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Evaluation of Multifocal Visual Evoked Potential in Normal Egyptian Population

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Short title: Multifocal VEP in normal Egyptian population

ABSTRACT

Background: Visual evoked potentials (VEP) s represents a valid electrophysiological tool in neurological pathologies. VEPs are the expression of the electrical activity of the visual pathways up to the optic nerve to the calcarine cortex. Multifocal visual evoked potential (mfVEP), a recent advancement in electrophysiology, has made it possible to document the visual field of an individual as a collection of evoked cortical responses.

Objectives: To assess multifocal visual evoked potential values in normal Egyptian population and their correlation with age, gender, laterality, and refraction.

Patients and methods: An prospective, observational, descriptive study was held on a sample of 100 healthy eyes of 50 cases attending Mansoura ophthalmic center outpatient clinic in the period from October 2020 till March 2022. Ophthalmic examinations included best corrected visual acuity, intraocular pressure measurement, slit lamp biomicroscopy, refraction, fundus. Multifocal VEP was evaluated by Reti-Scan 21.

Result: The mean age of studied cases was 33.82 years. There was 20 (40%) males and 30 (60%) females. Mean BCVA was 0.95 ± 0.115. Mean spherical equivalent was -1.07 ± 1.199. There was no significant correlation between spherical equivalent with multifocal visual evoked potential values ($p>0.05$). There was no significant correlation between IOP with multifocal visual evoked potential values ($p>0.05$). There was significant positive correlation between BCVA with amplitude at inferior nasal, while there was significant negative correlation between BCVA with latency at superior temporal. There was a significant negative correlation between spherical equivalents with latency at superior temporal.

Conclusion: There was significant positive correlation between BCVA with amplitude at inferior nasal, there was significant negative correlation between spherical equivalents with latency at superior temporal. Multifocal VEP technique is superior to conventional full-field VEPs in evaluating the integrity of the visual system, thus allowing more accurate detection of smaller visual field defects.

Keywords: Multifocal Visual Evoked Potential, Best Corrected Visual Acuity, Intraocular pressure.

INTRODUCTION

Non-invasive electrophysiological interfaces for the retina are important in the study of the retina and the visual system. Non-invasive electrophysiological investigations are widely used both for medical and research purposes[1].

Visual evoked potentials (VEP)s represents a valid electrophysiological tool in neurological pathologies. VEPs are the expression of the electrical activity of the visual pathways up to the optic nerve to the calcarine cortex[2].

The development of the multifocal visual evoked potential (mfVEP) has lagged behind the multifocal electroretinogram (mfERG). The large intersubject variability in mfVEP responses has discouraged its use for a period of time.Its usefulness has been extended with the development of an automated, computerized method of measuring the latency of the local mfVEP responses[3].

ISCEV provides guidelines for recording mfERG and recommended each lab to develop its own normative values for clinical use[4]. However, till now, there is no international guideline to standardize the use of mfVEP in clinical practice[5].

Were concerned with the maturation of the mfVEP in children. They observed maturation of latency and amplitude until the age of 13 years, which may be a reflection of greater recruitment of neurons in the striate cortex[6].

Multifocal visual evoked potential, a recent advancement in electrophysiology, has made it possible to document the visual field of an individual as a collection of evoked cortical responses. Multiple domains/loci of the visual field are simultaneously stimulated using a cortically scaled pseudorandomly reversing pattern stimulus. Visual evoked potentials corresponding to each of the loci of the visual field tested can be recorded within a short period of time to generate a perimetry of VEP. This technique has been successfully applied in adults to the detection of glaucoma and other diseases affecting the visual pathway[5,7].

The recording of mfVEP responses is a relatively novel technology that enables the simultaneous recording of many spatially localized VEP responses that are evoked by rapid, pseudorandom m-sequence stimulation with more than 30 pattern reversals per second. Accumulating evidence suggests that mfVEP is a promising tool for the objective assessment of visual function in patients with a variety of diseases affecting the visual pathway, including glaucoma, optic neuritis, and amblyopia[8].

