Multifocal visual evoked potential normative scaling in Egyptian adolescents

Elham N. Fayed[a], Neveen M. El-Fayoumy[a], Mohamed M. Al-Kanishy[b], Hossam Mohammed[c], Mona M. Nada[a], Amira M. El Gohary[a], Zeinab S. El-Sanabary[c], Saly H. Elkholy[a]

Departments of [a]Clinical Neurophysiology, [b]Ophthalmology, [c]Paediatric Diabetic Unit, Cairo University, Cairo, Egypt

Correspondence to Elham N. Fayed, Department of Clinical Neurophysiology, Cairo University, 11571 Cairo, Egypt
Tel: +201228588530;
e-mail: elham.salem@kasralainy.edu.eg

Received 23 April 2015
Accepted 28 August 2015

The Egyptian Journal of Neurology, Psychiatry and Neurosurgery 2016, 53(1):37–40

Background
The multifocal visual evoked potential (mfVEP) is a useful tool for evaluating optic nerve disease and visual defects secondary to optic nerve or retinal ganglion cell damage.

Objective
The aim of this study was to establish technical guidelines and normative values of the peak time and amplitude of the mfVEP in adolescents.

Participants and methods
This is a prospective study conducted on 20 healthy adolescents (40 eyes) 10 girls and 10 boys. Their age ranged between 10 and 15 years with a mean of 12.50 ± 1.48. Monocular mfVEP was obtained from each eye separately. The peak time and amplitude of the P1 wave of each individual response were measured and then expressed in the form of four quadrants.

Results
The peak time and amplitude of the P1 wave showed no statistical differences between the four quadrants and no correlation to the age. 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.

Conclusion
We obtained normative data of mfVEP of the adolescents in our lab as a preliminary work for further application in different neuro-ophthalmological disorders.

Keywords:
adolescents, amplitude, multifocal visual evoked potential, normal range, peak time

Egypt J Neurol Psychiat Neurosurg 53:37–40

1110-1083

Introduction

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 [1]. Its usefulness has been extended with the development of an automated, computerized method of measuring the latency of the local mfVEP responses [2,3]. ISCEV (2011) 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. Balachandran *et al.* (2004) [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.

The diagnostic utility in evaluating optic diseases and visual defects secondary to optic nerve or retinal ganglion cell damage can be enhanced by combining the use of mfVEP with mfERG [6]. The use of multifocal modalities in pediatric age groups has been limited by the intolerance of the children to the techniques and the effect of eccentric fixation [7]. Use of mfVEP in adolescents is another challenging point. Developing lab normative data will help in extending our work to include different diseases affecting the visual system as diabetes mellitus and retinal diseases in such particular age group.

Aim of work

The aim of this study was to establish technical guidelines and normative values of the peak time and amplitude of the mfVEP in normal adolescents.

 DOI: 10.4103/1110-1083.176369

Participants and methods

Participants

This is a prospective study conducted on 20 healthy adolescents (40 eyes) 10 girls and 10 boys. Their age ranged between 10 and 15 years with a mean of 12.50 ± 1.48 years. Approval of the research ethics committee of the Faculty of Medicine, Cairo University was taken in November 2013. Informed written consent was taken from each parent or guardian after full explanation of the aim of the study and the methodology which will be used.

Methods

Ophthalmological examination

Slit-lamp biomicroscopy (slit-lamp Haag-Streit machine, Koeniz, Switzerland) was performed for all participants to exclude anterior segment diseases. Fundus examination was done under full pupillary dilatation to exclude posterior segment pathology (retinal or optic nerve diseases). The best distance vision (with eyeglasses if used) for all participants was not less than 6/9 using Snellen chart. mfVEP was done using the Reti-Scan 21 (Roland Consult, Brandenburg a.d. Havel, Germany). mfVEP technique: the recording electrodes used were VEP cross-connection (Fig. 1) with a bridge electrode connection; electrode A was 2 cm above the inion and electrode C was 1 cm below the inion. Electrodes B and D were 1 cm above and 4 cm lateral to inion respectively. 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 adolescent 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.

