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Original Article

Relationship of the Pattern- reversal Visually Evoked P100 Wave Latency, Amplitude and duration to Head Size and Height

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ABSTRACT

Background and Aim: Transient Pattern-Reversal Visual Evoked Potentials (t-PRVEPs) used in evaluation of many neurological disorders are documented to be influenced by age, sex and body size and are best recorded over the occipital region. **Methods:** The present study has investigated the influence of head size and height on the main component P100 peak latency, amplitude and duration in Indian population. Occipito-frontal circumferences, heights of 146 healthy normal volunteers aged 1-75 years were measured and t-PRVEPs latency, amplitude and duration of P100 waveform of each eye (292 monocular tracings) recorded. **Results:** Results indicate that OFC and height of the individual correlates positively with the P100 latency and duration but negatively with its amplitude. **Conclusion:** In the 1st decade of development, P100 latency increases at a rate of around 2.3ms/cm increase in OFC and the most significant changes with respect to OFC and height are on the P100 amplitude contributing about 39% and 45% each respectively.

Key words: P100latency, Amplitude, Duration, Occipitofrontal circumference, Height, Indians.

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INTRODUCTION

Pattern- reversal visually evoked potentials (PRVEPs) have emerged as an important non invasive tool of investigation in detecting abnormalities of visual system in neuro-ophthalmic disorders. Since it is an objective and reproducible test for optic nerve function, it is not only useful for clinical neurophysiologist or ophthalmologist but also for neurologists and neuro-surgeons, as many of the neurological disorders present with visual abnormalities.[1]

These evoked potentials generated in the cortical and sub-cortical visual areas when the retina is stimulated with patterned- light are best recorded over the occipital region. However, before using it as a diagnostic tool, its proper statistical characterization and identification of PRVEP abnormalities in an appropriate neurologically normal population is required. Published normative data[2-8] have stated the influence of age, sex and body size on the main component P100. The present study has investigated the influence of head size and height on the P100 peak latency, amplitude and duration in Indian population.

MATERIALS AND METHODS

The study is an institutional cross-sectional study (October 2005 to Apr 2008) conducted in the Neurophysiology Lab, Department of Physiology, Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sewagram, Wardha, Maharashtra. Ethical clearance from the Institutional Ethics Committee, MGIMS, was taken and informed consent was also taken from the volunteers before the study.

The study population consisted of visually normal, 146 healthy subjects (38 females; 108 males), aged between 1-75 years which was further divided on the basis of their age into 5 groups of 60 eyes each except in Group E where it is only 52 eyes due to the paucity of normal subjects.

i. GROUP A : Children (1-15years)
ii. GROUP B : Young adults (16-25years)
iii. GROUP C: Adults (26-40 years)
iv. GROUP D: Middle-aged (41-60 years)
v. GROUP E: Old-aged (61-75 years):

Methodology proper

Each subject was given a thorough eye examination as a preliminary measure to exclude any eye pathology. Non-co-operative individuals or those with systemic or ocular diseases that might affect the normal values of PRVEPs were excluded from the study. The head circumference (in cms) recorded as the occipito-frontal circumference (OFC) was measured using an inch-tape and height (in cms) in upright position using a standard height-scale.

The t-PRVEPs of each eye amounting to 292 monocular tracings were recorded on an Evoked Potential Recorder (RMS-EMG.EP Mark-II) in accordance to the recommendations of International Federation of Clinical Neurophysiologists (IFCN)[9] and International Society for Clinical Electrophysiology of Vision (ISCEV).[10] As per 10-20 International system of EEG placement,[11-12] the montage used was Oz-Fz and

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grounded at the vertex, Cz. The stimulus was a full field B&W checkerboard pattern (check size 8x8), reversed at a rate of 1.71Hz with a sweep duration of 300ms. The filters were kept at 2 Hz - 100 Hz and sensitivity at 2μV. The electrode impedance was kept below 5 KΩ. The luminance (59cd/sqm.) and contrast level (80%) are kept constant for all the recordings in all the cases.

200 epochs were averaged and recorded twice for reproducibility. Specific attempt was made to ensure that the child / subject maintained his fixation at the central red point throughout the recording. Each subject was allowed to rest for 5-10 minutes after each recording, typically with their eyes closed.

Statistical Analysis of Data

Association of the latency, amplitude and duration of P100 waveform with the occipito- frontal head circumference and height were analysed using linear as well as non-linear polynomial regression studies. Significance levels were kept at $p<0.05$.