Many studies have introduced a multiple-channel recording system, rather than the single- channel recording system initially developed, to overcome inter-individual variations and to enhance the signal to-noise ratios (SNRs)of mfVEP responses[9,10]. Meigen and Kramer[11]. Analyzed the multichannel data using receiver operating characteristic (ROC) analysis to correct for multiple testing[12].

PATIENTS AND METHODS

Study Design

This was a prospective, observational, descriptive case series study conducted in Mansoura Ophthalmic Center, Mansoura University, Egypt.

Ethics and Consent

The research approval of the study was obtained from institutional review board (IRB) of Faculty of Medicine at Mansoura University before starting the study on 9 march 2019 (code number MS.19.02.508). All cases provided written informed consent prior to study participation.

Patients

This study was held on a sample of 100 healthy eyes of 50 cases attending Mansoura ophthalmic center outpatient clinic in the period from October 2020 till March 2022. Patients with the following criteria were included in this study, age from 20 to 50 years old, both genders, best corrected visual acuity≥ 6/9 and normal optic disc appearance using Volk 90D. Patients with the following criteria were excluded from this study, previous intraocular surgery or ocular injuries, patients with history of prematurity, neurologic, metabolic or other systemic diseases affecting visual pathway strabismus, amblyopia, retinal or optic nerve pathology, Glaucoma, Optic nerve cup disc ratio more than 0.5 or asymmetry more than 0.2 between two eyes and Media opacity.

Ocular Examination

Ophthalmologic examination included visual acuity assessment by Landolt's broken ring chart then converted to LogMAR for statistical analysis, anterior segment slit-lamp examination using Haag Streit BP 900 (Haag-Streit, Koeniz, Switzerland) was used to asses corneal clarity, depth of anterior chamber, lens morphology, pupillary reaction. Fundus examination using Volk 90D was used to assess retina and optic nerve head, intraocular measurement using Goldmann applanation tonometry. Multifocal VEP was evaluated by Reti-Scan 21 (Roland Consult, Brandenburg a.d. Havel, Germany).

MfVEP technique

The recording electrodes used were VEP cross-connection with a bridge electrode connection; the vertical channel electrodes are placed 3cm below inion and 3.5cm above inion. The horizontal channel electrodes are placed 4cm on either side of the inion. The ground electrode was placed over the forehead by using a rubber band. All electrodes were soaked in water and soap before starting application. In addition, forehead and scalp were cleaned by cleaning gel (Nuprep) and then by soap and water to get the best conductivity.

The impedance was kept below 10 kW. The pupil of the examined eye should not be dilated with average size of 4 mm. The fellow eye was occluded with light pressure to prevent blinking artifacts.

The patient was instructed to fixate his/her eye to a small black cross in the center of the stimulating screen. The stimulus

consisted of 61 segments, each with 16 checks (eight white and eight black). The luminance values for the black and white checks were 2 and 200 cd/m 2 respectively, while the background was set to 100 cd/m 2. The viewing angle was 30° and presented on a 20-inch LCD monitor at a viewing distance of 33 cm. Low and high amplifier cutoffs were set to 3 and 100 Hz respectively. Each eye session lasted for about 8 min with a video monitoring fixation check. To improve fixation, each session was broken into four cycles. An artifact level of 10% was accepted for a reliable examination. Raw trace data were analyzed with peak-to-trough amplitude and peak time of P1 wave. The amplitude and peak time of average P1 wave for the four quadrants were calculated.

Statistical Analysis: Data were checked, entered, and analyzed using Statistical Package for Social Science (SPSS) for data processing, version 22.0 (Armonk, NY: IBM Corp). The Data were expressed as number and percentage for qualitative variables and mean -+ standard deviation (SD) for parametric data after testing normality using Kolmogrov-Smirnov test. The two groups were compared with Student'test for parametric data and Mann Whitney test for non-parametric data. Pearson (parametric) and Spearman (non-parametric) correlations were used to correlate continuous data. Significance of the obtained results was judged at the (0.05) level.

