Standards for the assessment of visual evoked potentials in an ethnically heterogeneous adult population

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Summary

Visual evoked potentials (VEPs) were recorded by chequerboard pattern-reversal stimulation in 276 normal adult subjects aged 15 - 73 years. The sample comprised comparable white, coloured and black groups of both sexes. Significantly shorter latencies of the major positive component were found in both male and female black subjects compared with those in whites. No significant differences were found between the amplitudes in the different population groups, but females in each population group showed significantly higher amplitudes of the major positive component than males. There was a close relationship between latency and amplitude for both right and left eyes. Except in coloured females, a non-linear relationship of the major positive component with age was demonstrated, the shortest latency being at about 35 years of age. It is suggested that the following criteria be used in the evaluation of VEP recordings: latency as well as the difference between latencies and amplitudes of the two sides of the major positive component (P1) as compared with standardized values for ethnic, sex and age groups.

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During the last decade the usefulness of the evoked potentials in clinical neurology has been proved. By applying the technique of signal averaging to stimulus-coupled responses, extraction of the signal from background noise makes it possible to quantify its latency and amplitude. The reversing chequerboard pattern, in which dark and white squares are reversed, has become the standard stimulus for eliciting the visual evoked potential (VEP). Rotating mirrors,[1,2] television tubes[3] and light-emitting electrodes[4] have been used to produce the pattern reversal, each method having its own distinctive characteristics.

Stimulus characteristics and laboratory methods vary widely and markedly influence the parameters of the normal response.[5,6'] It is therefore necessary to adhere to a standardized procedure with well-established normal values derived from a sufficient number of healthy subjects.

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Published results reveal differences in normative values for VEP latencies and amplitudes related to age and sex.[6-12] In some studies the numbers of subjects are too small to allow statistical evaluation. Since most papers on this subject originate from the Western world, normative values for large non-white population groups have yet to be determined.

This article is concerned with the analysis of VEP parameters by age and sex in three different ethnic groups in the Cape Peninsula.

Subjects and methods

A group of 276 normal adult subjects was studied. White, coloured and black males and females were adequately represented (Table I). Thirty-one per cent of the subjects were between 15 and 29 years old, 32% between 30 and 44 years old, 28% between 45 and 59 years old and 9% older than 60 years. The mean age for females was 37 years and that for males 42 years, with a range of 15 - 73 years.

TABLE I. SAMPLE SIZES

	Ethnic group			Total
	White	Coloured	Black	
Male	49	42	40	131
Female	49	45	51	145
Total	98	87	91	276

Subjects with refractive errors were accepted when their visual acuity with spectacles could be corrected to 6/6 or better (Snellen chart), and colour-blindness was excluded by means of the Ishihara colour-chart test.

The subjects were adapted to a dimly lit room and placed in a comfortable, semi-recumbent position. If they used spectacles they were requested to keep them on. They were tested with one eye fixing on a central target dot; the other eye was occluded with a patch. Silver-silver chloride electrodes were applied at the midline 5 cm above the inion (inverting), the reference electrode was placed at FZ and an electrode attached to the wrist was grounded. Electrode impedance was kept below 5K ohms. The electrodes were connected to the input of a pre-amplifier (type AA6M) of a Medelec MS6 EMG machine. A band width of between 1,6 and 32 Hz and a gain of 20 μV per division was maintained.

Pattern stimulation with a chequerboard array was performed by a Medelec visual stimulus pattern grader. The pattern was displayed on a 625-line 50 Hz television screen. The stimulus was delivered at a rate of 1 per second and the contrast ratio was kept at 100%. The pattern on the television measured 53 cm horizontally and 39,5 cm vertically and was placed 1,50 m in front of the stimulated eye resulting in subtended arcs of approximately 20° and 15° respectively. The individual squares subtended 27,5 min arc horizontally and 25 min arc vertically.

The amplified signal of 128 responses for each eye was averaged by a DAV6 averager. A time base of 300 ms was used. Latencies and amplitudes of the VEP response were read digitally from an A X 62-type averager expander belonging to this machine. Amplitudes were measured from peak to peak, i.e. from the first negative peak (N1) to the first major occipital-positive peak (P1).*

Results

A repeated-measures analysis of variance was used to compare the different ethnic and sex groups with regard to latency and amplitude of P1 in the left and right eyes.