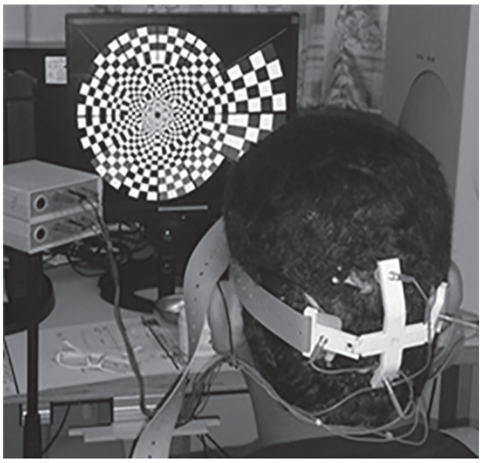
Abbreviation of quadrants

Q1: lower nasal, Q2: upper nasal, Q3: upper temporal, Q4: lower temporal (Fig. 2).

Statistical methods

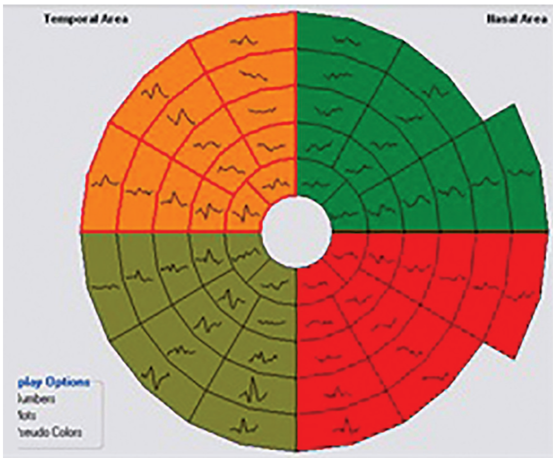
The data were coded and entered using the statistical package SPSS version 15. The data were summarized using descriptive statistics: mean, SD, minimal and maximal values for quantitative variables and numbers. Statistical differences between groups were tested using independent sample *t*-test for quantitative normally distributed variables while nonparametric Mann–Whitney test was used for quantitative variables which are not normally distributed. Correlations were

Figure 1



Stimulating screens of the multifocal visual evoked potential (VEP) with the cross-connection recording electrodes applied to a 12-year-old boy.

Figure 2



Quadrants, divisions of the multifocal visual evoked potential (VEP) from the left eye.Q1: lower nasal (red), Q2: upper nasal (green), Q3: upper temporal (orange), Q4: lower temporal (olive).

done to test for linear relations between variables. *P*-values less than 0.05 were considered statistically significant.

Results

Data were tabulated for minimum, maximum, mean and SD for the peak time (ms) and amplitude (nV/deg^2) — of P1 wave — for each quadrant in mfVEP (Table 1). There were no statistically significant differences between left and right eyes regarding the peak time and the amplitude of the P1 wave mfVEP tests.

mfVEP–P1-wave-peak time, comparative studies between the four quadrants were statistically insignificant ($P > 0.05$, Table 1). So we considered the normal accepted peak latency of the P1 wave for all quadrants to be ranged between 90 and 115 ms (mean ± 1 SD = 102.65 ± 12.39).

mfVEP–P1-wave-amplitude, comparative studies between the four quadrants were also statistically insignificant ($P > 0.05$, Table 1). So, the normal accepted amplitude of the P1 wave for all quadrants will be ranged between 2.5 and 5 nV/deg^2 (mean ± 1 SD = 3.5 ± 1.35).

No significant correlations could be found between either amplitude or peak time of P1 wave and the ages of the adolescents (Table 2).