RESULTS

Demographic features and clinical data among studied cases are represented in table (1) .(n = 50 patients, 100 normal eyes). The mean age was 33.82 ± 6.543 years. There was 20 (40%) males and 30 (60%) females with male to female ratio was 1: 1.5. The BCVA had mean of 0.95 ± 0.115. The Spherical equivalent had mean of -1.07 ± 1.199. The IOP had mean of 17.04 ± 1.652.

Table 1: Demographic features and clinical data among studied cases

All patients (n= 50) – All eyes(n=100)		
Age (years)		33.82 ± 6.543
Gender	**Male**	40.0% (20)
	Female	60.0% (30)

Data is expressed as mean and standard deviation or as percentage and frequency.

BCVA	0.95 ± 0.115
Spherical equivalent	-1.07 ± 1.199
IOP	17.04 ± 1.652

Data is expressed as mean and standard deviation.

The difference in amplitude at the four sides mentioned between male and female was statistically non-significant (p>0.05). The difference in latency at the four sides mentioned between male and female was statistically non-significant (p>0.05).

The amplitude at superior nasal had mean of 29.21 ± 3.360 in male and mean of 28.35 ± 4.261 in female. The amplitude at superior temporal had mean of 27.26 ± 4.881 in male and mean of 25.90 ± 4.561 in female. The amplitude at inferior temporal had mean of 27.24 ± 4.181 in the male and mean of 27.87 ± 4.643 in female. The amplitude at inferior nasal had mean of 23.91 ± 4.240 in the male and mean of 25.01 ± 5.865 in female.

The latency at superior nasal had mean of 50.32 ± 2.083 in male and mean of 49.88 ± 2.704 in female. The latency at superior temporal had mean of 50.22 ± 2.779 in male and mean of 49.53 ± 2.289 in female. The latency at inferior temporal had mean of 49.66 ± 2.411 in male and mean of 50.21 ± 2.263

in female. The latency at inferior nasal had mean of 50.76 ± 2.383 in male and mean of 50.10 ± 2.270 in female (table2).

Table 2: Effect of gender on amplitude and latency in the studied sample.

		Male	Female	95% CI	P
Amplitude	**Superior Nasal**	29.21 ± 3.360	28.35 ± 4.261	-0.7, 2.4	0.289
	Superior Temporal	27.26 ± 4.881	25.90 ± 4.561	-0.5, 3.3	0.160
	Inferior Temporal	27.24 ± 4.181	27.87 ± 4.643	-2.4, 1.2	0.497
	Inferior Nasal	23.91 ± 4.240	25.01 ± 5.865	-3.2, 1.0	0.313
Latency	**Superior Nasal**	50.32 ± 2.083	49.88 ± 2.704	-0.6, 1.4	0.387
	Superior Temporal	50.22 ± 2.779	49.53 ± 2.289	-0.3, 1.7	0.180
	Inferior Temporal	49.66 ± 2.411	50.21 ± 2.263	-1.5, 0.4	0.252
	Inferior Nasal	50.76 ± 2.383	50.10 ± 2.270	-0.3, 1.6	0.169

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean differencebetween both groups. P is significant when < 0.05.

There was no significant correlation between age with multifocal visual evoked potential values including amplitude at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05). Also, there was no significant correlation between age and multifocal visual evoked potential values including latency at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05) (table3).

Table 3: Correlation between multifocal visual evoked potential values with age

	Age	Correlation efficient	P
Amplitude	**Superior Nasal**	-0.192	0.055
	Superior Temporal	0.066	0.513
	Inferior Temporal	-0.178	0.076
	Inferior Nasal	-0.105	0.300
Latency	**Superior Nasal**	-0.109	0.283
	Superior Temporal	0.048	0.638
	Inferior Temporal	0.133	0.186
	Inferior Nasal	-0.109	0.282

P is significant when < 0.05.

Regarding amplitude, there was significant positive correlation between BCVA with amplitude at inferior nasal (r-0.334, p=0.001) while no significant correlation was found between BCVA with multifocal visual evoked potential values including amplitude at superior nasal, superior temporal, inferior temporal, and superior temporal (p>0.05).

