Original Article

Effect of age on pattern-reversal visual evoked potentials in Indian population

Jayshree Phurailatpam, Arun Kumar Sharma[1], Ramji Singh[2]

Departments of Physiology and [1]Radiotherapy, Regional Institute of Medical Sciences, Imphal, Manipur, [2]Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra, India

Abstract

Background and Aim: Functional declines of the visual system are probably the most obvious aging changes in humans. Normal non-pathologic aging causes senile miosis and media opacities which cannot entirely explain the age-related declines. Changes in the retina and its neuro-circuitary contribute to the visual decline, which can be evaluated by evoked potentials. We investigated the effects of age on various components of transient pattern-reversal visual evoked potentials (t-PRVEPs) and whether there is presence of any differential aging on t-PRVEPs in Indian population.

Methods: Monocular t-PRVEPs of 292 eyes from 146 normal subjects living in Wardha, Maharashtra and whose age ranges from 1-75 years, were recorded on an evoked potential recorder. Differences in latencies and amplitude were analyzed using one way analysis of variance (ANOVA) and polynomial regressions.

Results: Age affects the PRVEP components differently with the most significant changes encountered in the P100 amplitude. The present study demonstrated that statistically, at least 67% of these changes are contributed by age alone. Comparisons with studies abroad showed similar changes but suggest the existence of an aging difference in Indians by at least 5 years. Indian males and females also showed aging differences with the latter aging earlier by at least 6-7 years.

Conclusion: We therefore conclude that Indians seem to age faster compared to other populations and further research on possible causes for this difference in aging is warranted.

Key words: Aging, differential aging, Indians, light exposure, pattern-reversal visual evoked potentials

Received: 28th April, 2014; *Revised:* 10th June, 2014; *Accepted:* 18th June, 2014

INTRODUCTION

Each sensory system has its own time of maturation and aging.[1] One of the first obvious signs of aging is the failure of an individual to read the fine prints, such as smaller font on the label of a medicine bottle. This visual decline cannot be wholly explained by senile miosis and media opacities encountered during aging. It could probably be due to the changes in neuronal pathway concerned with vision.

Access this article online	
Quick Response Code:	Website: www.ijcep.org
	DOI: 10.4103/2348-8093.137416

Evoked potentials provide a measure of the functional changes of the sensory systems during different stages of life.[1] For the visual cells starting from the retina upto the visual cortex and beyond, the activities can be partly recorded by electroretinographs (ERGs) and partly by the visual evoked potentials (VEPs); ERGs measure the retinal activities and VEPs records the activity of the neuronal circuitary beyond it and the cortical responses.[2] Comparisons between pattern evoked ERG and cortical evoked potentials in the same individuals suggested that some neural change occurs between the retina and the striate cortex, though the exact location and nature of change was not established.[2]

Among the VEPs, the most sensitive measure of signal transduction is considered to be the transient pattern reversal VEPs (t-PRVEPs) showing 3 major waveforms-N70, P100, and N155.[3] However, amongst known physiological and physical parameters[3-6] that

Address for correspondence: Dr. Jayshree Phurailatpam, Department of Physiology, Regional Institute of Medical Sciences, Imphal - 795 004, Manipur, India. E-mail: drjayshreeph@gmail.com

are found to influence the t-PRVEPs, age and sex of the individual are considered to have a major effect. Therefore, the primary objective of the present study was to evaluate the effect of age and its individual contribution to the t-PRVEPs waveforms. Also, we have studied whether gender plays a role in this differential aging.

MATERIALS AND METHODS

The study was conducted in the Neurophysiology Lab (June 2005-Feb 2008), 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 starting the study.

Study population

Students and staffs of MGIMS, Wardha, volunteers and screened patients within the age range of 1-75 years attending Kasturba Hospital, MGIMS, Sevagram, Wardha. All subjects were assumped to be a representative sample of the neurologically normal population but no attempt was made to select an unusually healthy sample.

This cross-sectional study of visually normal 292 subjects (males = 216; females = 76) t-PRVEP recordings was carried out, consisting of people in and around Wardha, a place which is considered as one of those receiving the highest annual global solar radiation[7,8] by NASA (National Aeronautics and Space Administration). Each subject was given a thorough eye examination as a preliminary measure to exclude any eye pathology.

