed in Table 5, Table 1, and Table 6.

We found that VEP amplitudes were significantly higher in non-amblyopic eyes with the stimuli of 1-cpd spatial frequency at all contrast levels ($P < 0.05$), and there was a significant correlation between two groups ($P < 0.05$). By 2-cpd spatial frequency stimulus, there were significant differences between the two groups at all contrast levels except for 5% ($P < 0.001$). Correlation was also significant at the same contrast levels with this stimulus ($P < 0.05$). However, by 4-cpd spatial frequency stimulus, we only found a significant difference at 100 ($P = 0.002$) and 5% ($P = 0.017$), and correlation was only significant at 100% ($P = 0.042$) contrast levels.

STF, as we see in Fig. 1, shows the behavior of VEP amplitude with changes in spatial frequency of stimulus. VEP amplitude shows high spatial specificity in normal eyes. Its peak is at 2-cpd spatial frequency, and attenuation is noticeable in higher and lower spatial frequencies. However, we encounter different conditions when the stimulus contrast is 5% so that amplitude decreases with increasing of spatial frequency. On the other hand, there is no spatial specificity in amblyopic eyes in all contrast levels with the exception of 100% contrast, and amplitude attenuates more with spatial frequency.

Comparison of VEP P100 latency between amblyopic and non-amblyopic eyes showed the following results. By 1-cpd spatial frequency stimulus, latency was significantly delayed in amblyopic eyes at all contrast levels except for 100% ($P < 0.05$), and there was a significant correlation between amblyopic and non-amblyopic eyes at all contrast levels ($P < 0.01$). By 2-cpd spatial frequency stimulus, significant difference was only seen at 50 ($P = 0.031$) and 25% ($P = 0.049$) contrast levels, and correlation was significant between two groups at all contrast levels except for 5% ($P < 0.001$). Nonetheless, by 4-cpd spatial frequency stimulus, there was no significant difference between two groups at any contrast level and correlation was only significant at 100% contrast level ($P = 0.040$).

Discussion

Results obtained from VEP P100 amplitude showed that AURC is greatest when a stimulus of 2-cpd spatial frequency (15 min arc component size) at 50% contrast level is used (Table 1, Fig. 2). In the second place, a stimulus of 2-cpd spatial frequency at 25% contrast level has the greatest AURC. According to Youden Index, the sensitivity and specificity of these two stimulus settings are shown in Table 3. Cut-off amplitudes for these two stimuli were 8.65 μV for 50% contrast and 4.50 μV for 25% contrast (i.e. if P100 amplitude drops below these cut-off amplitudes, the eye is assumed amblyopic with the sensitivity and specificity mentioned in Table 3). Lim[25] found that VEP P100 latency can detect amblyopia with the sensitivity of 0.511, and the difference between amplitudes of two eyes can detect amblyopia with the

Table 6
Area under the ROC curve (AURC) data for visual evoked potential (VEP) P100 latency.

	SF = 1				SF = 2				SF = 4			
Contrast (%)	100	50	25	5	100	50	25	5	100	50	25	5
AURC	0.530	0.685	0.718	0.569	0.603	0.587	0.559	0.547	0.537	0.588	0.600	0.492
Significance	0.672	0.010	0.002	0.336	0.149	0.226	0.408	0.509	0.603	0.221	0.162	0.913
95% CI	0.390 to 0.671	0.555 to 0.815	0.592 to 0.843	0.426 to 0.712	0.466 to 0.741	0.448 to 0.725	0.419 to 0.700	0.406 to 0.689	0.396 to 0.678	0.448 to 0.727	0.463 to 0.737	0.351 to 0.634

AURC: Area under the ROC curve; CI: Confidence interval; SF: Spatial frequency.

sensitivity of 0.319. However, Lim used only one stimulus setting of 1.2-cpd spatial frequency and without manipulation of contrast. Our findings demonstrated that we may have more sensitivity in detecting amblyopic eyes if we select stimuli of 2-cpd spatial frequency at 50 or 25% contrast levels (0.758 and 0.697, respectively).

