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Research Article

EFFECT OF EXPERIMENTALLY INDUCED ANISOMETROPIA ON BINOCULAR VISION STUDIED BY PATTERN REVERSAL VISUAL EVOKED POTENTIALS

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ABSTRACT
Optimal binocular vision is associated with depth perception and enhancement of certain other aspects of vision. Binocular interaction can, however, be compromised when one of the monocular inputs is altered in conditions like anisometropia. We aimed to evaluate the effects of interocular refractive differences, electrophysiologically, by recording transient pattern reversal visual evoked potentials in normal and induced anisometropic conditions. Transient PRVEPs (pattern reversal visual evoked potentials) were recorded in 50 adults in the age group of 18-25 years. N75-P100 amplitude and P100 latency were studied in normal monocular, normal binocular conditions and after inducing simple myopic anisometropia (0.5 to 5 dioptres). Mean binocular amplitudes were compared in normal and anisometropic states using paired t-test. Binocular summation ratio was calculated for normal refractive states and anisometropia. Mean binocular N75-P100 amplitude decreased significantly ($p<0.0001$) in anisometropia compared to that in normal refraction, while P100 latency change was not statistically significant. Anisometropia of more than 2 dioptres reduced the binocular amplitude highly significantly ($p<0.0001$). Binocular summation ratio was 1.18±0.2 in normal refraction, while in anisometropic binocular conditions, it was 0.94±0.1. Anisometropia interferes with normal binocular interaction. Transient PRVEPs seem to be reliable electrophysiological measure to assess binocular interactions objectively. The study also emphasizes the importance of using a binocular approach in the treatment of anisometropic amblyopia.

Keywords: *Anisometropia, Binocular Vision, Visual Evoked Potential*

INTRODUCTION
Anisometropia is defined as a relative difference in the refractive states of the two eyes. It is well known to be associated with amblyopia (a disorder of visual function characterised by reduction of best-corrected visual acuity that cannot be directly attributed to structural abnormality of the eye). A considerable volume of literature supports that anisometropia is a significant risk factor for the development of amblyopia. About 6 to 38% of all cases of amblyopia are reported to be caused by anisometropia without strabismus (Phelps and Muir, 1977). Other such report suggests the cause of the amblyopia as strabismus in 38%, anisometropia in 37%, and both strabismus and anisometropia in 24% (Paediatric Eye Disease Investigator Group, 2002).

It has been argued that, amblyopia is intrinsically, a binocular problem and not a monocular one. Improvement in binocular function does not always occur, despite monocular vision improvement (Scheiman *et al.*, 2005). Accordingly, binocular problem involving suppression must be addressed first, if good binocular outcome is to be achieved. These facts strengthen the value of evaluating binocular functions in anisometropia. Majority of the studies have used the stereopsis tests to evaluate the effect of anisometropia on binocularity (Tomaç and Birdal, 2001; Weakley, 1999; Rutstein and Corliss, 1999). In other studies, anisometropia has been experimentally induced and its effect on binocular function has been demonstrated, using stereopsis tests (Oguz and Oguz, 2000; Dadeya *et al.*, 2001; Brooks *et al.*, 1996; Heo and Yoo, 1999). Evaluation of the effect of experimentally induced anisometropia on binocular functions by pattern reversal visual evoked potential tests have been documented in fewer studies, so far (Krumina and Caune, 2009; Lefebvre and Saint-Amour, 2008). Moreover, the electrophysiological approach has been successful using non-standard steady-state visual evoked potentials (VEPs) and

evidence from transient-VEPs are weaker (Bagolini *et al.,* 1994). The present study, therefore, was designed to assess the binocularity in the visual cortex in adult subjects with anisometropia, induced experimentally, using transient (PRVEPs) pattern reversal visual evoked potentials. The study, in this manner, also attempts to evaluate the potential effects of uncorrected anisometropia on binocular development in childhood. Binocular interaction has well been reported by pattern reversal visual evoked potentials (PRVEPs) in terms of amplitude as well as latency changes. Binocular summation is evident in the visual evoked responses, which refers to the larger amplitude of the P100 wave, under normal binocular viewing conditions. Hence, the study aimed to detect the extent of effect on the binocular vision objectively, in subjects with experimentally induced anisometropia of different degrees.