Discussion

Enrollment of adolescents in this study was a challenge in itself. They must be convinced with the usefulness of the technique used and its validity. Most of them complained about the tightness of the rubber band used to fix the electrodes of the mfVEP taking a period to adapt to it. Fixation is not an issue in this age group. Interrupting the session can be minimized or increased according to the adolescent's cooperation.

There are two main sources of intersubject variability. First, the position of the calcarine fissure relative to the external landmarks varies among individuals [8]. Second, individuals differ in the way the cortex is folded and how the primary visual area is positioned within these folds [9,10]. If intersubject variability is due to cranio-occipital variations, the mfVEP responses from the two eyes should be identical. The reason for this is purely anatomical; any point in the visual field projects to the nasal retina of one eye and the temporal retina of the other, but both points project to essentially the same region of the striate cortex [3]. In our work, mfVEP intersubject variability did not represent a great obstacle which may be due to the homogeneous group sample, the patience of the technician and the well experience of the examining doctor.

Table 1 Multifocal visual evoked potential–P1 peak time and amplitude

Variables	Minimum	Maximum	Mean	SD	*P*-value (rt/lt)
P1 peak time (ms)					
Q1 rt eye	90.6	110.4	99.7	8.25	0.44
Q1 lt eye	85.6	136.4	101.14	13.07	
Q1 Both eyes	85.60	136.40	99.89	10.79	
Q2 rt eye	83.7	117.5	98.97	12.82	0.42
Q2 lt eye	85.0	121	99.47	8.91	
Q2 Both eyes	83.70	121.00	104.47	12.08	
Q3 rt eye	80.2	122.5	102.1	12.25	0.43
Q3 lt eye	80	108	98.6	8.29	
Q3 Both eyes	80.00	122.50	102.28	10.83	
Q4 rt eye	84.6	134.4	104.0	15.81	0.42
Q4 lt eye	87.6	158.3	106.17	16.28	
Q4 Both eyes	84.60	158.30	103.97	15.85	
P-value quadrants	0.42	0.42	0.43	0.44	
P1 amplitude (nV/deg^2)					
Q1 rt eye	2	5.4	3.44	1.19	0.14
Q1 lt eye	2	6	3.84	1.17	
Q1 Both eyes	2.00	6.00	3.62	1.18	
Q2 rt eye	1.2	5	2.98	1.24	0.19
Q2 lt eye	1.8	7.7	3.48	1.49	
Q2 Both eyes	1.2	7.7	3.16	1.36	
Q3 rt eye	2	6	4.45	1.25	1.2
Q3 lt eye	2	6.1	4.03	1.2	
Q3 Both eyes	2.00	6.10	4.26	1.23	
Q4 rt eye	3	6.3	4.1	1.15	0.27
Q4 lt eye	2.1	10	4.52	2.04	
Q4 Both eyes	2.1	10.00	4.21	1.64	
P-value quadrants	0.17	0.17	0.19	0.14	

Comparative studies between the four quadrants from both right (rt) and left (lt) eyes as well as both eyes for peak time and amplitude were statistically insignificant; lt, left; Q1, lower nasal; Q2, upper nasal; Q3, upper temporal; Q4, lower temporal; rt, right.

Table 2 Correlation between the average amplitude (nV/deg^2), the peak time (ms) of P1 wave and the ages of the adolescents

P1 wave	mfVEP			
	Amplitude		Peak time	
	P-value	*r*	*P*-value	*r*
Q1	0.241	0.190	0.213	0.201
Q2	0.438	0.126	0.244	0188
Q3	0.990	−0.002	0.051	0.310
Q4	0.344	−0.154	0.525	0.104

mfVEP, multifocal visual evoked potential; *r*, Pearson's correlation coefficient.

Raw trace data were analyzed for each wave within the interval of 60–220 ms determined and compared among channels for every stimulated segment of the visual field. Amplitude and latency for each field sector of the mfVEP is determined [8].

