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Normative data of Electroretinogram and Visual Evoked Potential in Thai Population

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ABSTRACT

Objective: To define normal values of Electroretinogram [ERG] and Visual Evoked Potential [VEP] in different age groups using Viking Select Master Software V7.1.

Methods: ERG and VEP values were measured using Viking Select Master Software V7.1 in selected subjects without history of ocular and/or systemic diseases that affect ERG and VEP values. Results were studied in three groups of age: less than 10 years old, 11 to 40 years old and over 40 years old.

Results: There were 26 eyes in the first group with age range from 6-10 years old [mean 7.8 ± 1.52 years old]. In ERG : the normal values of photopic amplitude of ; a-wave was ≥ 18.57 microvoltage [μV] and b-wave was ≥ 23.82 μV, flickering amplitude of b-wave was ≥ 21.93 μV, scotopic amplitude of b-wave was ≥ 39.12 μV, mesopic amplitude of ; a-wave was ≥ 60.44 μV and b-wave was ≥ 96.84 μV. In VEP : transient flash amplitude was ≥ 20.58 μV and latency was ≤ 94.10 millisecond[ms], transient pattern size 2 amplitude was ≥ 8.61 μV and latency was ≤ 100.00 ms. There were 75 eyes in the second group with age range from 11-38 years old [mean 26.8 ± 7.35 years old]. The values of photopic amplitude of ; a-wave was ≥ 22.56 μV and b-wave was ≥ 20.14 μV, flickering amplitude of b-wave was ≥ 19.35 μV, scotopic amplitude of b-wave was ≥ 32.29 μV, mesopic amplitude of ; a-wave was ≥ 45.05 μV and b-wave was ≥ 78.97 μV, VEP- transient flash amplitude was ≥ 11.64 μV and latency was ≤ 96.78 ms, transient pattern size 2 amplitude was ≥ 4.82 μV and latency was ≤ 88.49 ms. There were 77 eyes in the third group with age range from 41-81 years old [mean 60.1 ± 11.54 years old]. The values of photopic amplitude of; a-wave was ≥ 19.12 μV and b-wave was ≥ 24.59 μV, flickering amplitude of b-wave was ≥ 18.76 μV, scotopic amplitude of b-wave was ≥ 35.60 μV, mesopic amplitude of ; a-wave was ≥ 40.90 μV and b-wave was ≥ 94.09 μV, VEP- transient flash amplitude was ≥ 10.07 μV and latency was ≤ 102.10 ms, transient pattern size 2 amplitude was ≥ 5.34 μV and latency was ≤ 96.00 ms.

Conclusion: We established normal ERG and VEP values in different age group using Viking Select Master Software V7.1 at Siriraj Hospital to distinguish between normal and pathological patients. The values are affected in relation to machine and environmental setting in different laboratory. It is essential for individual laboratories to set their own normal values.

Keywords: Electroretinography; electroretinogram; normal values; visual evoked potential

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Visualization of the fundus has progressed from simple ophthalmoscopy to highly technological devices. But for all the wealth of detail received from such techniques, information regarding the *functional* status of a specific retinal layer, the optic nerve, or visual cortex is lacking. Using light to produce electrical signals from different regions of the visual system can produce data with a high degree of specificity.

Electrophysiologic tests are the tests which using light to produce electrical signals from different regions of the visual system. They can produce information regarding the *functional* status of a specific retinal layer, the optic nerve and visual cortex. The most important thing of these tests is that they are *objective tests* which are more reliable than other subjective tests[1].

The standard electrophysiologic tests are composed of electrooculography [EOG], electroretinography [ERG] and visual evoked potential [VEP]. EOG represents electrical activity from retinal pigment epithelium. ERG [full-field or classical ERG] represents electrical activity from photoreceptor cells and mid-retinal layers [except ganglion cells]. VEP represents electrical activity from nerve fiber layer, optic nerve through visual cortex. The normal value of EOG is the standard value of Arden ratio [> 1.8]. The normal value of ERG and VEP are affected by many factors such as machine, environmental setting and techniques.

