



# OBJECTIVE ASSESSMENT OF PHYSIOLOGIC AGEING CHANGES BY PATTERN REVERSAL VISUAL EVOKED POTENTIALS

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## ABSTRACT

**Background:** Impairment of visual information processing is one of the profound physiologic effects of ageing. Visual evoked potentials can record electrophysiological alterations in the visual pathways that can occur due to ageing and the nature of the impact in the older adults can be evaluated. Rapidly increasing size of the older population further emphasizes the acquisition of the data for this proportion of population optimizing the clinical evaluation in this group.

**Methods:** Pattern-reversal visual evoked potentials (PRVEP) were recorded in 120 healthy subjects in the age-group of 20-80 years (60 males and 60 females). Mean P100 latencies and N75-P100 amplitudes were compared in different age-groups by one way ANOVA. Correlations of latencies and amplitudes with age were performed using Pearson correlation coefficient. Gender differences were studied by unpaired t test. P value < 0.05 was considered as statistically significant.

**Results:** Mean P100 latency increased with age (both eyes) (both the sexes) with statistical significance ( $p < 0.01$ ) while mean N75-P100 amplitude did not vary significantly ( $p > 0.05$ ). Males exhibited increased mean P100 latency as compared to females ( $p < 0.0001$ ) while increased mean N75-P100 amplitudes were recorded in females ( $P < 0.0001$ ).

**Conclusion:** Prolonged PRVEP P100 latency with age reflects electrophysiological alterations in visual pathways. Males demonstrate significant ageing changes earlier in life than females. Gender differences reveal increased P100 latency in males and increased N75-P100 amplitude in females in young as well as older adults. PRVEPs are useful objective measures to investigate the involvement of neural elements of visual system in the elderly individuals.

**Key Words:** Visual evoked potentials, Ageing, P100 latency, N 75-P100 amplitude

## INTRODUCTION

Physiologic ageing, a universal and natural phenomenon of gradual deterioration of physiologic functions with age has been of particular interest to the researchers studying the mechanism of ageing and age-related diseases. The effects of ageing are widespread in the body with brain as no exception. Slowing in visual processing speed is a common characteristic of ageing and has been a well-established phenomenon.<sup>1</sup> Visual abilities decline during normal (non-pathological) ageing. Many physiologic changes in the vision during ageing often represent same continuum as those due to disease. More objective criteria in defining normal ageing should be used by the investigators. Changes in the optical factors such as senile miosis and opacification of the ocular media cannot entirely account for the age-related declines in

the visual abilities and there might be involvement of retina or central visual pathways in the older subjects.

Visual evoked potentials (VEPs) can be a productive research methodology for studying such age-related visual declines owing to its objective and sensitive nature. They provide a measure of normal functioning of the visual system and also for assessing the changes during different stages of life.<sup>2</sup> Each sensory system has its own time of maturation and senescence. Visual evoked potentials can serve as a window into the central nature of neural processing and the pattern of age-related signal transmission delays in the visual system can be measured. Visual evoked potentials represent electrophysiologic responses to visual stimulation. Patterned visual stimuli are the preferred stimuli in various clinical settings. PVEP (pattern visual evoked potential) testing detects minor

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visual pathway abnormality with much greater sensitivity and accuracy than unpatterned stimuli.<sup>3</sup> Of the various VEP components described in normal subjects- the N75, P100, and N145, P100 is the most consistent and least variable peak and the most clinically useful measurements on the responses to monocular full-field stimulation are (1) the P100 latency and (2) amplitude (N75-P100) of the P100 component. Additional latency, duration, and amplitude are highly variable measures and generally add little to clinical interpretation.<sup>3</sup>