Latency

The analysis of P1 latency shows no significant difference between the two sexes ($P = 0,235$) and between left and right eyes ($P = 0,4632$). A pairwise comparison of the ethnic groups shows a significant difference between the black and white population groups ($P = 0,0143$) but no significant difference between the black and coloured groups or between the coloured and white groups ($P = 0,4011$ and $P = 0,1138$ respectively).

Table II shows the mean values with their standard deviations for the different groups as well as the correlation coefficients between the left and right eyes for P1 latency. The differences in P1 latency (and amplitude) between the right and left eyes did not follow a normal distribution and we therefore considered the median and range as descriptive measures. The median difference was 0 ms and the differences ranged from –6 to +6 ms. The normal upper limit for the absolute difference in latency between the two eyes is therefore 6 ms for all groups. Marginal means for ethnic and sex groups as well as the overall mean value for P1 latency are also shown in Table II.

TABLE II. MEAN VALUES FOR P1 LATENCY (ms)*

Ethnic group	Sex Male	Female	Means for ethnic groups
Black			
Left	97,68 (5,47)	96,61 (4,70)	
r	0,91	0,88	97,25 (4,98)
Right	98,15 (5,18)	96,86 (4,69)	
Coloured			
Left	98,10 (5,06)	97,64 (4,73)	
r	0,90	0,90	97,90 (4,76)
Right	97,81 (5,04)	98,04 (4,37)	
White			
Left	99,27 (4,10)	98,80 (4,40)	
r	0,92	0,90	98,96 (4,18)
Right	99,33 (4,26)	98,45 (4,03)	
Means by sex	98,44 (4,84)	97,72 (4,52)	98,06 (4,69)

*Standard deviations are shown in brackets and r is the correlation between the left and right eyes.

Amplitude

Mean amplitudes are shown in Table III. No significant differences were found between the amplitudes for the different ethnic groups ($P = 0,4154$), but a significant difference was

*The designation P100 is often used for this wave, because it appears about 100 ms after the pattern-shift stimulus. In other papers it is referred to as P2, on account of the fact that a sometimes demonstrable small positive wave precedes the major one.

TABLE III. MEAN AMPLITUDES (μV)*

Ethnic group	Sex Male	Female	Means for ethnic groups
Black			
Left	4,75 (2,49)	6,04 (3,07)	
r	0,56	0,76	5,43 (2,87)
Right	4,41 (2,28)	6,17 (3,57)	
Coloured			
Left	5,21 (2,71)	6,50 (2,58)	
r	0,89	0,79	5,87 (2,92)
Right	4,84 (2,93)	6,80 (3,03)	
White			
Left	4,41 (2,44)	6,60 (3,16)	
r	0,83	0,72	5,43 (3,03)
Right	4,47 (2,31)	6,25 (2,86)	
Means by sex	4,67 (2,52)	6,38 (3,05)	5,57 (2,94)

*Standard deviations are shown in brackets and r is the correlation between the left and right eyes.

demonstrated between males and females ($P < 0,0001$). The median difference in amplitude between the right and left eyes was 0 μV and the range was 16,6 μV ($-8,8 - 7,8$ μV). The marginal means for ethnic and sex groups as well as the overall mean value are also shown in Table III.

Relationship between P1 latency and age

The association between P1 latency and age was examined in the different sex and ethnic groups. Because of the highly correlated values of P1 latency in right and left eyes (Table II), this association was investigated only for the right eye.

In five of the six groups a second-order polynomial regression model showed significant improvement over a straight line regression model. An exception was the coloured female group — no association between P1 latency and age could be demonstrated. Table IV shows the squared multiple correlation coefficient (r^2) of the polynomial regression for the six ethnic and sex groups. Sparse data for those aged 60 years and older may account for some of the low r^2 values. For example, the black male group had the best representation (18%) in this age group, whereas the coloured female group had only 1 subject older than 60 years.

TABLE IV. SQUARED MULTIPLE CORRELATION COEFFICIENT (r^2)

Ethnic group	Sex Male	Female
Black	0,426	0,216
Coloured	0,218	0,088
White	0,243	0,357

Fig. 1 shows the non-linear association between P1 latency and age for the white male group. The 99% confidence intervals are also depicted. The regression function in Fig. 1 has the following formula: P1 latency = $108,45 - 0,59$ (age) $+ 0,0079$ (age^2). The standard error of this prediction is 3,789.