Our aim is to report the normal values of the Electroretinogram [ERG] and the Visual evoked potential [VEP] of Thai population in our laboratory at Siriraj hospital using Viking Select Master Software V7.1.

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TABLE 1. Normal values of ERG and VEP in group1.

Group I	**ERG**	Photopic	a wave amplitude[1] [μV]	≥18.57
			b wave amplitude[2] [μV]	≥23.82
		Flickering	b wave amplitude[1] [μV]	≥21.93
		Scotopic	b wave amplitude[2] [μV]	≥39.12
		Mesopic	a wave amplitude[2] [μV]	≥60.44
			b wave amplitude[2] [μV]	≥96.84
		OP*	op1 amplitude[1] [μV]	≥0.87
			op2 amplitude[1] [μV]	≥1.51
			op3 amplitude[1] [μV]	≥0.73
			op4 amplitude[2] [μV]	≥0.68
	VEP	Transient	amplitude[2] [μV]	≥20.58
			latency[3] [ms]	≤94.10
		Pattern size 2		
			amplitude[1] [μV]	≥8.61
			latency[4] [ms]	≤100.00

* OP = oscillatory potentials
1 = ≥ Mean - 1.645 SD
2 = ≥ Percentile 5
3 = ≤ Mean - 1.645 SD
4 = ≤ Percentile 5

MATERIALS AND METHODS

Data collection in this study was divided into two parts. The first part was retrospective study, we collected the data that was available at the beginning of the usage of this software [January 2004]. We selected cases that had disease or injury in one eye, the other eye was normal without systemic or ocular disease, and we used the normal eye for our study. The second part was prospective study from January 2005 to January 2006. We collected the data the same as the first part and included the data from healthy volunteers.

Inclusion criteria were normal eyes without systemic or ocular diseases that would affect the values of ERG and VEP. In young children, the participants were sedated by chloral hydrate 1 milliliter per kilogram of body weight before testing, and inform consents were signed by their parents. Exclusion criteria were the persons who were not co-operate to these tests and who had systemic or ocular diseases that would affect the normal values. We used Viking Select Master Software V7.1 to perform full-field ERG and VEP.

TABLE 2. Normal values of ERG and VEP in group 2.

Group II	**ERG**	Photopic	a wave amplitude[1] [μV]	≥22.56
			b wave amplitude[1] [μV]	≥20.14
		Flickering	b wave amplitude[1] [μV]	≥19.35
		Scotopic	b wave amplitude[1] [μV]	≥32.29
		Mesopic	a wave amplitude[1] [μV]	≥45.05
			b wave amplitude[1] [μV]	≥78.97
		OP*	op1 amplitude[1] [μV]	≥1.39
			op2 amplitude[1] [μV]	≥2.27
			op3 amplitude[1] [μV]	≥0.69
			op4 amplitude[2] [μV]	≥0.39
	VEP	Transient	amplitude[2] [μV]	≥11.64
			latency[3] [ms]	≤96.78
		Pattern size 2	amplitude[2] [μV]	≥4.82
			latency[3] [ms]	≤88.49

* OP = oscillatory potentials
1 = ≥ Mean - 1.645 SD
2 = ≥ Percentile 5
3 = ≤ Mean - 1.645 SD

The full-field flash ERG testing has five recommended international standard responses that established by the International Society for Clinical Electrophysiology of Vision [ISCEV]. We performed the full-field flash ERG in our study according to the ISCEV. It composed of

1. Rod single-flash response after dark adaptation with flash 2.5 log unit dimmer than standard flash
2. Maximal combined rod and cone single-flash response after dark adaptation
3. Oscillatory potentials with standard flash
4. Cone single-flash response after light adaptation with standard flash
5. Cone 30-Hz flicker response after light adaptation with standard flash

VEP was performed according to standard VEP recording which also established by the ISCEV. We used 2 types of stimulus for VEP response: flash stimulus and pattern stimulus [checkerboard size 2].