RESULTS

The physical parameters of the subjects included in the study are shown in Table 1. The mean ± Standard Deviation (SD) of the age of the subjects in years, occipito-frontal head circumference and height in cm are depicted for males and females as well as the group trend in each of the five groups. The head circumference of all 146 subjects (age range 1.8 - 75years) ranges from 46 to 59cm with an average of 54.12cm. The height was 154.94cm in average and ranges from 83 to180cm. The age-related changes in height and head circumference of the study population are depicted in Figure A.

Head circumference and P100 parameters*:* Latency, duration and amplitude

Figure 1 shows the relation between occipito-frontal head circumference (cm) and P100 latency (ms). The P100 peak latency across the age span was 97.53ms. The best fit mathematical model was a *Linear Regression* described by the Equation: Y = 1.79903X. The corresponding variances of OFC and P100 latency were 5.68 and 25.15 respectively, with F being 17846.22. The Co-efficient of Determination, R^2 is 0.124 with a Standard Deviation (SD): 6.183 and a highly significant *P* (<0.0001). There is a positive correlation between the two showing that as head circumference increases, there is also a corresponding increase in the P100 latency.

Figure 2 shows the relationship between head circumference and P100 duration. Like its latency relationship, P100 duration also follows a positive correlation with increasing head circumference and is best described by the *Linear Regression as given by: Y = 1.42 X*. The SD is 12.61, $R^2 = 0.015$ and *P* <0.0001.

Figure 3 shows the relation between OFC (cm) and P100 amplitude (uV). The best fit mathematical model of this observed data is a polynomial equation of second degree, described as *Y = 314.58 -10.6X + 0.09X2* and shows a negative correlation between the two. The R-Square (COD) is 0.39261, Standard Dev: 3.05 and *P*<0.0001.

Height and P100 parameters: latency, amplitude and duration.

The relation between height and P100 amplitude (Figure 4) is best described by a second degree Polynomial Regression equation: $Y = 33.68 -0.24*X + 4.17E-4*X^2$. Here, the R-Square (COD) is 0.4527, with SD of 2.8997 and *P*<0.0001.

Figure 5 depicts the correlation between height and P100 latency. The best fit mathematical model was a Polynomial Regression of fifth Degree described by the Equation: $Y = 4734.03 - 185.04X + 2.89X^2 -0.02X^3 + 8.26E-5X^4 -1.25E-7X^5$. The calculated R-Square (COD) is 0.062 with SD =4.9 and P=0.0026.

The relationship between height and P100 duration is depicted in Figure 6. The data is best expressed by Polynomial Regression of fourth degree: $Y = 1376.87 - 44.7X + 0.56X^2 - 0.003X^3 + 5.85E-6X^4$. The R-Square (COD) is 0.04789 with SD being 11.98441 and P=0.0069.

Table 2 depicts the association and significant levels of P100 parameters with OFC and height. It is obvious that the influences of OFC and height are mostly on the amplitude showing 39% and 45% association respectively while their effects on latency and duration merely ranges from 1.5% to 12% only.

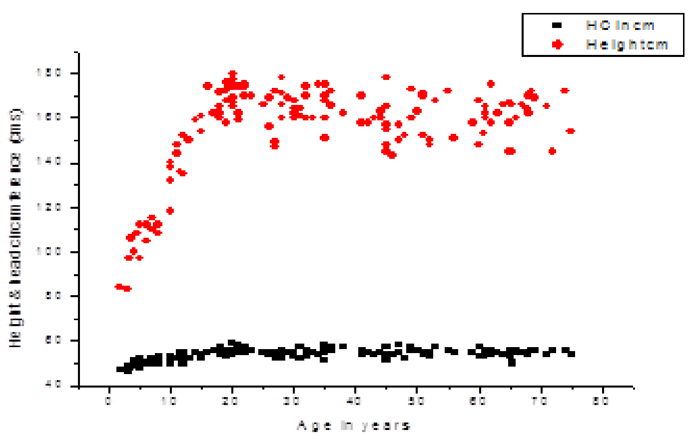


Figure A: Variation of head circumference and height as a function of Age.