Discussion

For the purpose of distinguishing between normal and patholo-

P₁(msec)
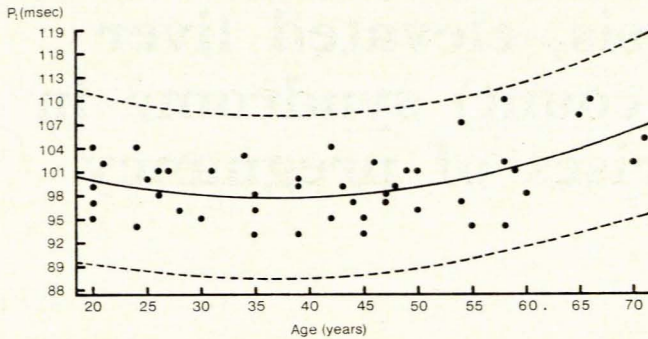
Fig. 1. P1 latency versus age (in right eyes) for white males — observed and predicted values. Dashes represent the 99% confidence limits.

gical values, reliable normative data on standard procedures are required.

Test results from the present study confirm the slightly shorter P1 latency in females reported earlier.[6-8] Hypotheses about the reason still have to be supported by facts. It is suggested, however, that genetic heterogeneity is not of relevance in this respect. Interesting is the small but significant difference between P1 latency in white and in black subjects, the latter group showing the shorter ones. This might be attributed to genetic factors, either intra- or extracerebral. Amplitudes have not usually been discussed in detail on account of the considerable variation among normal subjects. Females in the three ethnic groups had higher amplitudes than males. This is in agreement with findings from other laboratories.[6,8]

Fig. 1 is representative for five of the six population groups. Between 15 and 35 years of age P1 latency decreases slightly with a gradual increase after 35 years and a steeper gradient in those over the age of 60 years. In coloured females, however, no relationship between P1 latency and age could be demonstrated. Test results in the present study are in general agreement with those of other investigators as to the relationship between P1 latency and age.[2,6-9] Celesia and Daly[10] found a continuously ascending slope from the age of 18 to 79 years. Their technique was, however, unusual in some respects.

In those older than 60 years inconclusive results can be obtained in the absence of ophthalmic screening for age-related lesions. On account of this and the relatively small number of subjects in this age group, there is uncertainty concerning P1 latencies and amplitudes. A few authors have commented on variations of P1 amplitudes with age.[8,11,12] In most papers no data are provided in this respect. Our data do not show a relationship between age and amplitude. Relatively few subjects, however, are included in the highest age group.

Clinical applications

A number of clinical applications can be derived from the present study. Firstly, the range of normal P1 latencies for the age groups 15 - 73 years with all ethnic and sex groups included is 90 - 111 ms. Age-adjusted values should be used in setting the normal limits of latency for clinical testing. Multiple sclerosis, still the most important indication for referral for assessment of VEPs, usually manifests its initial signs and symptoms in young adults. The P1 latency here should not exceed 108 ms, although other factors such as difference in latency between the two eyes and the shape of the potentials should be taken into account.

Individual variations in VEP latency are much larger than the responses of each eye in the individual subject. Clinically this applies particularly to patients in whom the two eyes or optic nerves are affected unequally, as in multiple sclerosis or compressive lesions on the optic nerves. According to the present material the P1 latency difference between the two eyes should not be more than 6 ms.

There is a great variation between the individual P1 amplitudes, the lowest being 0,8 μV and the highest 18,4 μV. The difference between the two eyes, however, is much smaller, and in normal subjects should not exceed 8,3 μV.

Apart from improvements in the diagnosis of multiple sclerosis, the VEP technique[1-3,13] has many other clinical applications. Several diseases of the eye can influence VEP parameters.[14] Halliday[15] summarized a number of hereditary diseases in which the optic nerves can be involved. He also mentioned compression of the optic nerves and subacute combined degeneration as possible causes for abnormal findings. Abnormal results were also found in patients with Parkinson's disease.[16] Hydrocephalus due to posterior fossa tumours[3] and benign intracranial hypertension can distort VEPs due to non-local factors.

Regarding the applicability of our tables and figure in other laboratories, it must be borne in mind that parameters of normal responses are influenced by many stimulus characteristics.[5] These, as well as selection of patients, may affect the results obtained.

The VEP technique is non-invasive and constitutes a valuable addition to routine diagnostic procedures in neurological practice. Standardization is essential and the results should be interpreted in relation to age, sex and ethnic group.

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