Regarding latency, there was significant negative correlation between BCVA with latency at superior temporal (r=-0.215, p=0.032) while no significant correlation was observed between BCVA with other multifocal visual evoked potential values including latency at superior nasal, inferior temporal, inferior nasal (p>0.05) (table4).

Table 4: Correlation between multifocal visual evoked potential values with BCVA

	BCVA	Correlation efficient	P
Amplitude	**Superior Nasal**	-0.194	0.053
	Superior Temporal	0.112	0.267
	Inferior Temporal	-0.085	0.399
	Inferior Nasal	0.334	**0.001**
Latency	**Superior Nasal**	-0.082	0.418
	Superior Temporal	-0.215	**0.032**
	Inferior Temporal	0.028	0.785
	Inferior Nasal	-0.004	0.965

P is significant when < 0.05.

In the studied cases there was no significant correlation between spherical equivalent with multifocal visual evoked potential values including amplitude at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05). Regarding latency, there was significant negative correlation between spherical equivalent with latency at superior temporal (r=-0.249, p=0.015) while no significant correlation was observed between spherical equivalent with other multifocal visual evoked potential values including latency at superior nasal, inferior temporal, inferior nasal (p>0.05) (table5).

Table 5: Correlation between multifocal visual evoked potential values with spherical equivalent

Spherical equivalent		**Correlation efficient**	**P**
Amplitude	**Superior Nasal**	-0.114	0.272
	Superior Temporal	0.029	0.780
	Inferior Temporal	-0.175	0.090
	Inferior Nasal	0.083	0.425
Latency	**Superior Nasal**	-0.143	0.167
	Superior Temporal	**-0.249**	**0.015**
	Inferior Temporal	0.001	0.992
	Inferior Nasal	-0.163	0.114

P is significant when < 0.05.

Regarding IOP, There was no significant correlation between IOP with multifocal visual evoked potential values including amplitude at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05). Also, no significant

correlation between IOP with multifocal visual evoked potential values including latency at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05) (table 6).

Table 6: Correlation between multifocal visual evoked potential values with IOP.

	IOP	Correlation efficient	P
Amplitude	**Superior Nasal**	0.039	0.698
	Superior Temporal	0.074	0.461
	Inferior Temporal	-0.153	0.127
	Inferior Nasal	-0.070	0.491
Latency	**Superior Nasal**	-0.117	0.245
	Superior Temporal	-0.032	0.754
	Inferior Temporal	0.101	0.319
	Inferior Nasal	0.002	0.985

P is significant when < 0.05.

DISCUSSION

The multifocal visual evoked potential (mfVEP), a technique that allows the recording of scores of local VEP responses, provides a measure of these local losses[13]. For example, local losses in amplitude of the mfVEP have been demonstrated in optic neuritis/multiple sclerosis and glaucoma[14].

mfVEP combines visual evoked potential recordings in response to a dartboard-like pattern stimulus display that is subdivided into a number of sectors (up to 60) each with several checks, which covers over 40 degrees of the visual field[15].

In the current thesis demographic features of the studied 50 cases showed that, the mean age was 33.82 ± 6.543 years, there was 20 (40%) males and 30 (60%) females with male to female ratio was 1: 1.5. The BCVA had mean of 0.95 ± 0.115. The Spherical equivalent had mean of 1.07 ± 1.199. The IOP had mean of 17.04 ± 1.652.

In agreement Ishikawa et al. aimed to establish optimal conditions for recording multifocal visual evoked potentials in fifty-six Japanese individuals (110 eyes; 54 right eyes and 56 left eyes) with normal or corrected-to-normal visual acuity participated in the mVEP study, the patients included 82 males, ranging in age from 21 to 85 (mean ± SD; 56.1 ± 17.2) years, and 118 females, ranging in age from 20 to 87 (52.7 ± 18.2) years[8].