MATERIALS AND METHODS

We studied 50 adults (22 males and 28 females) in the age group of 18-25 years with refractive errors ranging from -0.5 to -5 dioptres). Approval from the institutional ethical committee was taken to carry out the research work. All the subjects underwent stereopsis testing with synaptophore. None had a history of strabismus or amblyopia. A complete neuro-ophthalmologic examination of each subject was done after obtaining a written informed consent and a detailed clinical history.

Inclusion Criteria

Adult subjects with refractive errors (not < -0.5 D), with normal stereopsis, normal fundus and visual field examinations.

Exclusion Criteria

Subjects with metabolic , endocrine or demyelinating pathologies; glaucoma, strabismus, amblyopia, optic neuropathies , inherited or acquired neurological disorders, compressive lesions of anterior visual pathways, HIV infections, history of drug- abuse and history of cerebro-vascular accidents.

Pre-Test Evaluation

For the best results of VEP testing, subjects were advised to come without applying oil or any hair chemical to the scalp, asked to put on their usual glasses for monocular VEP. Subjects were instructed to have an adequate sleep the previous night to prevent the effect of drowsiness on the responses. Subjects were explained about the test to ensure full cooperation and to avoid subject's inattention and defocusing during the test procedure. Subjects were also instructed to avoid any mydriatic or miotic drug 12 hours before the test. Preparation of scalp skin was done before electrode application.

VEP Recording

VEP was recorded with Allengers-Scorpio EMG EP NCS system in a specially equipped electro-diagnostic procedure room made dark and sound attenuated for the test. Subjects were seated comfortably about 85 cm away from a video-monitor with a 23×25 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^2 and contrast 70%). The checks/pattern elements reversed alternately at the rate of 2 Hz. The visual angle subtended by the checks was 1° (58 min×63 min) and the screen subtended a visual angle of 16 degrees (15.5°×16.85°). The signals were amplified (gain 20,000), filtered with a system band pass filter of 2-100 Hz and 100 responses were averaged. Standard disc surface electrodes were placed according to the International 10/20 system of electrode placement with active electrode at Oz, reference electrode at Fz and ground electrode at Fpz (Odom *et al.,* 2010). Volunteers were instructed to fix the gaze on a small red square at the center of the screen of video-monitor. Subject's fixation at the screen center was continuously monitored during the recording. Monocular stimulation was done by testing each eye separately with an eye-patch covering the other eye. Normal binocular stimulation was done, with both the eyes, in corrected refractive state and fixating at the target simultaneously. Binocular VEP, after experimentally induced simple myopic anisometropia was recorded by putting spectacles (with corrective lenses) on the right eye while the left eye was in uncorrected refractive state (0.5 to 5 dioptres) and both fixating at the target simultaneously. To verify the reproducibility of the waveform, two responses were recorded and superimposed.

The latency of major positive peak P100 (most consistent and least variable peak) and N75-P100 amplitude (peak-peak) were the parameters for study. Mean P100 latency and N75-P100 amplitudes were calculated in normal monocular, normal binocular conditions as well as binocular conditions after induced anisometropia. Binocular summation ratio was calculated as: 2 × [Amplitude of P100 under binocular conditions/Amplitude of Right eye + Amplitude of Left eye] (Leguire *et al.,* 1987). Based on the degree of induced simple myopic anisometropia, three groups were made. Group 1 (fifteen subjects) had anisometropia in the range of 0.5 to 2 dioptres, group 2 (twenty subjects), with anisometropia of >2 but <3.5 dioptres and group 3 (fifteen subjects) with anisometropia varying from 3.5 to 5 dioptres.