Exclusion criteria

Individuals with ptosis, strabismus, amblyopia, glaucoma, papilloedema within one disc margin of the macula, lens or corneal opacities, hereditary disorders/retinitis pigmentosa, albinism, past history of serious visual problems (traumatic optic nerve atrophy, acute attacks of retro-bulbar neuritis, multiple sclerosis), recent eye medications with mydriatics or cycloplegics in the past 12 hrs prior to test, visual acuity less than 6/6 (uncorrected with glasses) were excluded from the study. No subject had a history of relevant neurological, diabetic, heart disease, or of drug abuse. 'Normal' was more difficult to define in the older age-group as slight ocular opacities may inevitably be present, but all had a visual acuity better than 6/6.

Aged individuals more than 75 years were also excluded as it was found that prevalence of impaired vision increased markedly above this age.[9]

Recording techniques

After a detailed briefing about the procedure, the subject was seated comfortably in an air-conditioned, sound-proof, quiet, and dark room at a distance of 1 m from the monitor screen. In case of infants and small children, they are seated in the mother's lap and the same distance of 1 m was maintained between the eye and the monitor screen. Each subject was instructed to avoid blinking, any mental activity such as counting or thinking as far as possible, as it has been known to produce muscle artifacts during the recording, or decrease the latencies and increases the amplitude of the VEP waveforms. Subjects wearing corrective glasses, if any were allowed to keep them on during the test.

Then, a monocular recording separately for the left and the right eyes was done on an evoked potential recorder (RMS-EMG.EP Mark-II). The montage used was Oz-Fz and grounded at the vertex (Vx). The stimulus was a full field black and white (B and W) checker-board pattern (check size 8 × 8) with a central red fixation point, reversed at a rate of 1.71 Hz with a sweep duration of 300 ms. The filters were kept at 2 Hz–100 Hz and sensitivity at 2 μV. 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

Differences in latencies and amplitude were analysed using one way analysis of variance (ANOVA) and polynomial regressions.

RESULTS

As shown in Figure 1a, the most consistent of the three waveforms is P100 with very little variations in its latency as age increases and N155 latency is the most variable of the three. However, wider variations in P100 duration was observed [Figure 1b].

Figure 2a depicts the ageing changes of P100 amplitude with significant changes occurring in individuals at particular ages. The initial change is a drastic reduction of amplitude seen in between 10-15 years of age ($P < 0.01$) which then stabilizes remaining almost constant up to 45 years. Thereafter, it shows a gradual decline to almost half of its adult value at the age of 75.

The degree of goodness of statistical fit is normally evaluated by the co-efficient of determination, R^2. The best fit mathematical model of this observed data, as depicted in the scattered diagram [Figure 2b] is a polynomial equation of second degree with R^2 value of 0.67. This implies the extent of correlation of age with

the P100 amplitude and shows that among the various confounding factors; at least 67% of the changes in P100 amplitude are accounted for by age alone.

The values observed in the present study [Table 1] were comparable to those reported by other workers. Slight variations may be attributed to the difference in sample sizes and age-groups studied.

Gender-wise comparison [Figure 3] showed insignificant differences in P100 latency all throughout, though the onset of latency prolongation which marks the declining