Determining the standards of normality for the visual evoked potentials is necessary, owing to the profound ageing effects on the visual evoked potential values during clinical interpretation of the tests. Assessment of various neurological diseases by the test becomes more reliable if the ageing effects have been taken into account. The clinical utility is required to be considered in the light of these physiologic effects. Moreover, it has been suggested that visual evoked potential (VEP) results are difficult to transfer even if stimulating and recording conditions are similar, due to the poorly understood effects of variation in stimulus conditions, as compared to the somatosensory and auditory evoked potential values.<sup>4</sup> Furthermore, the recent trends in the increase in the older population emphasizes the importance of acquisition of the data for this proportion of population for better clinical evaluations of this group of subjects. The maturation and senescence of different sensory system reflects different patterns. Glimore R (1995) who studied the process of senescence in sensory system found that the latencies of visual evoked potentials prolong by 2-4 ms/decade after age 40 years.<sup>5</sup> In a study by Allison T et al (1983), VEP P100 latency did not change between 20 and 59 years.<sup>4</sup> Also, there are strong evidences for the fact that the gender differences in young adults characteristically reveal increased P100 latency in males while increased N75-P100 amplitude in females.<sup>6,7</sup> The characteristic variations have also to be investigated and ascertained in the older groups. The present study hence, is an attempt to contribute to the researches and share our investigations and findings by performing an objective evaluation of the visual functions in the subjects with the older age-group by way of pattern reversal visual evoked potentials (PRVEPs).

## MATERIALS AND METHODS

The study was conducted on 120 healthy adults in the age group of 20-80 years (60 males and 60 females) with normal or corrected visual acuity. It was a cross-sectional analytical study. PRVEP was recorded in Electrophysiology laboratory in the department of Physiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. Approval from the institutional ethical committee was acquired to carry out the research work. A written informed

consent was obtained. Subjects underwent complete neuro-ophthalmological examination after taking a detailed clinical history.

Inclusion criteria for the study were adult healthy subjects in the age group of 20-80 years with normal or corrected visual acuity, normal fundus and visual field examinations while exclusion criteria were subjects with metabolic, endocrine or demyelinating pathologies; glaucoma, optic neuropathies, inherited or acquired neurological disorders, compressive lesions of anterior visual pathways, HIV infections and history of cerebro-vascular accidents.

VEP testing was optimized by instructing the subjects to come without the application of hair-oil or any hair chemical to the scalp and asked to wear their usual glasses or corrective lens. To prevent the effects of drowsiness on the VEP responses, they were advised to have an adequate sleep, the previous night. Before starting the procedure, they were explained about the test to ensure optimum cooperation. It was also ensured that no mydriatic or miotic drug 12 hours before the test was given to them. Application of electrodes was done after proper cleaning of the scalp skin.

VEP (visual evoked potential) was performed on Allengers Scorpio EMG, EP, NCS system in a specially equipped electro-diagnostic procedure room with dark and sound attenuated environment for the test. Subjects were seated comfortably about 95 cm away from a video-monitor with a 30 cm screen. The video-monitor presented a black and white checker-board pattern with a fixation spot in the center of the screen (mean luminance 50 candela/m<sup>2</sup> and contrast 70%). The checks reversed alternately at the rate of 2 cycles/sec. The visual angles subtended by the checks and the screen were 54.6 min and 19 degrees respectively. The signals were amplified (gain 20,000) and filtered with a system band pass filter of 2-100 Hz. Number of epochs were 100. Standard disc surface electrodes were placed and the electrode placement was according to the International 10/20 system with active electrode placed at Oz, reference electrode at Fz and ground electrode at Fpz.<sup>3</sup> Volunteers were instructed to focus on a small red square at the center of the screen of video-monitor. Monocular stimulation was performed. To validate the reproducibility of the waveform, two responses were recorded and superimposed. P100 latency difference within 2.5 ms and N75-P100 amplitude within 15% difference in replicated responses was accepted.<sup>3</sup> Parameters for the study were P100 latency and N75-P100 amplitude. The data was expressed as mean  $\pm$  S.D.

The subjects were classified into six different age-groups: Group I (20-30 years), Group II (31-40 years), Group III (41-50 years), Group IV (51-60 years), Group V (61-70 years) and Group VI (71-80 years). The effect of age in different age groups on PRVEP P100 latency and N75-P100

amplitude in both the eyes (total 120 subjects/240 eyes) was compared and analyzed using one way ANOVA and post hoc tests (Tukey multiple comparison tests). Correlations of age with PRVEP latency and N75-P100 amplitude were obtained using Pearson correlation coefficient. The effect of gender was obtained by unpaired t test. Statistical analysis was done by using SPSS (Statistical package for social science) version 20.0 statistical software. The analysis was done at 5% level of significance.

