Original Article

Normative values of visual evoked potential in adults

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Purpose: Visual evoked potentials (VEP) are used to determine the function of visual pathway from the optic nerve to visual cortex. Various factors may affect VEP response, viz., technical and environmental. The aim of this study is to obtain the normative value of VEP latency and amplitude parameters in adulthood in Indonesia, as well as the relationship of height, weight, body mass index (BMI), head circumference, and visual acuity with the variety of latency and amplitude values of VEP parameters. **Methods:** It is a cross-sectional study on 120 healthy subjects consisting of 60 males and 60 females between 18 and 65 years old. Height, weight, BMI, head circumference, and visual acuity were measured and continued with VEP examination using a 26′ checkerboard pattern on the left and right eyes alternately. All data were collected and analyzed with the Shapiro–Wilk test using statistical software R version 3.5.2. **Results:** Mean value of P100 latency (interocular latency) of left and right eye were 104.6 ± 3.4 ms and 104.1 ± 3.4 ms, respectively, as well as 9.8 ± 4.7 μV and 10.3 ± 5.4 μV for the amplitude. There was no significant difference between the male and female group, as well as on the age group. Female significantly exhibited a higher P100 amplitude than male. The greater the age, the lower amplitude of P100 significantly. **Conclusion:** Gender and age do not affect the P100 latency value but only affect P100 amplitude. Height, weight, BMI, head circumference, and visual acuity also do not affect the P100 latency and amplitude.

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Visual evoked potential (VEP) is an electrical wave, triggered by a visual stimulus, produced by electrical activity in the visual cortex, and recorded by the electrodes on the scalp. VEP represents a functional visual pathway from the retina, optic nerves, and optic tracts to the occipital cortex. Therefore, it can aid in diagnosing and determining the prognosis in certain neurological cases such as multiple sclerosis, optic nerve glioma, traumatic optic neuropathy, and several other diseases that can attack the visual system.[1]

The latency and amplitude of VEP are affected by subjective factors (age, gender, head circumference, and subject attention) and technical factors (types of stimulus monitor, size of stimulus box, the distance between stimulus point and the subject's eye, and room lighting).[1,2] Normal VEP response to a stimulus is a positive peak that occurs at a mean latency of 100 ms. Therefore, each laboratory is expected to demonstrate its own VEP normative values, which can be used as parameters.[1-4]

This study is expected to provide information regarding normal values of latency and amplitude of VEP in adult subjects in Manado, Indonesia, which can be used as a reference for VEP examination in the clinical neurophysiology laboratory of Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia in the future. Therefore, the objective of this research is to determine normative value distributions of VEP wave latency and amplitude in adults in Indonesia and determine normative value distributions of VEP wave latency and amplitude related to age, height, weight, head circumference, visual acuity, and body mass index (BMI) in adults in Indonesia.

Methods

Research design

A cross-sectional study with a nonrandom sampling method was conducted in the neurophysiology laboratory of Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia in October 2018–December 2018. This study used primary data from healthy adult subjects aged 18–65 years, who reported to the neurology clinic and met the inclusion criteria, including ophthalmoscopy using direct ophthalmoscope, field of view using confrontation test and Amsler Grid, normal color vision using Ishihara color card, and willing to participate in VEP examination in the Clinical Neurophysiology Department of Prof. Dr. R. D. Kandou General Hospital. The exclusion criteria include the following: history of intracranial neurological disorder, history of routine alcohol consumption, chronic kidney disease (proven by urea and creatinine levels in blood by laboratory examination), thyroid disease, malignancy, epilepsy, eye disease (cataract/glaucoma), diabetes (proven by blood glucose level), smoking, mental disorder and growth and developmental disorder based on anamnesis, consumption of drugs such as antidepressant, antipsychotic, sedative and opioid within the last month, and uncooperative or reduced awareness.