Table 1: Physical parameters in males and females in each age groups (mean±SD)

Parameters	Age (years)			Head circumference (cm)			Height (cm)		
	Males	Females	Group trend	Males	Females	Group trend	Males	Females	Group trend
Group A	7.8±3.5	9.2 ±4.7	8.25±3.9	50.8 ±2.5	51.1 ±1.9	50.9 ±2.3	118.9 ±19.8	127 ±28.6	121.6 ±22.9
Group B	20 ±2	18 ±0.5	20 ±2.9	55.8 ±1.2	53.8 ±0.8	55.5 ±1.3	170 ±5.3	161 ±2.97	169± 6.2
Group C	32 ±3.44	28.9 ±3.02	31.3 ±3.52	55 ±1.7	54 ±1.4	55±1.8	167.5 ±5.4	156 ±7.7	164.8 ±7.7
Group D	48.1 ±5.12	49.7 ±5.9	48.7 ±5.4	55.5 ±5.14	53.8 ±1.5	54.8 ±1.7	164 ±7.5	151 ±5.6	159 ±9.3
Group E	65.9 ±4.13	64.6 ±1.8	66±4	55±1	54±3	55±1	163±7	152 ±8.12	162 ±8.1

Table 2: Association of OFC and Height with P100 parameters.

Parameters		COD: R^2
Occipito-Frontal Circumference vs	P100 Latency	0.124***
	Amplitude	0.39261***
	Duration	0.015***
Height vs	P100 Latency	0.062**
	Amplitude	0.4527***
	Duration	0.04789**

COD: co-efficient of Determination, P: level of significance**<0.01,***<0.001

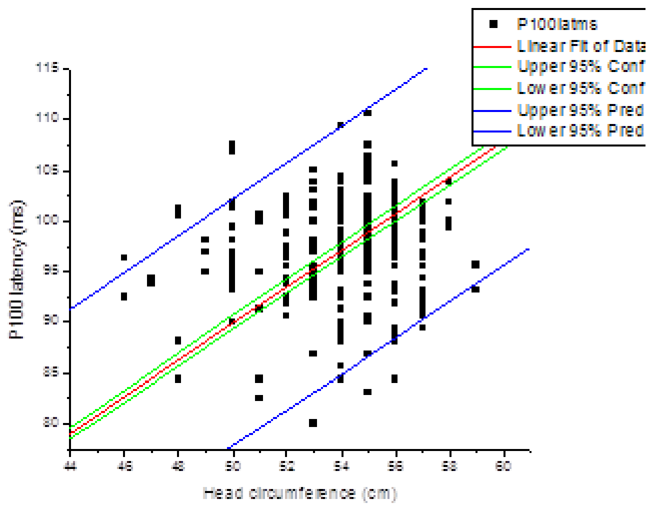


Figure 1: P100 latency (ms) as a function of Head circumference (cm)

DISCUSSION

VEPs have various utility in many neurological disorders and established use in clinical conditions such as Multiple Sclerosis, not only in its diagnosis but also can provide prognostic information.[13] However, it is known to be influenced by many physical and physiological parameters and valid identification of its abnormalities requires a proper statistical characterization especially concerning the main influencing factors like age, gender and body size.[10]

In our study done in Indian population (Central India), we found that head circumference measured as the occipito-frontal circumference has a positive correlation with P100 latency and duration showing that as head circumference increases, there is also a corresponding increase in the P100 latency and duration. Our population has an average occipito-frontal head circumference increasing on an average from 48.9cm in the 1-5year group to 50.9cm in the 6-10year group and 52.9cm in the 11-15years group. This increase is reflected by an increase in mean P100 latency (msec) of 95.36 in the 1-5year group which increases to 100.01 in the 6-10year group and can be accounted for by the gradual lengthening of the visual pathway with the growth of the child and increase in the head circumference.[5] It is observed that a difference of 2cm in OFC correlates to an increase of around 4.6ms in the P100 latency in this age-group. In the 11-15 years group, the OFC increases again by another 2cm to 52.9cm but the P100 latency reduces to 97.9ms.

This may indicate the rapidity of nervous growth and sensory pathway lengthening in the first decade and thereafter an accountable maturation of the visual pathway beyond 10years. Beyond this age span upto 75 years, the OFC averages around 54.54cm while the latency of P100 averages

