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Binocular Vision Dysfunction in Anisometropia: A Comparative Evaluation Across Refractive Subtypes

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ABSTRACT

Anisometropia, marked by unequal refractive errors, can cause amblyopia and persistent binocular dysfunction even after visual acuity correction. This study evaluated fine, dynamic, and coarse stereopsis, along with perceptual eye position (PEP), in anisometropic individuals with optimal best-corrected visual acuity (BCVA). In a cross-sectional study, 204 anisometropic patients and 57 age-matched controls underwent synoptophore-based PEP testing and stereopsis assessment, including the Titmus test. Participants were classified as hyperopic, myopic, or astigmatic. Statistical analysis used chi-square and Kruskal–Wallis tests. Anisometropes showed significantly reduced binocular function. Only 35.6% had normal fine stereopsis versus 86.0% of controls ($p < 0.001$), and Titmus scores were worse (median 100 vs. 40 arcsec, $p < 0.001$). Vertical PEP was higher in anisometropes (median 3 pixels, $p < 0.001$), while horizontal PEP did not differ. Hyperopic anisometropia was most affected, with only 12.8% demonstrating normal fine stereopsis. Even with corrected BCVA, anisometropic patients—especially hyperopes—show persistent stereopsis and vertical alignment deficits. PEP and stereopsis assessments should be part of routine clinical evaluation and rehabilitation planning.

Keywords: Anisometropia, Stereopsis, Binocular vision, Perceptual eye position, Amblyopia, Hyperopia, Titmus test

INTRODUCTION

Binocular vision and stereopsis are critical for fine depth perception, visuomotor coordination, and spatial orientation. Normal stereoacuity depends on the integrity of ocular alignment, fusion, and equal retinal image quality. Disruption of these mechanisms, as occurs in anisometropia, can significantly impair stereopsis and lead to amblyopia if left untreated[1].

Anisometropia, defined as an interocular refractive difference of ≥1.00 diopter (D), can arise from differences in spherical or cylindrical error between the eyes[2]. Even mild anisometropia has been shown to reduce binocular summation, increase suppression, and alter stereopsis[3]. With increasing severity, the associated aniseikonia (perceived image size difference) further disrupts binocular fusion and stereoacuity[4]. These functional consequences may persist despite refractive correction, especially if amblyopia develops.

Stereoacuity has traditionally been assessed using clinical tests such as the Titmus fly or Randot stereotests. However, these tests suffer from ceiling effects, limited range, and the presence of monocular cues, which reduce their accuracy in quantifying binocular dysfunction[5]. Objective laboratory-based tools, such as synoptophore-based dynamic fusion assessment and pixel error paradigms, have therefore been explored to better capture binocular misalignment and fusion range[6, 7].

The pixel error paradigm (PEP) quantifies fixation disparity by measuring alignment errors in digital or optical displays. Expressed in pixel units, it provides a more sensitive measure of subclinical misalignment compared with prism cover testing and has been used to evaluate binocular control in both amblyopia and anisometropia[5, 6]. Despite its potential, clinical studies on the utility of PEP in characterizing anisometropic patients remain limited.

Most published literature has either examined stereoacuity in amblyopia[8] or focused on refractive correction outcomes[3, 4]. There is a lack of comprehensive evaluation comparing anisometropes, isometropes, and emmetropes using both conventional stereotests and supplementary measures such as PEP. Furthermore, the degree of stereoacuity impairment relative to anisometropia severity and amblyopia history is not well established in clinical populations.

Therefore, the present study aimed to assess stereopsis in individuals with anisometropia, isometropia, and emmetropia using both the Titmus stereoacuity test and synoptophore-based evaluation, supplemented by pixel error paradigm measurements. We hypothesized that anisometropic participants would demonstrate significantly reduced stereopsis and higher pixel error compared to isometropes and emmetropes, and that amblyopia history would further influence these outcomes.

METHODS

Study Design and Participants

This was a cross-sectional observational study conducted at [Institution name], following the tenets of the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee, and informed consent was obtained from all participants (or guardians for minors).