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Besides the chronic kidney disease and diabetes, each exclusion criterion was checked by anamnesis, physical examination, and neurological examination. Normal alcohol consumption was categorized as normal if alcohol consumption was less than 200 mL per day for 12% alcohol and the frequency is not every day for 1 year (WHO, 2000).[5] Height, weight, head circumference, and visual acuity (limited to ≥6/60 m with or without corrective lens) were measured.

The sample size was calculated using the following formula:

$$n = n_{(1)} + n_{(2)} \quad (1)$$

where $n_{(1)}$ was male subject and $n_{(2)}$ was female subject. The minimum subject was calculated based on the following formula:

$$n_{(1)} = n_{(2)} = 2\delta^2 \frac{(Z1 - \frac{\alpha}{2} + Z1 - \beta)^2}{(\mu_{(1)} - \mu_{(2)})^2} \quad (2)$$

$$\delta^2 = \frac{\delta^2_{(1)} + \delta^2_{(2)}}{2} \quad (3)$$

where (1) and (2) are the sample groups; $Z1 - \alpha/2 = 1.96$ for $\alpha = 0.05$; $Z1 - \beta = 1.28$ for $1 - \beta = 0.90$ and $\mu(1) - \mu(2)$ = the magnitude of the desired effect (Lemeshow, 1990).[6]

Previous study by Sharma *et al*.[2] showed that the effect size of 4 ms is adequate to detect $\mu(1) - \mu(2)$. Based on that, we got the estimate of $\delta^2 = 45.535$ and $n_{(1)} = n_{(2)} = 59.81$ or rounded up to 60 and eventually the sample size will be 120 people. The ethics committee has approved the ethical clearance on September 28, 2018.

VEP examination

VEP examination was conducted using a Dantec® machine (Alliance Biomedica, Chennai, India), with a calibrated 24-in DELL® LCD monitor (Dell, Round Rock, USA). VEP examination was conducted monocularly for each eye alternately with 80% contrast using a white–black checkerboard with a 26-mm squares pattern and 2-Hz frequency. The distance between the subject and the monitor was 1 m, with a visual fixation in the middle of the stimulus monitor. The recording was conducted using a band pass 1–100-Hz system, with 250-ms analysis duration. The recording was repeated twice with 200 stimuli per response (sweeps averaged). The best wave result was collected for the study. If the first and second results were similar, then the first recording was taken. Electrodes were mounted according to the international system of 10–20 with impedance under 5 Ω for each electrode. Room lighting was measured at 60 lx. The VEP parameters recorded were latencies to N75, P100, and N145 waves and peak-to-peak amplitude of P100 wave. The study was performed to determine the normative values and to investigate the effect of gender, height, weight, BMI, head circumference, and vision on VEP.

Statistical analysis

All data were collected and analyzed using statistical software R version 3.5.2. The correlation between variables was considered significant if $P < 0.05$. The Shapiro–Wilk test was conducted to determine numerical data normality, and data transformation was performed to normalize the abnormal distribution of data. Numerical data were presented in means and standard deviations.

Results

One hundred and twenty subjects with a comparable gender and various ethnicity participated in this study, with an average age of 43.3 ± 13.4 years [Table 1]. The majority of ethnicity was Minahasa (65.8%), followed by Bolaang Mongondow (11.7%), Batak (5.8%), Talaud (5%), Sangihe (4.2%), Java (3.3%), and Siau (2.5%), while Makassar was the least (1.7%). The majority of subjects were in the normal category, according to the results of BMI with a mean value of 24.8 ± 3.8 kg/m^2. Table 1 represents that males, as expected, tend to measure 10 cm higher (mean 167.1 ± 6.3 cm vs. 157.2 ± 3.8 cm, $P < 0.001$) and heavier than female (mean 71.8 ± 13.7 kg vs. 59.1 ± 8.3 kg, $P < 0.001$). Male subjects demonstrated approximately 2 cm