We found that AURC in assessment of area under the logarithm of contrast sensitivity function (AULCSF) obtained from psychophysical contrast sensitivity test, as a diagnostic test for detecting amblyopia, is significant (Table 5). Moreover, AURC for psychophysically examined spatial frequencies (2 and 4-cpd) were significant, too. Obviously, VEP results had greater AURCs with two select stimulus settings mentioned above. This finding could be due to deficient visually evoked responses to suprathreshold stimuli in amblyopic eyes, while there is no such deficit in suprathreshold psychophysical responses. Levi[15,17] suggested that suprathreshold compensating mechanisms in amblyopic visual system occur in a level higher than the area of origination of the VEPs. Thus, the results of these mechanisms would not influence VEP responses.

Our results in assessment of spatial tuning function, which demonstrates the changes of VEP amplitude with spatial frequency (Fig. 1), showed that the peak of amplitude in non-amblyopic eyes was at 2-cpd spatial frequency at all contrast levels except for 5%. This finding confirms previous studies.[18,19] The greatest difference between P100 amplitudes of amblyopic and non-amblyopic eyes was at 2-cpd spatial frequency at 50 and 25% contrast levels. These are exactly the same stimuli that have maximum sensitivity and specificity for detecting amblyopia. Accordingly, our findings about sensitivity and specificity at theses stimulus settings seems reasonable. Although previous studies had not examined different contrast levels, they implied that the greatest difference between amblyopic and non-amblyopic eyes occurs at 2-cpd spatial frequency.[18,19] Therefore, assessment of spatial tuning function again confirms that the best protocol for VEP testing for detecting amblyopic eyes is to use stimuli of 2-cpd spatial frequency at 50 and 25% contrast levels.

Perception of low contrast stimuli is predominantly mediated by magnocellular pathway. Since magno system is the main liable for recognition of the close to threshold stimuli and probably forms the basis of the CSF,[26] loss of contrast sensitivity is probably the result of a defect in magno system. As all of the individuals who attended our study were mild anisometropic amblyopes (visual acuity 0.1 to 0.4 logMAR), and magnocellular pathway is intact in mild amblyopia,[18,27] psychophysical contrast sensitivity test that measures the threshold demonstrates poorer sensitivity and specificity than VEP.

To form the VEP wave, parvo neurons contribute with magno cells. It has been proven that there is a considerable overlap at the nerve endings receiving magno and parvo axons in the 4c layer in V1 striate cortex. This anatomic

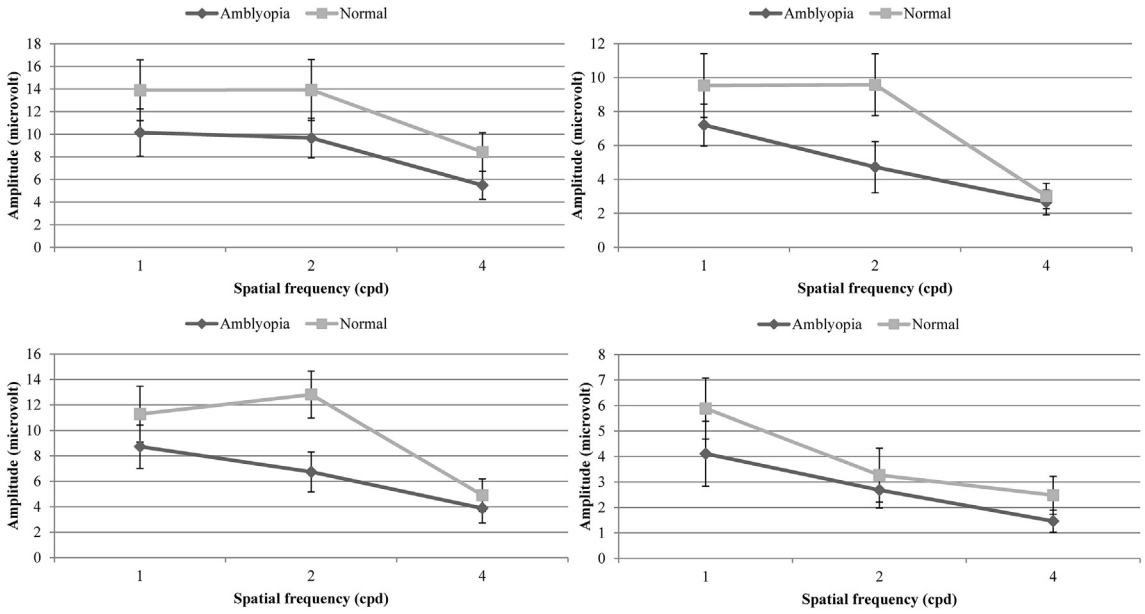

Fig. 1. Spatial frequency tuning functions (STF) in four contrast levels represents visual evoked potential (VEP) amplitudes as a function of spatial frequency. cpd: cycles-per-degree.