The results were classified by age into three groups [group 1: ≤ 10 years old, group 2: 11-40 years old and group 3 : > 40 years old]. For normal distribution data, we use mean-1.645 SD for calculation the normal values and percentile 5 for non normal distribution data. Because there is no upper limit of amplitude of both ERG and VEP, so the normal values are the ones that greater than or equal to the aforesaid calculated values except the VEP latency that the normal values are lesser than or equal to them. The study protocol was approved by the research ethics committee of Siriraj Hospital, Mahidol University.

RESULTS

There were 26 eyes in the first group which the mean age ± SD was 7.8 ± 1.52 years old [range from 6-10 years old]. Normal values of the ERG and VEP in this group are shown in Table 1. In the second group 75 eyes were enrolled in our study. The mean age ± SD of the participants was 26.8 ± 7.35 years old [range from 11-38 years old] and the normal values of the ERG and VEP in this group are shown in Table 2. There were 77 eyes in the third group, which the mean age ± SD was 60.1 ± 11.54 years old [range from 41-81 years old]. Normal values of the ERG and VEP in this group are shown in Table 3.

DISCUSSION

The full-field electroretinogram [ERG] records the electrical responses from the retina stimulated by a flash stimulus. It measures the overall rod- and cone- generated responses. It is the only electrophysiologic test that assesses rod-generated activity. Numerous diseases including Leber congenital amaurosis, achromatopsia, congenital stationary night blindness and others abnormalities of photoreceptor cells use the ERG in conjunction with an ocular examination in diagnosis.[2,3] The ERG waveform represents overall activities of all cells in the retina except from ganglion cells. So any localized defected or isolated macular lesion is not affected the full-field ERG response. In such cases, testing with focal or multifocal ERG is helpful.

According to the ISCEV, there are 5 types of ERG recordings as mention above. We can isolate the information of both photoreceptor cells which are rod cells and cone cells by using specific stimulations. To assess rod-generated activity, we used single-flash 2.5 log unit dimmer than standard flash [dim blue light] after dark adaptation which is called scotopic ERG. Cone cells function can be assessed

TABLE 3. Normal values of ERG and VEP in group 3.

Group III ERG	Photopic	a wave amplitude[1] [μV]	≥19.12
		b wave amplitude[1] [μV]	≥24.59
	Flickering	b wave amplitude[1] [μV]	≥18.76
	Scotopic	b wave amplitude[1] [μV]	≥35.60
	Mesopic	a wave amplitude[1] [μV]	≥40.90
		b wave amplitude[1] [μV]	≥94.09
	OP*	op1 amplitude[1] [μV]	≥1.20
		op2 amplitude[1] [μV]	≥2.30
		op3 amplitude[2] [μV]	≥1.04
		op4 amplitude[1] [μV]	≥0.17
VEP	Transient	amplitude[2] [μV]	≥10.07
		latency[3] [ms]	≤102.10
	Pattern size 2	amplitude[2] [μV]	≥5.34
		latency[4] [ms]	≤96.00

* OP = oscillatory potentials
1 = ≥ Mean - 1.645 SD
2 = ≥ Percentile 5
3 = ≤ Mean - 1.645 SD
4 = ≤ Percentile 5

by 2 types of responses that are photopic ERG and Flickering ERG. Photopic ERG is the response by using standard white flash stimulation and flickering ERG is the response by using 30-Hz flicker stimulation after light adaptation. The maximal combined rod and cone response is elicited by a single bright flash stimulation after dark adaptation which is called mesopic ERG. It is the biggest response generated by both rod and cone cells across the entire retina. The oscillatory potentials [OP] usually consist of three larger wavelets followed by a smaller one during the ascending phase of the b wave in mesopic ERG. They can be isolated or designated in order of occurrence as OP1, OP2, OP3 and OP4. The oscillatory potentials represent inner retinal circulation. Normal values should be established by each laboratory for specific ERG responses, because the difference in recording equipment and techniques such as electrode type.