Table 1: Characteristics of subjects

Variable	Total (*n*=120)		Male (*n*=60)		Female (*n*=60)		*P**
	n (%)	Mean±SD	*n* (%)	Mean±SD	*n* (%)	Mean±SD	
Age (years)	*	43.3±13.4	*	42.8±12.9	*	43.8±13.5	0.663
Height (cm)	*	162.1±7.5	*	167.1±6.3	*	157.2±4.8	<0.001
Weight (kg)	*	65.4±12.7	*	71.8±13.7	*	59.1±8.3	<0.001
BMI (kg/m^2)	*	24.8±3.8	*	25.6±4.1	*	24.0±3.5	0.007
<18.5	7 (6)	*	0 (0)	*	7 (12)	*	<0.001
18.5-25	69 (57)	*	36 (60)	*	33 (55)	*	
>25	44 (37)	*	24 (40)	*	20 (33)	*	
Head circumference (cm)	*	55.4±2.2	*	56.6±2.2	*	54.2±1.9	<0.001
Left eye vision							
Normal	49 (41)	*	31 (52)	*	18 (30)	*	0.026
Myopia	71 (59)	*	29 (48)	*	42 (70)	*	
Right eye vision							
Normal	49 (41)	*	31 (52)	*	18 (30)	*	0.026
Myopia	71 (59)	*	29 (48)	*	42 (70)	*	

SD=Standard deviation, **t*-test or Mann-Whitney *U* test according to distribution normality

longer head circumferences ($P < 0.001$) than female subjects. The observation data showed that the variance of the BMI, body height, body weight, and head circumference were typical of Indonesian people.

The VEP assessment result of a healthy woman aged 43 years old showed that the P100 latency value of the left and right eye on the Oz-Fz channel is 101 ms and 98.3 ms, respectively, while the P100 amplitude value of the left and right eye on the Oz-Fz channel is 14.8 μV and 13.8 μV, respectively [Fig. 1]. The P100 wave amplitudes were significantly smaller in the male group [Table 2] (mean 8.0 ± 3.6 μV vs. 11.5 ± 5.1 μV for the left eye, mean 8.3 ± 3.9 μV vs. 12.3 ± 5.9 μV for the right eye; $P < 0.001$ for both eyes). This could be because females have smaller head circumference, which also affects the brain volume.[7] Few hypotheses also suspect that the hormones play a role, but it needs more evidences. The P100 wave amplitude [Table 3] was significantly lower in the 61–65-year age group compared to the other age groups ($P < 0.001$). This could be due the degenerative process of optical neural system at the old age.[8]

Table 4 represents an insignificant relationship between body height, body weight, head circumference, and BMI and vision based on latency and amplitude P100. Positive correlation was observed between BMI and P100 latency and negative correlation between BMI and P100 amplitude, both were not significant. The differences suggest the uncertainty between anatomy and hormonal factors to P100 latency and amplitude. The negative correlation between BMI and N75 and N145 latency was not used for clinical matter as it is inconsistent and unreliable due to many ambiguous factors, such as vision and subject's focus.[8-10] Thus, we did not discuss deeper in this article.