Statistical analysis: All the data was expressed as mean ± S.D. The statistical significance of the data was assessed by t-test and p value <0.05 was considered as statistically significant. The statistical software used was IBM SPSS version 20.

RESULTS AND DISCUSSION

Results

The study was conducted in 50 adults (22 males and 28 females) with refractive errors ranging from -0.5 to -5 dioptres. P100 latency and N75-P100 amplitude were recorded in normal monocular, normal binocular conditions (corrected visual acuity) and after inducing simple myopic anisometropia. In normal binocular conditions, mean binocular N75-P100 amplitude (10.2±3.84 µv) is significantly greater than the mean of monocular amplitude (8.65±2.16 µv) (P=0.0121), also mean binocular P100 latency (101.80±5.08 ms) is significantly lesser than that monocular (104.46±3.39 ms (P=0.0022) by paired t-test (Table-1).

Table 1: Mean monocular and binocular amplitude (N75-P100) and P100 latency (with corrected visual acuity in both the eyes)

	Mean N75-P100 amplitude (µv) ± S.D.	*Mean P100 latency* (ms) ± S.D.
Monocular VEP	8.66±2.16	104.46±3.39
Binocular VEP	10.2±3.84	101.8±5.08

P value=0.0121 (<0.05), when means of normal *monocular and binocular N75-P100 amplitude* were compared (paired t test). *P100 latency decreased* in normal binocular stimulation as compared with those in monocular, with *p value of 0.0022 (<0.01)*.

When mean binocular N75-P100 amplitude was compared between normal binocular (10.20±3.84 µv) and induced anisometropic binocular states (7.83±3.08 µv), a statistically significant decrease is evident in the latter with p-value<0.0001 (highly significant). Mean binocular P100 latency increased in induced anisometropic conditions (102.56±4.98 ms) as compared to those in normal binocular state (101.8±5.08 ms) but the difference was not statistically significant (p>0.05) by paired t-test. Binocular summation ratio in normal binocular state was 1.18±0.2, while in anisometropic binocular conditions; it was 0.94±0.1 (Table-2).

Table 2: Mean binocular amplitude (N75-P100) and P100 latency in normal binocular conditions (with corrected visual acuity) compared with experimentally induced anisometropia

	Mean binocular N75-P100 Amplitude (µv ± S.D.)	Mean binocular P100 latency (ms ± S.D.)	Binocular summation ratio
Normal binocular conditions	10.2±3.84	101.8±5.08	1.18±0.2

Induced anisometropia	7.83±3.08	102.56±4.98	0.94±0.1

P value is<0.0001 for the decrease in the binocular amplitude in anisometropic conditions compared with those in normal binocular (paired t test), while p=0.14, (> 0.05) for the increase in the mean binocular latency in the anisometropic state as compared to that in normal binocular state

The decrease in mean binocular N75-P100 amplitude in anisometropia, when assessed in three different groups (based on the degrees of induced myopic anisometropia) was found to be statistically significant in all the three groups. For group I, (12.33±5.35 µv vs. 9.94±3.88 µv), p value = 0.015, while in group II (8.42±2.36 µv vs. 6.91±2.13 µv) and group III (10.46±2.43 µv vs. 6.41±2.24 µv), p value<0.0001 (highly significant) by paired t-test (Table-3). The increase in mean binocular P100 latency (in all the three groups) with induced anisometropia, however, was not statistically significant (p>0.05) (Table-4).