## RESULTS

Mean age of the study group (with 60 males and 60 females) was  $50.14 \pm 17.23$  years. Demographic and anthropometric data for males and females revealed no statistically significant differences in mean ages for males ( $50.5 \pm 17.1$  years) and females ( $49.83 \pm 17.5$  years), while height (males:  $170.4 \pm 6$  cms, females:  $158.5 \pm 7.01$  cms), weight (males:  $65.1 \pm 11.2$  kgs, females:  $55.8 \pm 8$  kgs) and head sizes (measured from nasion toinion) (males:  $34.29 \pm 0.8$  and females:  $32.63 \pm 1.1$  cms) were statistically significantly different ( $p < 0.05$ ).

Mean P100 latency in ms (milliseconds)  $\pm$ SD and N75-P100 amplitudes in  $\mu$ v (microvolts)  $\pm$ SD for both right and left eyes were compared among the subjects in six different age-groups (Group I: 20-30 years, group II: 31-40 years, group III: 41-50 years, group IV: 51-60 years, group V: 61-70 years and group VI: 71-80 years) (table 1, figure 1 and 2). Mean P100 latency increased with age (both eyes) with statistically significant differences ( $p < 0.01$ ) (one way ANOVA). The statistical significance was found between group I and group IV, group I and V and group I and group VI. Similarly, mean P100 latency in group II and group III varied significantly from VI (post hoc tests) (table 1). The differences in mean N75-P100 amplitude (both eyes), did not show statistical significance with age ( $P = 0.197$  and  $P = 0.15$  for right and left eyes respectively) (table 1). Correlation studies for age and mean P100 latencies revealed a statistically significant positive correlation ( $p < 0.0001$ ) for right as well as left eyes with age (table 2). Correlation studies for age and mean N75-P100 amplitudes revealed a negative correlation with age, but with no statistical significance ( $p > 0.05$ ) (table 2).

Age-related changes in males and females were analyzed separately. The increase in mean P100 latency with age was significant ( $p < 0.01$ ) in both males and females for both right and left eyes and for mean of both the eyes (mean of right eye and left eye were not statistically significant) (table 3) (figure 3). In males, within the group comparisons revealed significance between group I and V and that with VI (both the eyes) (post hoc test) (table 3). In females, within the group comparison revealed significance between group I and VI, within group II and VI and within group III and VI (post hoc test) (table 3). Hence, in males, it was group V (61-70

years) in which significant aging changes became evident first as compared to the young adults (20-30 years) while in females; the same could be noticed in 71-80 years of age-group. Similar aging changes in males and females for mean N75-P100 amplitude variations could not be found (table 4).

The influence of gender was assessed by comparing the mean P100 latencies and N75-P100 amplitudes in males and females (figure 4). The comparison between males and females was performed in different age-groups and among total males and females as well. Mean P100 latency in both the eyes were found to be greater in males as compared to females with statistically significant difference ( $p < 0.05$ ) in majority of the age-groups (unpaired t test) (table 3).  $p < 0.0001$ , when mean P100 latency was compared between total males ( $n = 60$ ) and total females ( $n = 60$ ) (table 3). On the other hand, mean N75-P100 amplitudes exhibited decreased values in males as compared to females in all the age-groups ( $p < 0.05$ ) and in total subjects as well ( $P < 0.0001$ ) (unpaired t test) (table 4).

## DISCUSSION

Rapidly increasing size of the older adult population worldwide, accentuates the need to extend and elaborate the researches on aging changes in the older adults. Visual declines are among the most common changes due to senescence. These age-related declines cannot solely be explained on the basis of the changes in various optical characteristics in the older subjects, but neural elements of the visual system and visual pathway affection can be important factors in the aged. Visual evoked potentials are objective measures investigating the functional integrity of the visual system and can provide important information regarding the physiologic and pathologic changes in the visual system. The study hence, included healthy subjects in a wider age-group including the elderly subjects in an attempt to find the electrophysiologic pattern of variations with ageing by pattern reversal visual evoked potentials.