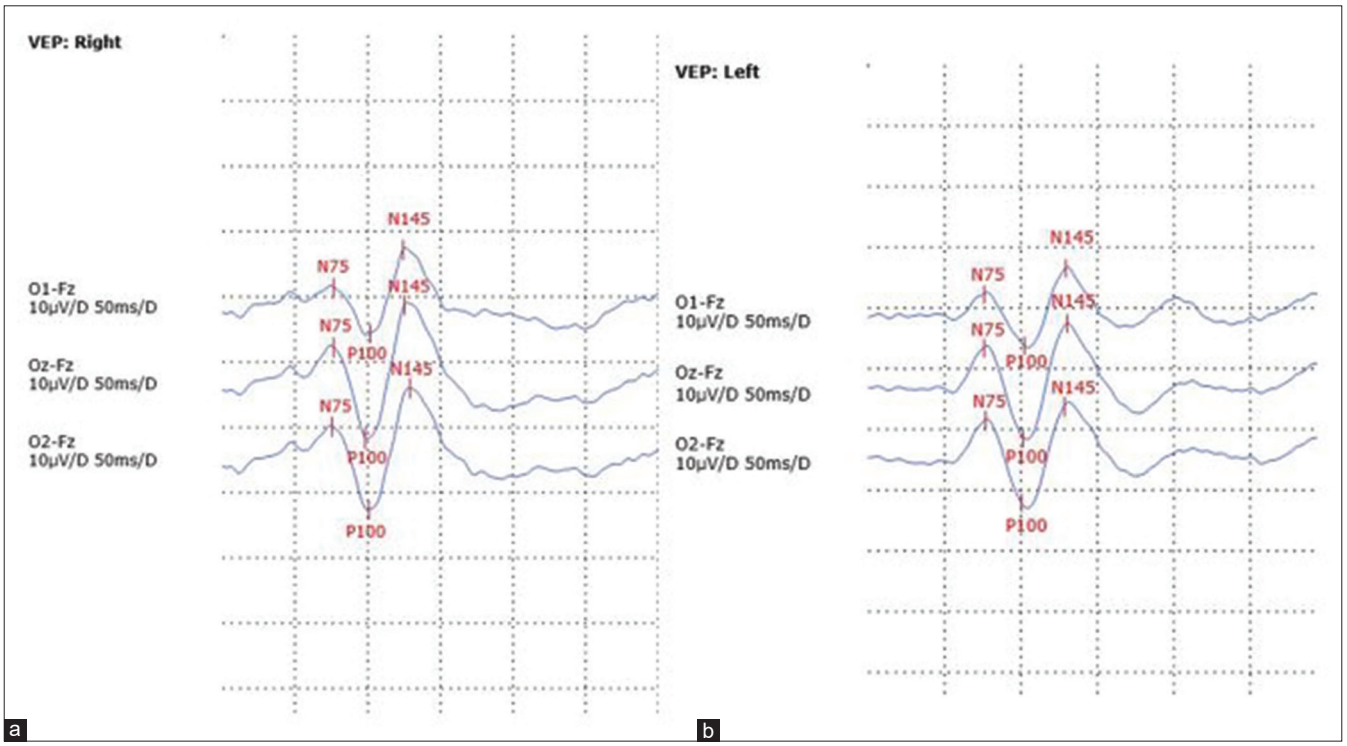

Figure 1: VEP assessment result of a healthy woman aged 43 years old

Table 2: VEP parameters according to gender

VEP parameter	Mean±SD			*P**
	Total (*n*=120)	Male (*n*=60)	Female (*n*=60)	
Left eye				
N75 latency (ms)	78.5±4.0	79.4±4.8	77.5±2.6	0.010
P100 latency (ms)	104.6±3.4	104.5±3.7	103.8±3.0	0.130
N145 latency (ms)	140.9±6.5	141.5±7.3	140.4±5.5	0.355
P100 amplitude (μV)	9.8±4.7	8.0±3.6	11.5±5.1	<0.001
Right eye				
N75 latency (ms)	78.3±3.9	79.0±4.6	77.2±2.6	0.002
P100 latency (ms)	104.1±3.4	104.8±3.6	103.5±3.0	0.133
N145 latency (ms)	140.4±6.5	141.3±7.4	139.5±5.4	0.121
P100 amplitude (μV)	10.3±5.4	8.3±3.9	12.3±5.9	<0.001

SD=Standard deviation, **t*-test or Mann-Whitney *U* test according to distribution normality

