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Evaluation of Fixation and Smooth Pursuit Eye Movement in Non-Amblyopic Anisometropic Children

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ABSTRACT
Anisometropia is a refractive condition characterised by a greater refractive error in one eye than the other. If left untreated, this condition potentially disrupts bifoveal fusion and impacts children's visual development and eye movement control. Current studies focus on eye movements in anisometropic amblyopia, but little is known about the effect of anisometropia on non-amblyopic children. Thus, the present study aimed to examine the eye movement characteristics in non-amblyopic anisometropia children, and to compare the characteristics with the control group. Fifteen children with non-amblyopic anisometropia and 15 healthy controls underwent horizontal smooth pursuit (SP) and fixation eye movement recordings using the Tobii Pro Fusion-120Hz eye tracker. SP gain and SP root mean square error (RMSE) were calculated to evaluate SP performance, while fixation performance was assessed by dwell time percentage. The SP gain for non-anisometropic and anisometropic children was 0.980±0.046 and 0.973±0.082, respectively. The RMSE was 1.803±0.149 for non-anisometropic children and 2.266±0.318 for anisometropic children. An independent t-test showed a significant difference in RMSE ($p<0.001$) but no difference in SP gain ($p=0.793$). The Mann-Whitney test revealed that non-anisometropic children-maintained fixation within 2° of the target center longer than anisometropic children ($p=0.004$). Anisometropic children have greater difficulty maintaining stable eye fixation compared to non-anisometropic children, indicated by higher tracking errors and less time spent within the area of interest. However, their SP gain is like non-anisometropic children.
Keywords: Anisometropia, eye movement, fixation stability, gain, smooth pursuit

ABSTRAK
Anisometropia ialah keadaan refraktif di mana satu mata mempunyai ralat refraktif yang lebih tinggi berbanding mata yang lain. Jika tidak dirawat, keadaan ini boleh mengganggu penyatuan bifoveal serta menjejaskan perkembangan visual dan kawalan pergerakan mata kanak-kanak. Kajian terdahulu menumpukan kepada pergerakan mata dalam kalangan kanak-kanak ambliopia anisometropik, namun terdapat keterbatasan mengenai kesan anisometropia terhadap kanak-kanak tanpa ambliopia. Oleh itu, kajian ini bertujuan untuk menyelidiki ciri pergerakan mata dalam kalangan kanak-kanak anisometropia tanpa ambliopia serta membandingkannya dengan kumpulan kawalan. Seramai 15 kanak-kanak anisometropia tanpa ambliopia dan 15 kanak-kanak kawalan telah menjalani rakaman pergerakan mata bagi penjejakan lancar mendatar (*smooth pursuit*, SP) dan fiksasi menggunakan peranti penjejakan mata Tobii Pro Fusion-120Hz. Nilai nisbah kelajuan penjejakan lancar (*SP gain*) dan ralat punca min kuasa dua (*root mean square error*, *RMSE*) dikira untuk menilai prestasi SP, manakala prestasi fiksasi dinilai berdasarkan peratusan tempoh fiksasi (*dwell time*). Nilai *SP gain* bagi kumpulan tanpa anisometropia dan anisometropia masing-masing ialah 0.980±0.046 dan 0.973±0.082. Nilai *RMSE* ialah 1.803±0.149 untuk kumpulan kawalan dan 2.266±0.318 untuk kumpulan anisometropia. Ujian t bebas menunjukkan perbezaan signifikan bagi *RMSE* ($p<0.001$), tetapi tiada perbezaan bagi *SP gain* ($p=0.793$). Ujian Mann-Whitney menunjukkan bahawa kanak-kanak tanpa anisometropia mengekalkan fiksasi dalam lingkungan 2° dari sasaran lebih lama berbanding kanak-kanak anisometropia ($p=0.004$). Kanak-kanak anisometropia menghadapi kesukaran dalam mengekalkan fiksasi stabil, seperti yang dibuktikan melalui ralat penjejakan yang lebih tinggi dan tempoh fiksasi yang lebih singkat. Namun, *SP gain* mereka setanding dengan kanak-kanak tanpa anisometropia.
Kata kunci: Anisometropia, pergerakan mata, kestabilan fiksasi, nisbah penjejakan, penjejakan lancar

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Introduction

Anisometropia, a refractive condition where the interocular refractive error differs by ≥ 1D, is widely associated with impairments in visual development and binocular function in children (Kuswandari, 2023; Zhuang et al., 2024). Previous studies have revealed that anisometropia is a common risk factor for unilateral amblyopia due to the suppression of the eye with higher refractive error, causing a reduction in vision for that particular eye (Meng et al., 2021; Tegegne et al., 2021). A significant magnitude of anisometropia can also disrupt binocularity, leading to the reduction in stereoacuity, especially in the case of anisometropic amblyopia (Khan et al., 2022). Besides, eye movement is another visual function that can be affected by anisometropic amblyopia as it impairs the coordination between the two eyes (Fan et al., 2024; Murray et al., 2022). These visual disfunctions associated with anisometropia may affect children's learning skills and quality of life (Webber, 2018).