The study reveals age-related changes in PRVEP mean P100 latency with statistical significance ( $p < 0.0001$ ) for both right and left eyes. The increase in mean P100 latency with age was statistically significant after the fifth decade of life as compared to the young adults (20-30 years) (table 1) (figure 1). The findings comply with previous similar studies.<sup>8-13</sup> In the present study, P100 latency increased at the rate of 0.82 to 1.8 ms per decade after the fifth decade. Stockard JJ et al (1979) reported an increase of 2.5 ms per decade after fifth decade of life while Glimore R et al (1995) reported a prolongation of 2-4 ms/decade after the age of 40 years.<sup>5,8</sup> According to Kuba M et al (2008), pattern-reversal VEP latencies increased only 0.25 ms/year in healthy subjects with 19-83 years of age.<sup>12</sup> On the other hand, Allison T

et al (1983) demonstrated no significant change in VEP P100 latency between 20 and 59 years.<sup>4</sup>

Mean N75-P100 amplitude variations with age did not show statistical significance ( $P>0.05$ ) (table 1). The findings conform to the study by Mitchell KW et al (1987) who studied the subjects in 40-80 years of age-group and could not find age changes in VEP amplitudes.<sup>9</sup> Similarly, Tobimastu S et al (1993) studied the subjects (19-84 years) and reported no aging effects in P100 amplitudes.<sup>10</sup> In a study by Wright CE et al (1985), the amplitudes were constant from the twenties onwards, showing no further consistent age changes.<sup>13</sup>

Correlation studies further supported the findings as mean P100 latencies showed statistically significant positive correlation with age ( $P<0.0001$ ) and a negative correlation obtained for N75-P100 amplitude with age did not reveal a statistical significance (table 2). Aging effects in males as well as females studied separately also revealed significant increase in P100 latency in both the sexes ( $P<0.01$ ). However, males appeared to age, a decade earlier (61-70 years of age) as compared to females (71-80 years) (table 3). Similar gender differences due to aging were also reported by Allison T et al (1984) with greater aging changes in males.<sup>11</sup>

The age-related delay in the central conduction time obtained in the form of P100 latency prolongation with aging in the present study can be attributed to visual declines due to aging.<sup>2,11,14</sup> Neuronal loss, changes in cell membrane composition and senile plaques present in older subjects have been speculated. Reduction in retinal illuminance due to the decrease in pupillary diameter with age has also been suggested.<sup>13,15</sup> Few other age-related changes documented in the neural elements of the aging visual system such as age-related loss of rods and cones, reduction in the number of cells in the primary visual cortex to about 25 % at the age of 60 and atrophy of the retinal ganglion cells can also be involved in the electrophysiologic alteration in the visual pathways.<sup>16-18</sup>

In the present study, gender comparison among the subjects reveals that the males have increased latency as compared to females in majority of the age-groups (table 3). The finding is in agreement with many studies in the past.<sup>14,19,20</sup> The difference in the head sizes of males and females has been accounted for the differences in the P100 latency.<sup>6,7,20</sup> N75-P100 amplitude, however exhibited increase in females as compared to males in the present study when compared between total males and females and also when compared in different age-groups (table 4). This characteristic increase in amplitude in females is a relatively more consistent finding as compared to latency variation in gender and is supported by a number of studies in the past.<sup>7,9,14,21</sup> Hormonal differences have been suggested to play role in the amplitude increase in females as compared to males.<sup>22</sup> Anthropometric differences in males and females have little role to play in

the same. Genetically determined sex differences in neuro-endocrinological systems and factors specific to CNS (central nervous system) processing of visual stimuli rather than global CNS anatomic or physiological factors have been suggested as the possible explanation for the amplitude change in the gender.<sup>23</sup>

## CONCLUSION

Aging documents increase in PRVEP P100 latency with significant influence after the fifth decade of life. Effects on P100 latency are stronger in comparison with N75-P100 amplitude changes. Males demonstrate significant alterations in P100 latency earlier in life than females. The results of gender comparison in the form of increased P100 latency in males and increased N75-P100 amplitude in females, which are relatively consistent findings in young adults, are also the characteristic features in the elderly subjects. Pattern reversal visual evoked potentials are useful objective investigations to acquire evidences for electrophysiologic variations in the elderly individuals.