Table 3: VEP parameters according to age

VEP parameter	Age (years) Mean±SD					*P**
	18-30 (*n*=30)	31-40 (*n*=24)	41-50 (*n*=23)	51-60 (*n*=29)	61-65 (*n*=14)	
Left eye						
N75 latency (ms)	77.4±3.8	79.2±3.8	78.1±4.1	79.4±4.6	78.1±2.4	0.302
P100 latency (ms)	104.1±3.0	103.8±3.4	104.1±3.3	104.5±3.5	104.1±3.6	0.134
N145 latency (ms)	140.3±7.6	139.5±7.0	142.8±7.0	140.7±4.8	142.2±4.8	0.413
P100 amplitude (μV)	11.4±3.9	12.1±5.0	10.0±4.1	9.0±4.2	3.8±2.2	<0.001
Right eye						
N75 latency (ms)	78.0±3.3	79.0±4.1	78.2±4.4	78.5±4.3	77.3±2.5	0.782
P100 latency (ms)	103.0±3.0	102.9±3.1	104.0±2.7	104.0±3.8	104.9±3.0	0.158
N145 latency (ms)	141.5±7.3	137.3±6.5	142.4±6.9	139.5±5.2	141.6±4.8	0.052
P100 amplitude (μV)	12.1±4.9	12.9±5.8	10.1±4.1	9.8±4.9	3.70±1.9	<0.001

SD=Standard deviation, **t*-test or Mann-Whitney *U* test according to distribution normality

Table 4: Correlation between VEP parameters and height, weight, BMI, head circumference, and vision

Correlation	Height (cm)	Weight (kg)	BMI (kg/m²)	Head circumference (cm)	Left eye vision	Right eye vision
Left eye						
N75 latency (ms)	0.160	0.068	−0.002	0.141	0.046	0.046
P100 latency (ms)	0.093	0.097	0.109	0.145	−0.092	−0.092
N145 latency (ms)	−0.106	0.088	0.121	−0.021	0.028	0.028
P100 amplitude (μV)	−0.111	−0.068	−0.087	−0.064	−0.259	−0.259
Right eye						
N75 latency (ms)	0.328	0.160	0.005	0.179	0.055	0.055
P100 latency (ms)	0.095	0.075	0.054	0.078	−0.197	−0.197
N145 latency (ms)	0.167	0.204	0.155	−0.013	−0.007	−0.007
P100 amplitude (μV)	−0.161	−0.005	−0.088	−0.069	−0.260	−0.260

*Pearson/Spearman test

Discussion

VEP is an important procedure in assessing visual function objectively and is highly sensitive in determining any disorder of the visual system in the optic nerve and optic chiasm.[11]

One hundred and twenty samples were used, with a male: female ratio of 50:50 and the average age of 43.3 ± 13.4 years. The majority of subjects were in the normal category of BMI. Height, weight, BMI, and head circumference data in this study demonstrated higher means in males compared to females and were not much different compared to the general Indonesian population. Thus, this can be considered a reference for the Indonesian population. More than half of the subjects exhibited myopia, and females were more affected. This result was in accordance to the data from the World Health Organization in 2012, in which the highest vision reduction in the world was caused by refraction disorder, and the data from Riskesdas in 2013, in which the prevalence of vision reduction patients was higher in females.[2,12]