Peak latency between 90 and 115 ms is accepted as a normal range. The amplitude ranged from 2.5 to 5 nV/deg^2. Less than 50% reduction of amplitude is the accepted limit of difference between quadrants.

There is no significant correlation between the age of the adolescents, sex, the eye laterality and the amplitude or the peak time of P1 wave in mfVEP test. The only available published work in the same age group to be compared with is that of Balachandran *et al.* (2004) [5] who tested 70 normal children between 5 and 16 years in whom the latency of the dominant peak showed a decrease with age reaching a plateau at 13 years of age which is almost the mean age of our adolescents. They had a large variation in full field amplitude between children, with no significant correlation with age. These findings suggest an increasing complexity of physiological response during maturation, extending at least into early adolescence. On the same hand, Wolff *et al.* (2010) [11] found minimal effect of age on mfVEP peak time and amplitude in their normal control between 25 and 45 years of age. Despite the large interindividual variation captured by Klistorner and Graham (2000) [12], the adult signal amplitude did not decline with age. They added that children under the age of 10 years had smaller signals than the adult ones. This point still needs further evaluation in a wider age range.

Conclusion

We obtained normative data of the mfVEP test of the adolescents in our lab as a preliminary step to apply multifocal tests as a diagnostic tool in different ophthalmologic, general and neurological diseases with ophthalmologic manifestation in such age group.

Acknowledgements

The authors are thankful to Mrs HalaEltoukhy, the nurse in the Ophthalmic Diagnostic and Laser Unit, Cairo University Hospitals, for her great effort.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Baseler HA, Sutter EE, Klein SA, Carney T. The topography of visual evoked response properties across the visual field. Electroencephalogr Clin Neurophysiol 1994; **90**:65–81.

2 Hood DC, Ohri N, Yang EB, Rodarte C, Zhang X, Fortune B, Johnson CA. Determining abnormal latencies of multifocal visual evoked potentials: a monocular analysis. Doc Ophthalmol 2004; **109**:189–199.

3 Hood DC, Zhang X, Rodarte C, Yang EB, Ohri N, Fortune B, Johnson CA. Determining abnormal interocular latencies of multifocal visual evoked potentials. Doc Ophthalmol 2004; **109**:177–187.

4 Hood DC, Bach M, Brigell M, Keating D, Kondo M, Lyons JS, *et al.* ISCEV standard for clinical multifocal electroretinography (mfERG) (2011 edition). Doc Ophthalmol 2012; **124**:1–13.

5 Balachandran C, Klistorner AI, Billson F. Multifocal VEP in children: its maturation and clinical application. Br J Ophthalmol 2004; **88**:226–232.

6 Hood DC, Greenstein VC. Multifocal VEP and ganglion cell damage: applications and limitations for the study of glaucoma. Prog Retin Eye Res 2003; **22**:201–251.

7 Zhang B, Stevenson SS, Cheng H, Laron M, Kumar G, Tong J, Chino YM. Effects of fixation instability on multifocal VEP (mfVEP) responses in amblyopes. J Vis 2008; **8**:16.1–16.14.

8 Steinmetz H, Fürst G, Meyer BU. Craniocerebral topography within the international 10–20 system. Electroencephalogr Clin Neurophysiol 1989; **72**:499–506.

9 Brindley GS. The variability of the human striate cortex. J Physiol 1972; **225**:1P–3P.

10 Stensaas SS, Eddington DK, Dobelle WH. The topography and variability of the primary visual cortex in man. J Neurosurg 1974; **40**:747–755.

11 Wolff BE, Bearse MA Jr, Schneck ME, Barez S, Adams AJ. Multifocal VEP (mfVEP) reveals abnormal neuronal delays in diabetes. Doc Ophthalmol 2010; **121**:189–196.

12 Klistorner A, Graham SL. Objective perimetry in glaucoma. Ophthalmology 2000; **107**:2283–2299.