As regard effect of gender on amplitude and latency in the studied sample. The difference in amplitude at the four sides mentioned between male and female was statistically non-significant (p>0.05). Also, the difference in latency at the four sides mentioned between male and female was statistically non-significant (p>0.05).

Fayed et al. observed that, there were no statistically significant differences between girls and boys or between left and right eyes regarding the peak time and the amplitude of the P1 wave [6]. Ishikawa et al. demonstrated that, neither gender nor age affected the ability of the best channel combinations to discriminate the mVEP signal from noise[8].

Alshowaeir et al.[7] evaluated mfVEP changes in ON and fellow eyes during the first year after the attack. They examined 87 patients with clinically diagnosed typical acute unilateral ON (27 of 87 patients were considered low risk, and 60 of 87 patients were considered high risk for developing MS) and 25 healthy controls. Their results indicate that both

amplitude and latency of the mfVEP at superior nasal had a mean 25.94 ± 2.157 and 47.26 ± 3.852 respectively.

As regard effect of gender on amplitude and latency in the studied sample. The difference in amplitude at the four sides mentioned between male and female was statistically non-significant (p>0.05). Also, the difference in latency at the four sides mentioned between male and female was statistically non-significant (p>0.05)[7].

It has also been reported by Emmerson-Hanover et al. that females have larger amplitudes for both traditional VEPs and mVEPs when compared to males[16]. Klistorner and Graham. reported that the sex difference that can characterize average amplitude was eliminated when the local mVEP responses were scaled by amplitude of the EEG[17]. Fortune et al. also found that both RMS signal amplitude and RMS noise amplitude were larger in females[18].

No significant correlation between age with multifocal visual evoked potential values including amplitude at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05). Also, no significant correlation between age with multifocal visual evoked potential values including latency at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05).

In agreement Fayed et al. reported that no significant correlations could be found between either amplitude or peak time of P1 wave and the ages of the adolescents[6]. Also, many previous reports. Klistorner et al. and Fortune et al. have asserted that age had little or no effect on mVEP responses or on the amplitude of the traditional VEPs[15-18].

Our results showed that, there was significant positive correlation between BCVA with amplitude at inferior nasal (r-0.334, p=0.001). There was significant negative correlation between BCVA with latency at superior temporal (r=-0.215, p=0.032). while no significant correlation was observed between BCVA with other multifocal visual evoked potential values including latency at superior nasal, inferior temporal, inferior nasal (p>0.05).

In agreement De Santiago et al. examined the variation in mfVEP amplitude observed that there was positive correlation between BCVA with amplitude at inferior nasal (p=0.021)[19]. Regarding latency, there was significant negative correlation between spherical equivalent with latency at superior temporal (r=-0.249, p=0.015). This was in agreed with several studies Pe´rez-Rico et al. Zafeiropoulos et al. Graham et al.[15-21-22] showed the same results.

In the present study no significant correlation between IOP with multifocal visual evoked potential values including amplitude or latency at superior nasal, superior temporal, inferior temporal, inferior nasal (p>0.05).

In a previous study Klistorner et al. reported that it should be noted that correlation between IOP with multifocal visual evoked potential values including amplitude at superior nasal are small and their significance is unclear[23]. Meigen et al. showed that, the correlation between IOP with multifocal visual evoked potential values was with no significant value (p=0.214)[11].

CONCLUSION

Multifocal VEP technique is superior to conventional full-field VEPs in evaluating the integrity of the visual system as it provides an independent measurement of multiple segments of visual field, thus allowing more accurate detection of smaller defects.

Declarations

Conflict of Interest

All authors have no conflicts of interest that are directly relevant to the content of this review.

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Reviewer Disclosures

No relevant financial or other relationships to disclose.

Declaration of Interest

No financial affiliations or financial involvement with any organization or entity with a financial competing with the subject matter or materials discussed in the review.

Consent for publication.

Not applicable

Availability of Data

All data generated during this review are included in this study.

Standards of Reporting

CONSORT guidelines were followed.

Authors contributions

Authors interpreted and discussed the data and wrote the first version of the manuscript. All authors read and approved the final manuscript.

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