The average latency of P100 in males was 104.5 ± 3.7 ms for the left eye and 104.8 ± 3.6 ms for the right eye. Females exhibited a mean latency of P100 of 103.8 ± 3.0 ms on the left eye and 103.5 ± 3.0 ms for the right eye. The total mean of the left eye was 104.6 ± 3.4 ms and 104.1 ± 3.4 ms for the right eye. An insignificant difference was found in the P100 latency value between males and females. This was concordant to Celesia *et al*.,[12] who obtained the total mean of 98.1 ± 4.4 ms (recording at 15′ squares) and 94.7 ± 5.0 ms (recording at 31′ squares). Tandon found a mean value of 95.4 ± 6.9 ms in males, 91.1 ± 7.4 ms in females, and 94.3 ± 7.1 ms in total, and Wijaya found a mean value of 100.2 ± 5.7 ms in males and 101.1 ± 5.8 ms in females.[7,13] These three authors did not find any significant difference in P100 latency value between adult males and females.[13,14] However, these results were different than Sharma who obtained a mean value of 93.2 ± 10.7 ms for males and 88.3 ± 8.8 ms for females, and he found that the P100 latency value was significantly shorter in females compared to males.[2] This study demonstrated that the P100 amplitude values in males were 8.0 ± 3.6 μV for the left eye and 8.3 ± 3.9 μV for the right eye. The P100 amplitude values in females were 11.5 ± 5.1 μV for the left eye and 12.3 ± 5.9 μV for the right eye. The total mean of the left eye was 9.8 ± 4.7 μV, and the right eye was 10.3 ± 5.4 μV. The results were higher in females than males ($P < 0.001$). These results were in line with Sharma obtaining mean values of 5.7 ± 0.5 μV for males and 6.4 ± 0.7 μV for females and Wijaya obtaining a mean value of 7.8 ± 3.2 μV for males and 11.3 ± 5.3 μV for females.[2,13] Both authors found that females exhibited a significantly higher P100 amplitude than males.[2] This may be due to the smaller head circumference in females compared to males and associated with brain volume. Several hypotheses also estimated a hormonal effect, albeit they cannot be fully proven.[7] The normative values of P100 latency and amplitude obtained in this study tend to be higher than normative values in other studies, as stated in this discussion.

This may be due to the difference in square size and subject age. The latency values of N75 and N145 were not used for clinical purposes, due to inconsistency and unreliability, and highly affected by confounding factors, especially the vision and focus of the subjects.[8-10] Therefore, these were not included in our discussion.

The differences in P100 latency value for each age group were not far adrift and insignificant. This was in accordance with a theory which stated that P100 latency was stable at 18 years old and started to lengthen above 70 years old due to prominent neuron cell death, especially the axon of the visual system, which occurred after the seventh decade. The P100 amplitude value in Table 3 shows a significant decrease in 61–65 age group ($P < 0.001$). This was in line with Sawaya obtaining a significant decrease of P100 amplitude value along with age.[8] This was also in accordance with a theory which stated that age above 28 years old will undergo a P100 amplitude decrease for each decade of life.[1,8,9,15,16]

The data in this study did not show a significant correlation between height, weight, head cir17cumference, BMI, and vision with latency and amplitude values of P100 [Table 4]. Sharma found a significant positive correlation between weight, BMI, and P100 latency in females, but not in males. Sharma did not find a significant correlation between height and head circumference with latency and amplitude of P100, neither in males nor females.[2,17,18] Wijaya found an insignificant correlation between head circumference (recording at 16′ and 32′ squares) and vision sharpness ((20/20–20/100 ft) recording at 16′ square) with P100 latency and amplitude. However, he found a significant negative correlation between vision sharpness (20/20–20/100 ft) and P100 latency (recording at 32′ square), a significant positive correlation between height and weight with P100 latency value (recording at 32′ square), and a significant positive correlation between BMI and P100 latency value (recording at 16′ and 32′ squares).[8,19] The differences of results obtained in this study with previous studies could be caused by differences in sample size, square size, method used, and other causal factors, including focus concentration. These differences proved that an uncertainty exists that anatomical and hormonal factors affected P100 latency and amplitude values.[2,19-21]

Although this study used laboratory examination performed on each sample to rule out undetected disorders during anamnesis and physical examination, it still demonstrated several limitations, that is, lack of adjunctive examination before VEP to rule out exclusion criteria, such as brain imaging or eye examination, or a more accurate neuro-ophthalmological examination like the use of campimetry in evaluating field of view and slide lamp to determine anterior condition of the eyes.

Conclusion

No significant differences were found between the P100 latency values of gender and age groups. However, the P100 amplitude was significantly higher in females compared to males and in age groups whereas amplitude decreased along with age. No significant correlation was found between height, weight, head circumference, BMI, and visual acuity with P100 latency and amplitude values.

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Conflicts of interest

There are no conflicts of interest.

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