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**Table 1: Mean P100 latency and mean N75-P100 amplitude in different age-groups**

Age group (years)	Mean P100 latency (ms ± SD)		Mean N75-P100 amplitude (µv± SD)	
	R	L	R	L
20-30	103.09±3.18	103.33±2.84	5.07±1.59	5.23±1.67
31-40	104.62±2.76	105±3.12	5.43±2.2	5.6±2.05
41-50	105.92±4.63	105.85±4.68	5.27±1.78	5.18±1.93
51-60	107.09±3.55	107±3.78	4.71±2.54	4.79±2.28
61-70	108.38±4.92	107.82±5.79	4.59±1.62	4.49±1.57
71-80	109.52±3.07	109.62±2.68	4.065±0.87	4.21±0.84

M- Males, F- Females, R-Right, L-Left.

*P*<0.0001 for the differences in mean P100 latency (both right and left eyes) in different age-groups (one way ANOVA). Group I revealed statistically significant differences from group IV, V and VI while group II showed the same for group VI and group III with group VI (post hoc test).

*P*>0.05 (*P*=0.197) for right and (*P*=0.15) left eye for the decrease in mean N75-P100 amplitudes with increasing age.

**Table 2: Correlation coefficient (r) for age and mean P100 latencies(ms ± SD) and N75-P100 amplitudes (µv± SD) (n=120)**

	Mean P100 latency		Mean N75-P100 amplitude	
	R	L	R	L
<b>r</b>	0.564	0.561	-0.14	-0.15
<b>P value</b>	<0.0001	<0.0001	0.13 NS	0.1 NS

n=number of subjects, R-Right, L-Left, NS-not significant

**Table 3: Mean P 100 latencies (ms ± SD)in males and females**

Age- group (years)	No.of subjects		Males		Females	
	M	F	R	L	R	L
20-30	10	10	104.1±3.07	104.65±2.31	102.08±3.1	102±2.79
30-40	10	10	105.85±3.14	106.26±3.5	103.54±1.72	103.75±2.18
41-50*	10	10	108.12±5.1	107.87±5.09	103.72±2.89	103.67±3.41
51-60	10	10	108.31±3.7	108.33±4.24	105.88±3.09	105.67±2.86
61-70*	10	10	110.85±4.87	110.3±5.57	105.9±3.7	105.24±5.12
71-80*	10	10	111±2.22	111.05±2.02	108.03±3.18	108.19±2.55
<b>Total**</b>	60	60	108.04±4.44	108.08±4.43	104.86±3.49	104.75±3.71

M- Males, F- Females, R-Right, L-Left.

\* $P < 0.05$  for the comparison of mean P100 latency between males and females(both eyes) (unpaired t test).

\*\*  $P < 0.0001$  for the comparison of mean P100 latency between males and females (both eyes) (unpaired t test).

$P < 0.01$  for differences in mean P100 latency in males with age (both the eyes). Within the group comparison revealed significance between group I and V and group I and VI, (post hoc test).

$P < 0.01$  for differences in mean P100 latency in females with age (both the eyes). Within the group comparison revealed significance between group I and VI, within group II and VI and within group III and VI (post hoc test).