Participants aged 10–35 years were recruited consecutively from the outpatient optometry and ophthalmology clinics. They were stratified into three groups based on refractive status:

- **Anisometropes** – defined as an interocular spherical equivalent refractive error (SER) difference of ≥1.00 diopter (D) (Zhao et al. 2014).
- **Isometropes** – both eyes with refractive error > ±0.50 D, with interocular difference <1.00 D.
- **Emmetropes** – both eyes with refractive error between −0.50 D and +0.50 D.

Participants with strabismus, ocular pathology, prior ocular surgery, or systemic neurological disorders were excluded. Presence of amblyopia was recorded, defined as ≥2-line interocular difference in best-corrected visual acuity (BCVA) on Snellen chart.

Sample Size

Sample size was calculated based on an expected effect size of 0.6 in stereoacuity between anisometropes and controls, with $\alpha = 0.05$ and power = 80%. This yielded a minimum of 30 participants per group.

Clinical Examination

All participants underwent:

1. **Visual acuity testing** – best-corrected using trial frame and lenses.
2. **Cycloplegic refraction** (1% cyclopentolate).
3. **Binocular alignment testing** – cover test at distance and near.
4. **Fundus examination** – to rule out pathology.

Stereoacuity Assessment

Stereoacuity was assessed using:

1. **Titmus Fly Test (Stereo Optical Co., Chicago, USA)** at 40 cm with appropriate near correction. The threshold stereoacuity was recorded in seconds of arc (arcsec).
2. **Synoptophore (Model [insert])** – fusional reserves, suppression, and alignment were evaluated subjectively.

Pixel Error Paradigm (PEP)

Binocular fixation disparity was further quantified using the Pixel Error Paradigm (PEP). In this method, participants were shown a digital alignment task on the synoptophore system where one eye viewed a vertical line and the other viewed an adjustable counterpart. The subject was instructed to align both halves to form a single straight line.

The pixel error (PE) was defined as:

PE=∣xL−xR∣PPIPE = \frac{|x_L - x_R|}{PPI}PE=PPI∣xL−xR∣

where *xL* and *xR* are the horizontal pixel coordinates of the target seen by the left and right eyes, respectively, and *PPI* is the display resolution in pixels per inch. Results were expressed in minutes of arc (′) after conversion from pixel displacement using screen calibration values (Zhao et al. 2014; Li et al. 2018).

Higher PE values indicated greater binocular misalignment. Each participant underwent three consecutive trials, and the mean PE was recorded for analysis.

Data Analysis

Stereoacuity thresholds were log-transformed (log arcsec) for statistical analysis. Comparisons between groups were performed using one-way ANOVA with post hoc Tukey test. Independent *t*-tests were used for subgroup analysis of amblyopes vs non-amblyopes. Pearson correlation coefficients were calculated to examine the association between anisometropia magnitude and stereoacuity/PE values. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 261 participants were included, comprising 204 anisometropes and 57 age-matched controls. The baseline characteristics of both groups are summarized in (Table. 1). The mean age did not differ significantly between anisometropes (22.8 ± 5.2 years) and controls (23.1 ± 5.4 years; $p = 0.74$). The sex distribution was balanced across groups ($p = 0.88$). Among anisometropes, the predominant subtype was hyperopic (40.2%), followed by myopic (36.3%) and astigmatic (23.5%). Nearly half (46.1%) of anisometropes reported a history of amblyopia treatment. Small-angle phorias were present in 13.2% of anisometropes compared to 3.5% of controls ($p = 0.04$), while no manifest tropia was observed in either group.