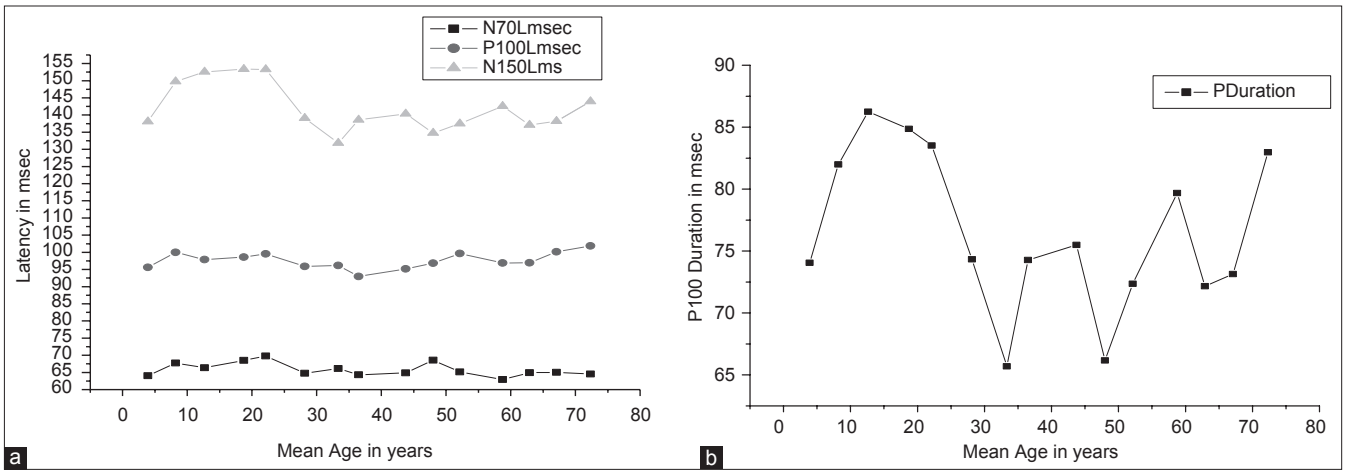

Figure 1: (a) Effect of age on PRVEP parameters: N70, P100, and N155 latencies and (b) P100 duration

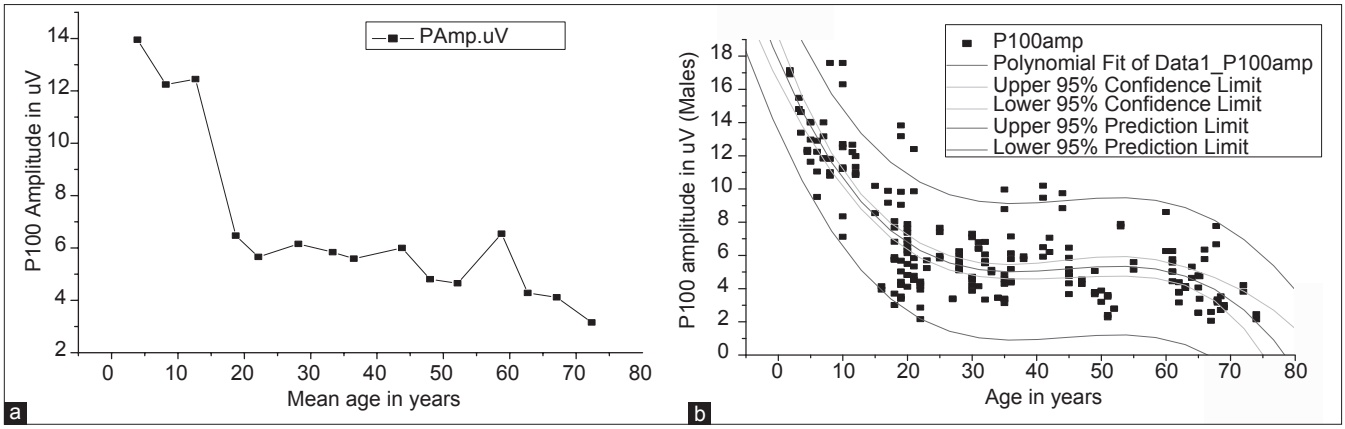

Figure 2: (a) Effect of age on P100 amplitude, (b) Correlation of age with P100 amplitude

Table 1: Comparative values of PRVEP parameters (present study *vs.* other's report)

Author/year	Recording montage	No. of subjects	Age (years)	PRVEP Observations
Celesia *et al.*, 1987	Oz- Fz	112	20-75	N70 latency=75.5±4.1 ms P100 latency=98.1±4.4 ms; Amp=9.9±5.9 uV
Guthkelch *et al.*, 1987	Oz -Fz	16	18-30	P100latency=100.04±3.9 ms
Misra and Kalita, 1999	Oz-Fpz	58 (M-38, F-20)	15-58	P100 latency=96.9±3.6 ms; Amp=12.4±1.2 uV, P100duration=55.9±7.7 ms
Shih *et al.*, 1988	Oz-M1 and M2	30	Adults	P100latency=107ms (M);106 ms (F) Amp.=6.4±2.3 uV
O.P.Tandon, 1989	O1-A1 and O2-A2	27 (M-20, F-7)	17-35	P100 latency (ms) = 95.3±6.8 (M); 91.07±7.4 (F); Amp.= 6.53±2.44 uV N1 latency (ms) = 75.72±7.86 (M); 71.35±6.3 (F) N2 latency (ms) = 124.75±10.5 (M) 117±10.04 (F)
Present study, 2008	Oz-Fz	146 (M-108, F-38)	1-75	N70 latency (ms) = 65.77±2.04; 99% TL=71.89 ms P100 latency (ms) = 97.6±2.3; 99% TL=104.44 ms Amp=6.79±3.3 uV; 99% TL=16.75 uV Duration (ms) = 76.38±6.3; 99% TL=95.2 ms N155 latency (ms) = 142.2±7.1; 99% TL=163.5 ms

ms: Milliseconds, μV: Microvolts, Amp: Amplitude, M: Male, F: Female, TL: Tolerance limits