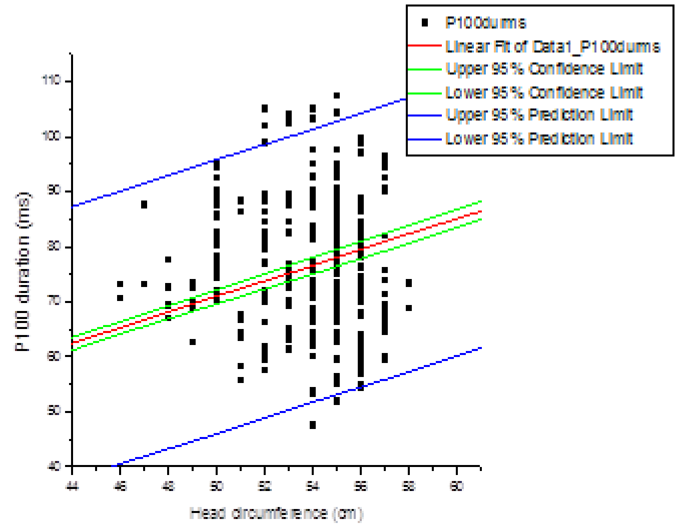
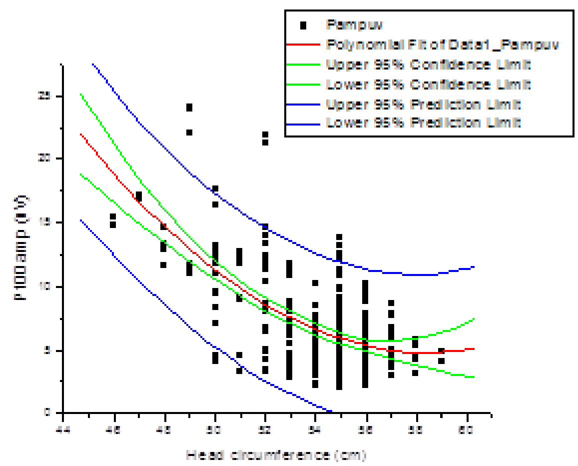


Figure 2: P100 duration (ms) as a function of Head circumference (cm)



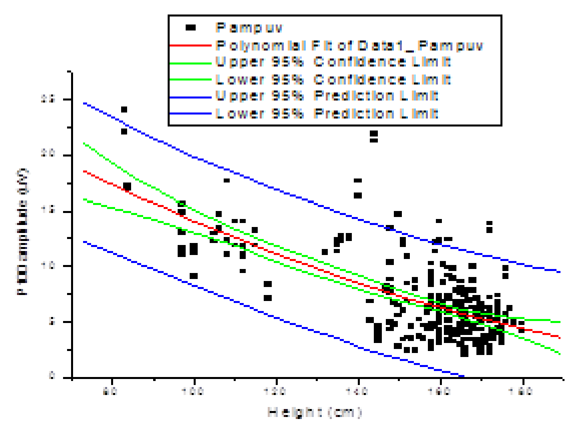


Figure 3: P100 amplitude as a function of Head circumference and Height **(Figure 4).**

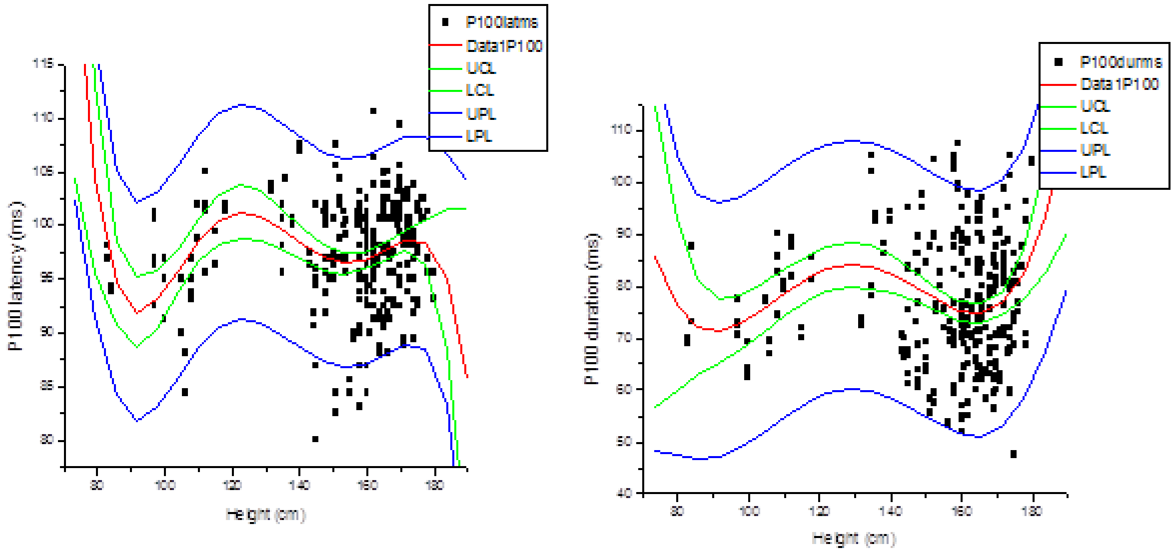


Figure 5: P100 latency and P100 duration (**Figure 6)** as a function of Height.

98.45ms in 16-25yrs, 96.12ms in 26-60 yrs and 98.92ms in 61-75yrs age span.