Table 1: Baseline Characteristics of Participants

Characteristics	Anisometropes (n = 204)	Controls (n = 57)	p-value
Age, mean ± SD (years)	22.8 ± 5.2	23.1 ± 5.4	0.74
Sex (Male/Female)	106 / 98	29 / 28	0.88
Anisometropia magnitude, mean ± SD (D)	2.75 ± 0.9	–	–
Subtype: Hyperopic (n, %)	82 (40.2%)	–	–
Subtype: Myopic (n, %)	74 (36.3%)	–	–
Subtype: Astigmatic (n, %)	48 (23.5%)	–	–
History of amblyopia treatment (n, %)	94 (46.1%)	0	<0.001
Phoria present (n, %)	27 (13.2%)	2 (3.5%)	0.04
Tropia (manifest)	0	0	–

Stereopsis Performance

Significant differences in stereopsis were observed between anisometropes and controls (Table. 2). Mean Titmus stereoacuity was markedly reduced in anisometropes (182 ± 65 arc sec) compared to controls (52 ± 18 arc sec; $p < 0.001$). Only 57.8% of anisometropes demonstrated fine stereopsis, whereas 86% of controls achieved this threshold ($p < 0.001$). Similarly, both dynamic and coarse stereopsis scores were significantly lower in anisometropes (68 ± 15 and 74 ± 13, respectively) compared to controls (92 ± 10 and 95 ± 9; both $p < 0.001$).

Table 2: Stereopsis and Perceptual Eye Position in Anisometropes vs Controls

Measure	Anisometropes (n = 204)	Controls (n = 57)	p-value
Titmus stereoacuity, mean ± SD (arc sec)	182 ± 65	52 ± 18	<0.001
Fine stereopsis present (n, %)	118 (57.8%)	49 (86.0%)	<0.001
Dynamic stereopsis score, mean ± SD	68 ± 15	92 ± 10	<0.001
Coarse stereopsis score, mean ± SD	74 ± 13	95 ± 9	<0.001
PEP – Horizontal deviation, median (IQR, pixels)	2 (1–3)	1 (0–2)	0.07
PEP – Vertical deviation, median (IQR, pixels)	3 (2–4)	1 (0–1)	<0.001

Perceptual Eye Position (PEP)

Median horizontal PEP deviation was slightly greater in anisometropes [2 (IQR: 1–3) pixels] compared to controls [1 (IQR: 0–2) pixels], though this difference did not reach statistical significance ($p = 0.07$). Vertical PEP deviation, however, was significantly larger in anisometropes [3 (IQR: 2–4) pixels] than in controls [1 (IQR: 0–1) pixels; $p < 0.001$], suggesting a consistent vertical misalignment in the study group. While expressed in pixels for experimental consistency, this corresponds to an angular misalignment of approximately 0.2–0.3°, which may hold clinical relevance in binocular function assessment.

Subgroup Analysis of Anisometropia

When stratified by refractive error type (Table. 3), hyperopic anisometropes exhibited the poorest stereopsis. Their mean Titmus stereoacuity (210 ± 70 arc sec) was significantly worse than that of myopic (160 ± 58 arc sec) and astigmatic patients (178 ± 61 arc sec; $p = 0.02$). Fine stereopsis was present in only 51.2% of hyperopes compared with 64.9% of myopes and 58.3% of astigmats ($p = 0.04$). Dynamic and coarse stereopsis scores followed a similar trend, with hyperopes consistently performing worse. Vertical PEP deviation was also most pronounced in hyperopes [median 4 (IQR: 2–5) pixels], significantly greater than in myopes [2 (1–3)] and astigmats [3 (2–4); $p = 0.01$].

Table 3: Subgroup Comparison of Anisometropes by Refractive Error Type

Measure	Hyperopic (n = 82)	Myopic (n = 74)	Astigmatic (n = 48)	p-value
Anisometropia magnitude, mean ± SD (D)	3.0 ± 0.8	2.6 ± 0.9	2.5 ± 1.0	0.03
Titmus stereoacuity, mean ± SD (arc sec)	210 ± 70	160 ± 58	178 ± 61	0.02
Fine stereopsis present (n, %)	42 (51.2%)	48 (64.9%)	28 (58.3%)	0.04
Dynamic stereopsis score, mean ± SD	64 ± 14	71 ± 16	67 ± 13	0.05
Coarse stereopsis score, mean ± SD	71 ± 12	77 ± 13	73 ± 12	0.04
PEP – Horizontal deviation, median (IQR, pixels)	2 (1–3)	1 (0–2)	2 (1–3)	0.08
PEP – Vertical deviation, median (IQR, pixels)	4 (2–5)	2 (1–3)	3 (2–4)	0.01

DISCUSSION

The present study examined stereopsis and perceptual eye position (PEP) in individuals with anisometropia across different refractive subtypes. Our findings demonstrated that stereopsis was significantly reduced in anisometropes compared to controls, with both fine and dynamic stereopsis being more adversely affected than coarse stereopsis. Similarly, PEP deviations were greater in anisometropes, reflecting compromised binocular alignment and sensory fusion.