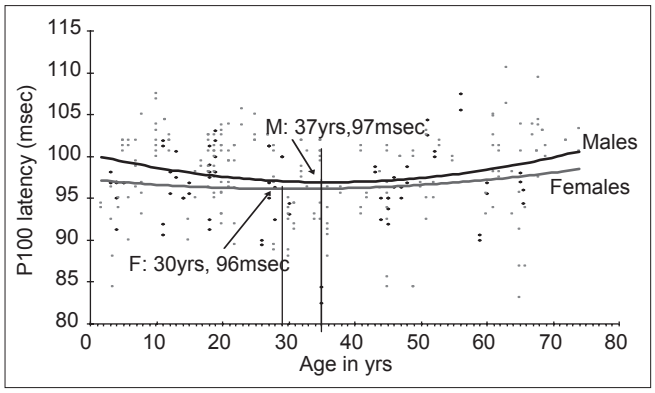

Figure 3: Gender-wise effect of age on P100 latency

conductivity of the visual system appears earlier in females by 7-8 years beginning at around 30 years as compared to 37-38 years in males. These aging trends of Indian males and females are interestingly different as the onset of aging are at almost similar P100 latencies (males: 97 ms, females: 96 ms).

DISCUSSION

Our study demonstrates that the early changes and amplitude reduction in the pubertal age group of 10-15 years, as depicted in Figures 1 and 2, could be due to the developmental and maturation phases of the visual system. The stabilization of amplitude from around 20 years to 40-45 years may suggest the attainment of the adult level and the gradual decline thereafter may indicate a slow decline due to the effects of aging. A similar trend is seen in studies reported by other workers.[3-6,10-12] However, slight variations in latencies and amplitude may be attributed to the difference in sample sizes and age-groups studied.

As shown in Figure 3, we also observed that the studied Indian population presents certain aging differences in between sexes and also as compared to available data obtained from other countries.[3] Both Indian males and females showed slightly longer P100 latencies (97 ms and 96 ms respectively) at the onset of aging and females seem to precede males by at least 6-7 years. However, in contrast, it was reported that western males appear to reflect greater aging changes than females[3] though the mechanism for the difference was not explained.

The aging differences demonstrated in the present study could be due to anthropometric, environmental, dietary, and genetic differences. Males generally are considered to have a larger head size than females, hence shorter P100 latencies are expected in females when compared to males.[6] The aging changes in the P100 latencies and amplitude in both sexes may also be partly explained by age-related visual declines.[1,3-5] Changes in ocular media lead to reductions in illuminance of the visual stimulus and neurons showing senile changes with age, but an important determinant of retinal aging is the cumulative exposure to high energy photons from solar radiation[13] which may accelerate the process of aging in tropical countries like India.

A long-term cumulative exposure to high energy photons from solar radiation in the study region as reported by NASA,[7,8] are reported to cause apoptotic damage or death of photoreceptors and neurons in retinal diseases due to the hyper-excitation toxicity of the visual cells.[14-17] Besides this environmental light stress, dietary stress in the forms of deficiency, especially of Vitamin A[18] appears to activate photo-transduction at a higher rate and in a continuous manner which may result in prolonged lower concentration of the calcium ions causing death of rods and neurons.

A possible role of difference in individual genetic constitution may also be considered. Studies have reported the possible role of certain genes such as neuronal *Rac-1*[19] and *rdy*[20] to increase the photo-oxidative stress and damage, whereas arrestins[21] and 1,3-dimethyl thiourea (DMTU)[22] reduces the photo-oxidative stress, in experimental animals. Therefore, a high radiation exposure, a still rampant Vitamin A and/or protein deficiency in India or it could be genetic constitution of our Indian population that may contribute to the aging differences in the visual system in Indians when compared to others.

Limitations of the study

Due to the less sample size, especially of females and unavailability of resources, the methods to study the effect of environmental, dietary, and genetic aspects of the population has not been studied.

CONCLUSION

Our study concludes that Indians show similar aging trends in the visual system as indicated by the changes in PRVEP parameters, as in other populations but suggests the existence of an aging difference by at least 5 years earlier. Therefore, future research in this area with a larger sample size studying the environmental, dietary and genetic aspects are warranted to establish the possible cause of difference in the visual aging pattern and may reveal more information on how to prevent or delay this aging process of the visual system.