and functional overlap occurs for stimuli that do not selectively excite magno or parvo systems.[26] Thus, both neural pathways contribute when VEP is recorded with nonselective stimuli, and a defect in either of each pathway may affect the outcome. Consequently, parvo deficiency may lead to a decrease in VEP amplitude as well.

To understand why maximum sensitivity and specificity achieved using stimuli of 2-cpd spatial frequency at 25 and 50% contrast levels, we have investigated the stimuli employed in VEP examination from the aspects of spatial frequency and contrast level. According to previous studies, amplitude is lower with high spatial frequency stimuli in both amblyopic and non-amblyopic eyes.[15,19] The highest spatial frequency stimulus we used was 4-cpd. In support of previous studies, we found reduced amplitude in amblyopic eyes, but this reduction was not more than that of other examined spatial frequencies.[14–20] Since reduction of contrast sensitivity at high spatial frequencies is probably due to visual acuity loss in many other visual system disorders,[28] and owing to high dispersion index of our findings of amplitude at 4-cpd spatial frequency, we can conclude that high spatial frequencies are not such appropriate stimuli for detecting amblyopia. Although higher spatial frequencies excite parvo system more selectively,[24,26] they do not have good sensitivity and specificity in detecting amblyopic eyes, according to our findings. This can be due to pre-neural factors like optics, or to contribution of higher levels of visual processing beyond Lateral Geniculate Nucleus (LGN) to form VEPs.[14]

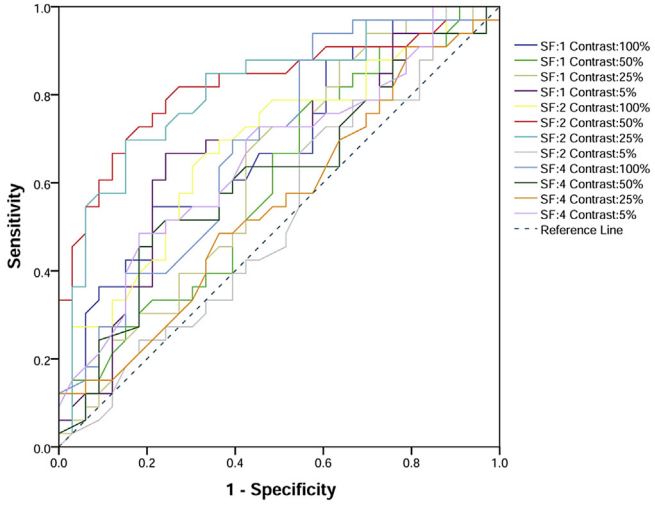

Fig. 2. Receiver Operating Characteristic (ROC) curve for visual evoked potential (VEP) P100 amplitude as a diagnostic measurement for detection amblyopia. SF: Spatial frequency.

VEP responses to stimuli with different spatial frequencies originate from distinct activities in visual system. Spatial frequencies above 1.5-cpd evoke responses that are primarily contrast specific, while those below 1.5-cpd evoke responses that are mostly arise from local luminance changes. Amblyopia involve contrast specific mechanisms more strictly rather than luminance mechanisms.[20] Moreover, low spatial frequency stimuli generally activate magnocellular pathway,[24,26] and it is well accepted that magnocellular pathway is less affected in amblyopic visual system.[18,27] Accordingly, using low spatial frequency stimuli may not lead to prominent VEP loss in amblyopic eyes. However, magno and parvo systems contribute to response to intermediate spatial frequency stimuli.[24] Thus, according to parvocellular defect in amblyopia,[18,27] abnormal VEPs are expected in response to such stimuli.

Our findings showed that stimuli with low contrast had poor sensitivity and specificity. The reason may be associated to the stimulus nature so that stimuli with below 10% contrast

activate magno system selectively.[26,29] Since the magno system is not considerably affected in mild anisometropic amblyopia,[18,27] stimuli with less than 10% contrast are not such good discriminators for detecting amblyopic eyes.