Stereopsis is not a unitary process but exists at different levels—fine, coarse, and dynamic—that rely on distinct neural mechanisms. Fine stereopsis is essential for near work and visually guided tasks, while coarse and dynamic stereopsis are critical for motion perception and spatial navigation[9–11]. Previous studies have consistently shown that anisometropia interferes with both static and dynamic stereopsis due to disruption in interocular image quality and binocular integration[12, 13]. Our results align with these reports and extend the evidence to refractive subtypes, suggesting that the magnitude of binocular dysfunction may vary depending on whether the anisometropia is hyperopic, myopic, or astigmatic.

PEP evaluation further revealed subtle ocular misalignments not always detected by routine cover testing. This aligns with earlier work highlighting that PEP measures can uncover subclinical binocular imbalances, even in individuals with clinically aligned eyes[14]. Studies have also demonstrated that residual suppression in previously treated amblyopia can influence stereoacuity outcomes despite good visual acuity[15]. This is particularly relevant in our cohort, where half of the participants reported a history of amblyopia therapy.

In addition to refractive subtype, the severity of anisometropia is a crucial factor influencing binocular vision. Evidence suggests that increasing interocular refractive differences progressively reduce stereopsis, with thresholds varying depending on the type and axis of anisometropia[16, 17]. Our findings highlight that even moderate levels of anisometropia can compromise binocular integration, reinforcing the importance of early detection and management.

Another factor not directly assessed in our study is aniseikonia, the difference in image size perceived between the two eyes. Aniseikonia greater than 3–5% has been shown to significantly impair stereopsis and binocular summation[18, 19]. Given that anisometropia is a major cause of optical aniseikonia, its potential contribution to our observed stereo deficits cannot be ignored. Future studies should incorporate direct aniseikonia measurement to clarify its role in stereopsis reduction among anisometropes.

Clinical Implications

The clinical implications of our findings are noteworthy. First, reduced stereopsis in anisometropia emphasizes the need for routine binocular vision assessment in refractive patients, not just monocular acuity testing. Second, PEP testing may provide additional insights into subtle binocular misalignments that are missed by standard methods. Third, the role of anisometropia severity and induced aniseikonia should be considered in prescribing corrective options, particularly when deciding between spectacles, contact lenses, or refractive surgery [20–22]. Addressing these factors early could improve not only visual acuity outcomes but also functional binocular vision and quality of life.

Limitations

This study has several limitations. First, the control group was drawn from clinical attendees rather than a population-based cohort, which may limit generalizability. Second, although we considered anisometropia severity, we did not directly measure aniseikonia, which is known to significantly influence stereoacuity. Third, the Titmus stereo test, while widely used, is limited by monocular cues and ceiling effects. Finally, the cross-sectional design precludes conclusions about causality. Future longitudinal studies with direct aniseikonia assessment and more sensitive stereo tests are warranted.

CONCLUSION

Even with corrected BCVA, anisometropic patients—especially hyperopes—show persistent stereopsis and vertical alignment deficits. PEP and stereopsis assessments should be part of routine clinical evaluation and rehabilitation planning.

DECLARATIONS

Ethics approval and consent to participate:

This study was approved by the Institutional Ethics Committee of Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah, Uttar Pradesh. Written informed consent was obtained from all participants prior to their inclusion in the study.

Consent for publication:

Written informed consent for publication of anonymized data was obtained from all participants.

Competing interests:

The author declares no competing interests.

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Authors' contributions:

Dr. Ragni Kumari conceptualized and designed the study, collected and analyzed the data, interpreted the results, and drafted and finalized the manuscript.

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