The P100 latency relationship with height appears to be more complex, requiring a higher polynomial fitting of fifth degree and is difficult to explain. Our study shows a statistical significance of p=0.0026 but we are of the opinion that the influence of height on the speed of conduction inside the cranium may be less profound and different from its influences on the peripheral nerve conduction. The positive correlation between P100 latency and increasing head circumference and height may all reflect the increase in length between the optic nerve head and the visual processing areas- the striate and the extra striate cortex which are the main generators of the various PRVEP waveforms.[16-19]

P100 duration reflects the extent of temporal dispersion of the visual information in the cortex (Onofroj and Bodis-Wollner, 1982; Livingstone *et al.* 1981). In our study, P100 duration follows a highly significant (p<0.0001) positive linear correlation with increasing head circumference while its relation with height is more complex but still statistically significant (p=0.006).

Jon S. Larsen (1978) found a significant correlation not only between head circumference and axial eye length but also between height and axial eye length. These differences existed even between the sexes.[5] These two factors may influence the VEP parameters as larger head circumference indicates a larger brain size and a longer conduction pathway thus prolonging VEP latencies. Assuming that the variation is isometric, differences in all dimensions will be proportional and any pathway in the brain will vary in length as the cube root of brain volume.[14]

Stockard *et al.* (1979) reported that individuals with the longest nasion-inion distances (NID) tended to have the longest latencies though the differences were not statistically significant.[4] Guthkelch *et al.* (1984) found that those with the shortest latency to P100 also tended to have the lowest OFC[15] and postulated that gender differences were depended on OFC, which is an easily measurable indicator of brain volume. Later, it was shown that P100 latency clearly depends on gender and OFC[3] and not on NID which was barely correlated with latency of P100.

Our findings are supportive of the assumptions of Allison T *et al.* (1984) that observed latency changes are a valid measure of the speed of axonal and synaptic conduction and the rise time of post synaptic potentials in sensory pathways and cortex. A decrease in latency with age (negative slope) reflects increasing conduction velocity or a change in neural processes associated with the maturation of the nervous system. An increase in the latency with age (positive slope) reflects a decrease in conduction velocity or a change in degenerative processes associated with aging, other things being equal though this may not be the case in children below 17 years where increase in latency probably reflect only increases in length of the conduction pathway. It must be noted that impedance of the body is mainly resistive (Plonsey, 1969) and changes with age in the conductive media surrounding the nervous system likely do not produce artifactual changes in latency.

Turner, (1948) and Yakovlev, 1962 hypothesized that in the area of morphological brain changes during development, those areas of the brain to develop later in childhood are the "silent' or the associational areas. The apparently delayed maturation at around 25-35 years may possibly be explained by incomplete myelination of the cortical neuropil till the third decade of life or later (Yakovlev and Lecours, 1967). The aging changes observed after 70years may be due to prominent ganglion cell loss after the seventh decade (Dolman *et al.* 1980).

We however found that the occipito-frontal circumference as well as the height exerts a negative correlation with the P100 amplitude in our study. In our previous work,[20] we studied the effect of age on PRVEP in the same population and observed that the most significant changes encountered were of P100 amplitude. Statistically, it was shown that 67% of this change could be contributed by age alone. In this present study which investigates changes in head circumference and height of the individual as a part of growth and aging and its association with the P100 parameters, we further found that a considerable 39% and 45% of the changes in P100 amplitude could be due to correlated with changes in OFC and height respectively. Previous investigators have found that amplitudes of some occipital VEP waves were maximum at about 8 years of age when neuronal density is highest in the human visual cortex. However, a strong tendency to reduce VEP amplitude has been documented in young children which rapidly decrease in strength with age and stabilises by 14years of age. This is consistent with our present observation of reduction in amplitude at around 15years of age in the study. Moreover, it is at ages 15-16 that adult level mental performance emerges. Thereafter the gradual reduction seen in older age group may reflect the degenerative changes in the CNS as already discussed.

To conclude, our study shows an obvious positive influence of OFC and height on P100 latency and duration but a negative effect on its amplitude. An increase in P100 latency of 2.3ms per cm increase in OFC in the first decade of life is hereby documented. It is also shown that of the 3 P100 parameters, the most significant changes with respect to OFC and height are on the P100 amplitude contributing about 39% and 45% each respectively.

CONFLICT OF INTEREST

The author declare no conflict of interest.

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Nil

ABBREVIATIONS USED

CM: Centimetre; **MS:** Milliseconds; **COD:** Co-efficient of determination.

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