Our findings in assessment of latency showed that maximum AURC occurred with 1-cpd spatial frequency stimulus at 25% contrast level (Table 6, Fig. 3). According to Youden Index, at the cut-off latency of 116 ms, we had maximum sensitivity and specificity (Table 4). Sokol[20] found little but significant increase in latency in amblyopic eyes with a 2-cpd spatial frequency stimulus. He found a mean difference of 4 ms between the two eyes. However, according to our findings, latency is not such an appropriate discriminator for detection of mild anisometropic amblyopia. Since participants in this study were mild anisometropic amblyopes (minimum visual acuity of 0.4 logMAR), and parvo system is more affected in mild amblyopia, a decrease in amplitude is expected in response to low contrast stimuli. Nevertheless, a magno system that mediates responses to a flicker of suprathreshold stimuli remains almost intact in mild amblyopia.[18] Hence, we do not expect an increase in latency. Our findings also confirmed that despite amplitude reduction in mild anisometropic amblyopia, there is no significant difference in latencies between amblyopic and non-amblyopic eyes at most spatial frequencies and contrast levels.

Magnocellular neurons are selectively activated with below 10% contrast stimuli. With reduction of contrast, parvo activity gradually ceases and magno activity increases. In addition, magno neurons tend to saturate with an increase of contrast, and the activity of more numerous parvo neurons begins. As a result of parvo activity, synaptic delay reduces (probably by means of a probability summation mechanism).[26] Therefore, according to insignificant reduction of latency in our findings, we can conclude that in mild anisometropic amblyopia even parvocellular pathway is not affected severely. Thus, absence of elevated latency in amblyopia indicates minor impairment of parvo and intactness of magno system. This implies a suitable condition for treatment. Thus, latency can be used as a parameter to estimate prognosis (not diagnosis).

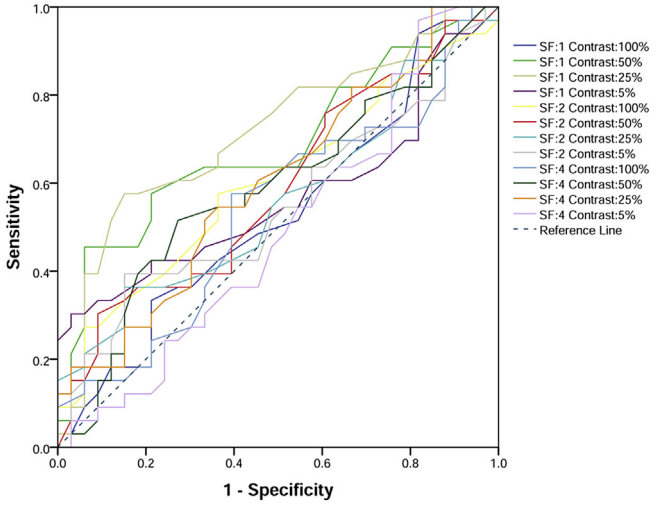

Fig. 3. Receiver Operating Characteristic (ROC) curve for visual evoked potential (VEP) P100 latency as a diagnostic measurement for detection amblyopia. SF: Spatial frequency.

In conclusion, according to our findings in assessment of VEP amplitude, stimuli of 2-cpd spatial frequency at 50 and 25% contrast levels have maximum sensitivity, specificity, and AURC in detecting amblyopic eyes. Thus, these stimulus settings can be use as the protocol of choice for diagnosis of amblyopia electrophysiologically.

Latency findings did not show satisfactory sensitivity and specificity in detecting amblyopic eyes. Since in more severe amblyopia, magnocellular system is also affected,[18] an increase in latency would be expected. Hence, we suggest further studies on patients with more severe amblyopia and to evaluate the latency as a prognostic parameter in treatment of amblyopia.

Unfortunately, the time-consuming nature of electrophysiological measurements, especially when we want to record numerous measurements, made our recording procedure exhausting to some extent for patients. This limited us to using more spatial frequencies in our procedure. Furthermore, although all of the individuals who attended our study were pure anisometropic amblyopes, a greater sample size could be better to rely on the results and more powerful statistical analyses.

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