**Table 4: Mean N75-P100 amplitudes (µv ± SD) in males and females**

Age- group (years)	No. of subjects		Males		Females	
	M	F	R	L	R	L
20-30*	10	10	4.34±1.56	4.5±1.35	5.8±1.32	5.95±1.7
30-40*	10	10	4.28±1.69	4.52±1.45	6.57±2.13	6.68±2.04
41-50*	10	10	4.13±1.17	4.14±1.08	6.6±1.15	6.52±1.52
51-60*	10	10	3.01±1.04	3.26±1.06	6.4±2.47	6.32±2.16
61-70*	10	10	3.77±1.24	3.72±1.34	5.4±1.59	5.25±1.46
71-80*	10	10	3.58±0.5	3.53±0.42	4.55±0.89	4.89±0.53
<b>Total**</b>	60	60	3.85±1.29	3.95±1.22	5.89±1.78	5.94±1.72

M- Males, F- Females, R-Right, L-Left.

\* $P < 0.05$  for the comparison of mean N75-P100 amplitudes between males and females (both eyes) (unpaired t test)

\*\* $P < 0.0001$  for the comparison of mean N75-P100 amplitudes between males and females (both eyes) (unpaired t test).

$P > 0.05$  for differences in mean N75-P100 amplitudes in males with age ( $P=0.17$  and  $P=0.095$ ) for right and left eyes respectively.

$P > 0.05$  for differences in mean N75-P100 amplitudes in females with age ( $P=0.06$  and  $P=0.11$ ) for right and left eyes respectively.

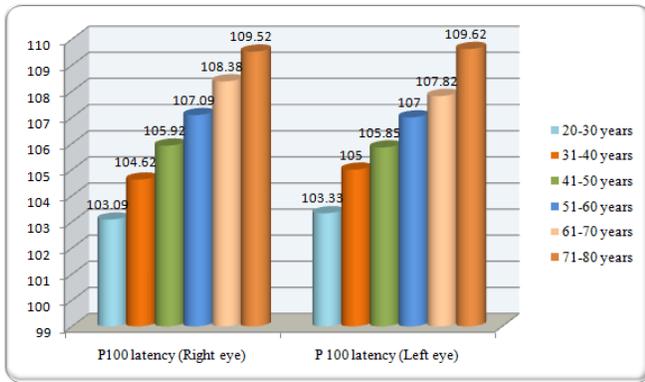


Figure 1: Mean P100 latency (ms) for right and left eyes in different age-groups.



Figure 3: Mean P100 latency (mean of right and left eye) (ms±SD) in relation with age in males and females.

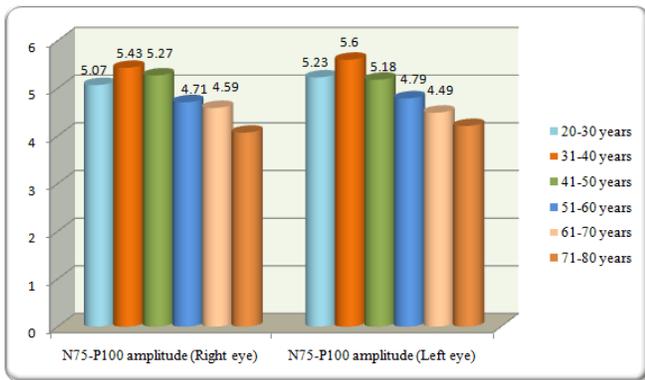


Figure 2: Mean N75-P100 amplitude (µV) for right and left eyes in different age-groups.

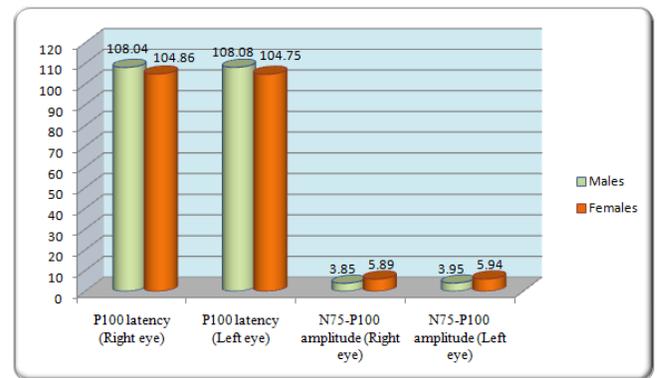


Figure 4: Mean P100 latency (ms) and mean N75-P100 amplitude(µV) in males (n=60) and females (n=60).