Visual Evoked Potential [VEP] is the signal elicited by visual stimuli which are recorded with cutaneous electrodes placed on the scalp in the occipital region. It is the only electrophysiologic test that assesses visual cortical activity, and standard for VEP recording has been established by the ISCEV. In clinical usage, VEP is commonly performed to detect visual pathway deficits or unexplained visual loss. An impaired VEP can be produced by a deficit anywhere along the visual pathway including the retina, optic nerve and brain. Therefore, an impaired VEP is anatomically non-specific unless it is used in combination with a complete ocular examination and other clinical investigations such as visual field, ERG and neuroimaging. VEP should not perform in place of a comprehensive ophthalmic examination or neuroimaging. Impaired VEP responses may be produced in some normal persons by poor fixation, defocusing or conscious suppression[2]. There are three standard responses in clinical VEP testing: Pattern reversal VEP [by using checkerboard stimulation], Pattern onset/offset VEP, and Flash VEP. The normal values should be established by each laboratory like the normal values of ERG.

In our laboratory we used skin electrodes in both ERG and VEP recordings. The machine with software name Viking Select Master Software V7.1 that has Ganzfeld stimulation was used in this study. To obtain reproducible responses, the stimulus and background light should be homogeneous and cover the entire retina, so all of the receptors are stimulated or adapted in a relatively homogeneous manner. The Ganzfeld stimulator represents such a stimulus and has been recommended by the ISCEV. We performed the stimulation for VEP [Pattern reversal VEP and Flash VEP] with nondilated pupil, and then ERG was done with fully dilated pupil by using standard specific stimulations as mention above. We collected the values from the normal eye of patient as the normal values as well as values from normal participants.

As the maturation and aging are influenced on electrophysiologic responses, we analyzed normal values for three different age groups; group 1: ≤ 10 years old, group 2: 11-40 years old, group 3: > 40 years old. More than 50 percents of participants in the first group were more than 6 years old because children under 6 years old could not cooperate with the tests. This is the limitation for using these normal values in infants and very young children. The number of participants in group 1 is less than group 2 and group 3. This due to the small amount of cases in children below 10 years old and no normal volunteer in this group. In this study, we found that almost the amplitudes of waves from group 1 were larger than ones from group 2 and group 3 [as shown in Table 1, 2 and 3]. The amplitudes of waves from children are bigger because the cells in young age group are fully developed and still healthy.

In conclusion, these electrophysiologic responses are variable among persons, group of age, difference laboratory and techniques. Each laboratory should obtain their normal values and age-related normative values for each electrophysiologic test to facilitate clinical interpretation. These tests will help or support the diagnosis for the clinician only when correlate with complete ocular examination. Slit-lamp biomicroscopy and ophthalmoscopy are important parts of the clinical routine, but without support from *functional findings* it can be a less accurate indicator. We encourage each laboratory of electrophysiologic tests of vision to establish normal values of their own.

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บทคัดย่อ

ค่าปกติของ Electroretinogram และ Visual Evoked Potential ในคนไทย

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วัตถุประสงค์: เพื่อหาค่าปกติของ Electroretinogram [ERG] และ Visual Evoked Potential [VEP] ในแต่ละกลุ่มอายุ โดยใช้เครื่องมือตรวจ Viking Select Master Software V7.1 ที่โรงพยาบาลศิริราช

วิธีการ: ทำการเก็บค่าของ [ERG] และ [VEP] จากการใช้เครื่องมือตรวจ Viking Select Master Software V7.1 ในคนที่ไม่มีโรคทางตาหรือโรคทางร่างกายอื่น ๆ ที่จะมีผลต่อค่าของ ERGและ VEP จากนั้นนำค่าที่ได้มาคำนวณหาค่าปกติโดยแบ่งตามกลุ่มอายุดังนี้ กลุ่มที่ 1 อายุน้อยกว่า 10 ปี, กลุ่มที่ 2 อายุ 11-40 ปี และกลุ่มที่ 3 อายุมากกว่า 40 ปี