Table 3: Mean binocular amplitude (N75-P100) in normal binocular conditions compared with experimentally induced simple myopic anisometropia in three different groups

	Group I (0.5 to 2 dioptres)	Group II (>2 to 3.5 dioptres)	Group III (>3.5 to 5 dioptres)
Mean binocular N75-P100 amplitude (µv) ± S.D. (corrected visual acuity)	12.33±5.35	8.42±2.36	10.46±2.43
Mean binocular N75-P100 amplitude (µv) ± S.D. (induced myopic anisometropia)	9.94±3.88	6.91±2.13	6.41±2.24

In group I, P-value was 0.0153 (<0.05), for the comparison between normal and induced anisometropic binocular amplitudes, while in group II and group III, it was <0.0001 (highly significant by paired t test)

Table 4: Mean binocular P100 latency in normal binocular conditions compared with experimentally induced simple myopic anisometropia in three different groups

	Group I (0.5 to 2 dioptres)	Group II (>2 to 3.5 dioptres)	Group III (>3.5 to 5 dioptres)
Mean binocular P100 latency (corrected visual acuity)	102.77±4.47	99.86±3.8	103.42±6.45
Mean binocular P100 latency (induced myopic anisometropia)	103.49±4.96	101.48±4.93	104.27±5.17

P value was >0.05 in all the three groups, when normal binocular latency was compared with binocular latency in anisometropia (paired t test).

Discussion

Anisometropia is a significant risk factor for the development of amblyopia. Association of anisometropia with subnormal binocular vision emphasizes the value of assessing the binocular functions in anisometropes. In this study, we recorded PRVEP in 50 adults in normal (corrected visual acuity) conditions as well as in induced simple myopic anisometropic states and the extent of effect on binocular vision was evaluated.

The normal binocular PRVEP when compared with the monocular values provides the evidence of summation of visual signals binocularly, in terms of significant increase in amplitude and shortening of P 100 latency (Table-1). In induced anisometropes, a significant decrease in binocular N75-P100 amplitude when compared with that in normal binocular states is clearly evident as p-value <0.0001. The reduction in the amplitude was found to be significant separately in the all the three groups too, with p value as<0.05 for the group I (with induced anisometropia in the range of 0.5 to 2 dioptres) and p<0.0001 for >2

dioptres of anisometropia (group II and III). The increase in the latency in induced anisometropia did not show statistical significance. These findings conform with a similar study by Krumina and Caune (2009). The statistically insignificant increase in latency may partly be attributed to the influence of size of the pattern elements on the latency as only one check size (60 min) was used for stimulation in this study. Binocular summation ratio in our study was 1.18±0.2 for normal binocular condition while in anisometropes the ratio was 0.94±0.1 (binocular suppression). However, in another such study by Lefebvre, Saint-Amour (2008), although binocular suppression was found in anisometropes but normal binocular amplitude did not show significant difference with the binocular amplitude in the induced anisometropes. The report still reflects binocular deficits in the form of binocular suppression in anisometropia.

The amplitude alteration, in our study, although significant for all the three anisometropic groups, the levels of significance were more for groups more than 2 dioptres of simple myopic anisometropia. Krumina and Caune (2009), found decreased binocular evoked potential for anisometropia greater than 1 dioptre. In other studies evaluating the different forms of binocular interaction, binocular suppression has been found to begin between 2 and 4 dioptres of refractive differences (McKerral *et al.*, 1995-1996; Levi *et al.*, 1980; Srebro, 1978).

The level of binocular summation is believed to be determined by some binocular cells in the visual cortex that respond only when both eyes are stimulated simultaneously (AND cells) (Grusser and Grusser-Cornehls, 1965). These binocular AND cells respond best to similar inputs from the two eyes and inhibition is strongest when inputs differ. The interocular differences in image quality as a consequence of refraction anomalies in anisometropia cause incongruity between the inputs from the two eyes, which may account for suppression and the decrease in the level of binocular performances.

Conclusion

The results of this study, in the form of significant reduction in the mean binocular N75-P100 amplitude and binocular summation ratio<1 (binocular inhibition) found in the anisometropic conditions, suggest the presence of interference in the mechanism of binocular interaction. Transient VEPs seem to be reliable objective measures of assessing the binocular vision. These findings also have clinical implications to use binocular approach in the treatment of anisometropic amblyopia. The degree of suppression should be quantified and the mode of treatment should not only aim at reducing monocular acuity deficits but strengthening and re-establishment of binocular vision should be taken into account.

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