REFERENCES

1. Onofrj M, Thomas A, Iacono D, D'Andreamatteo G, Paci C. Age-related changes of evoked potentials. Clin Neurophysiol 2001;31:83-103.

2. Spear PD. Neural bases of visual deficits during aging. Vision Res 1993;33:2589-609.
3. Emmerson-Hanover R, Shearer DE, Creel DJ, Dustman RE. Pattern reversal evoked potentials: Gender differences and age-related changes in amplitude and latency. Electroencephalogr Clin Neurophysiol 1994;92:93-101.
4. Allison T, Hume AL, Wood CC, Goff WR. Developmental and aging changes in somatosensory, auditory and visual evoked potentials. Electroencephalogr Clin Neurophysiol 1984;58:14-24.
5. Celesia GG, Kaufman D, Cone S. Effects of age and sex on pattern electrorentinograms and visual evoked potentials. Electroencephalogr Clin Neurophysiol 1987;68:161-71.
6. Guthkelch AN, Bursick D, Sclabassi RJ. The relationship of the latency of the visual P100 wave to gender and head size. Electroencephalogr Clin Neurophysiol 1987;68:219-22.
7. NASA surface Meteorology and solar energy. Available from: http://eosweb.larc.nasa.gov/sse/RETScreen/. [Last updated on 2008 Mar 26].
8. Solar irradiation data in India. Available from: www.eai.in/club/users/krupali/blogs/627. [Last accessed on 2012 Jul 7].
9. Congdon N, O'Colmain B, Klaver CC, Klein R, Munoz B, Freidman DS, *et al*. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477-85.
10. Tandon OP, Sharma KN. Visual evoked potential in young adults: A normative study. Indian J Physiol Pharmacol 1989;33:247-9.
11. Misra UK, Kalita J, editors. Visual evoked potentials. In: Clinical Neurophysiology. 1st ed. Churchill Livingstone, New Delhi; 1999. p. 255.
12. Shih PY, Aminoff MJ, Goodin DS, Mantle MM. Effect of reference point on VEPs: Clinical relevance. Electroencephalogr Clin Neurophysiol 1988;71:319-22.
13. Werner JS, Peterzell DH, Scheetz AJ. Light, vision, and aging. Vis Sci 1990;67:214-29.
14. Organisciak DT, Darrow RM, Barsalou L, Darrow RA, Kutty RK, Kutty G, *et al*. Light history and age-related changes in retinal light damage. Invest Ophthalmol Vis Sci 1998;39:1107-16.
15. Hajkova D, Imanishi Y, Palamalai V, Rao KC, Yaun C, Sheng Q, *et al*. Proteomic changes in the photoreceptor outer segment upon intense light exposure. J Proteome Res 2010;9:1173.
16. Van Norren D, Gorgels TG. The action spectrum of photochemical damage to the retina: A review of monochromatic threshold data. Photochem Photobiol 2011;87:747-53.
17. Organisciak DT, Vaughan DK. Retinal light damage: Mechanisms and protection. Prog Retin Eye Res 2010;29:113-34.
18. Fain GL. Why photoreceptors die (and why they don't). Oessays 2006;28:344-54.
19. Haruta M, Bush RA, Kjellstrom S, Vijyaysarathy C, Zeng Y, Le YZ, *et al*. Depleting Rac-1 in mouse rod photoreceptors protects them from photo-oxidative stress without affecting their structure or function. Proc Natl Acad Sci U S A 2009;106:9397-402.
20. Organisciak DT, Li M, Darrow RM, Farber DB. Photoreceptor cell damage by light in young Royal College of Surgeons rats. Curr Eye Res 1999;19:188-96.
21. Chen J, Simon MI, Matthes MT, Yasumura D, LaVail MM. Increased suspectibility to light damage in an arrestin knockout mouse model of Oguchi disease (stationary night blindness). Invest Ophthalmol Vis Sci 1999;40:2978-82.
22. Darrow RA, Darrow RM, Organisciak DT. Biochemical characterization of cell specific enzymes in light-exposed rat retinas: Oxidative loss of all-trans retinol dehydrogenase activity. Curr Eye Res 1997;16:144-51.

How to cite this article: Phurailatpam J, Sharma AK, Singh R. Effect of age on pattern-reversal visual evoked potentials in Indian population. Int J Clin Exp Physiol 2014;1:152-6.

Source of Support: Nil, **Conflict of Interest:** Nil.