ผลการศึกษา: ในกลุ่มที่ 1 มีจำนวน 26 ตา มีอายุตั้งแต่ 6-10 ปี โดยมีอายุเฉลี่ย 7.8 ± 1.52 ปี ค่าปกติของ Photopic amplitude ของ a wave มากกว่าหรือเท่ากับ 18.57 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 23.82 ไมโครโวลต์, Flickering amplitude ของ b wave มากกว่าหรือเท่ากับ 21.93 ไมโครโวลต์, Scotopic amplitude ของ b wave มากกว่าหรือเท่ากับ 39.12 ไมโครโวลต์, Mesopic amplitude ของ a wave มากกว่าหรือเท่ากับ 60.44 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 96.84 ไมโครโวลต์ ส่วนค่าปกติของ VEP ใน Transient flash amplitude มากกว่าหรือเท่ากับ 20.58 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 94.10 มิลลิวินาที และใน Transient pattern size 2 amplitude มากกว่าหรือเท่ากับ 8.61 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 100.00 มิลลิวินาที ในกลุ่มที่ 2 มีจำนวน 75 ตา มีอายุตั้งแต่ 11-38 ปี โดยมีอายุเฉลี่ย 26.8 ± 7.35 ปี ค่าปกติของ Photopic amplitude ของ a wave มากกว่าหรือเท่ากับ 22.56 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 20.14 ไมโครโวลต์, Flickering amplitude ของ b wave มากกว่าหรือเท่ากับ 19.35 ไมโครโวลต์, Scotopic amplitude ของ b wave มากกว่าหรือเท่ากับ 32.29 ไมโครโวลต์, Mesopic amplitude ของ a wave มากกว่าหรือเท่ากับ 45.05 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 78.97 ไมโครโวลต์ ส่วนค่าปกติของ VEP ใน Transient flash amplitude มากกว่าหรือเท่ากับ 11.64 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 96.78 มิลลิวินาที และใน Transient pattern size 2 amplitude มากกว่าหรือเท่ากับ 4.82 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 88.49 มิลลิวินาที ในกลุ่มที่ 3 มีจำนวน 77 ตา มีอายุตั้งแต่ 41-81 ปี โดยมีอายุเฉลี่ย 60.1 ± 11.54 ปี ค่าปกติของ Photopic amplitude ของ a wave มากกว่าหรือเท่ากับ 19.12 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 24.59 ไมโครโวลต์, Flickering amplitude ของ b wave มากกว่าหรือเท่ากับ 18.76 ไมโครโวลต์, Scotopic amplitude ของ b wave มากกว่าหรือเท่ากับ 35.60 ไมโครโวลต์, Mesopic amplitude ของ a wave มากกว่าหรือเท่ากับ 40.90 ไมโครโวลต์ และ b wave มากกว่าหรือเท่ากับ 94.09 ไมโครโวลต์ ส่วนค่าปกติของ VEP ใน Transient flash amplitude มากกว่าหรือเท่ากับ 10.07 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 102.10 มิลลิวินาที และใน Transient pattern size 2 amplitude มากกว่าหรือเท่ากับ 5.34 ไมโครโวลต์ และมี latency น้อยกว่าหรือเท่ากับ 96.00 มิลลิวินาที

สรุป: ได้รวบรวมค่าปกติของ ERG และ VEP โดยใช้เครื่องมือตรวจ Viking Select Master Software V7.1 ที่โรงพยาบาลศิริราช ในแต่ละกลุ่มอายุ เครื่องมือที่ใช้ในการตรวจและสภาพแวดล้อมของห้องตรวจมีผลต่อค่าของ ERG และ VEP ดังนั้นห้องตรวจคลื่นไฟฟ้าของตาในแต่ละสถาบันควรจะมีค่าปกติเป็นของตนเองเพื่อใช้ในการแปลผล