Previous studies have shown different views on when eye movements reach maturity; 5-7 years of age (Langaas et al., 1998; Miladinović et al., 2022), 10-12 years of age (Armstrong et al., 2009; Irving et al., 2008) and 17-18 years of age (Katsanis et al., 1998). In this study, primary school-aged children were recruited considering their eye movements have typically attained adult-like developmental stages by this age and due to the fact that a low prevalence of anisometropia was reported in children under 6 years old (Nunes et al., 2021). This facilitates a more precise comparison between the healthy control group and those with anisometropia. It ensures that any differences in eye movement patterns are not due to the ongoing maturation of eye movement functions.

There are various types of eye movement systems, each with different characteristics and functions. Smooth pursuit (SP) and fixational eye movements are common parameters measured in eye movement studies. SP refers to the continuous voluntary eye movement that allows the eyes to track a moving object smoothly and maintain the image steadily on the fovea to ensure clear vision (Shafee, 2021). Fixational eye movements refer to small ocular movements made when attempting to focus on a static object or when maintaining fixation while tracking a smoothly moving object (Leigh & Zee, 2015).

Delayed SP initiation was reported in individuals with anisometropic amblyopia compared to visually normal participants due to the discrepancies in the processing of retinal velocity and retinal position signals between the normal and amblyopic eyes (Raashid et al., 2016). Additionally, fixation instability was also observed in anisometropic amblyopia which resulted from modifications in physiological fixational eye movements (FEMs) (Murray et al., 2022). Physiologic FEMs refer to small involuntary movements that are localised within the fovea, which do not affect the visual acuity (Putnam et al., 2005). However, in anisometropic amblyopia, the amblyopic eye showed an increase in the amplitude of rapid FEMs as compared to the fellow eye, which correlated with the fixation instability (Kang et al., 2019; Shaikh et al., 2016).

While extensive studies have explored eye movements in anisometropic amblyopia, there is limited information about the effect of anisometropia on eye movements among non-amblyopic children. Given the importance of eye movements in reading, attention and general visual processing, examining the impact of anisometropia on eye movement patterns in non-amblyopic children is crucial, especially during the primary school years, when visual and cognitive skills are critically developing.

Methods

Participants

Fifteen non-amblyopic anisometropic children (mean age: 10.00±1.73) and 15 control children (mean age: 9.93±1.53) who attended the International Islamic University Malaysia (IIUM) Optometry Clinic were recruited in this cross-sectional study. Before the study procedures, written consent was obtained from the parents. This study adhered to the tenets of the Declaration of Helsinki, and the study procedures were reviewed and approved by the IIUM Research Ethics Committee (IREC 2023-144).

In the present study, anisometropia was defined as a difference in refractive error between the two eyes, with a spherical equivalent (SE) difference of ≥ 1.00D (Zhou et al., 2022). Inclusion criteria were children aged between 7 and 12 years old (Aljohani et al., 2022; Mondal et al., 2022), interocular SE difference of < 1.00D for the control group and ≥ 1.00D for the anisometropic group (Yang et al., 2017), best corrected visual acuity of 6/6 at distance and near in both eyes (Caldani et al., 2020) and stereoacuity of 60 seconds of arc or better for the normal group measured using the TNO test (Zhou et al., 2022). Exclusion criteria included the history of amblyopia (Krarup et al., 2020), history of ocular disease and any ocular surgery or media opacity (Jamil et al., 2022). Children with a previous history of amblyopia therapy such as patching and orthoptic therapy were also excluded from this study to avoid confounding factors in the comparison between the groups (Tayah et al., 2022).

Before data collection, a detailed optometric examination, including refractive error measurement was conducted on all participants (Gebru et al., 2022; T. Krarup et al., 2021). To obtain an accurate measurement of refractive error, cycloplegic refraction was conducted using two drops of 1% cyclopentolate hydrochloride ophthalmic solution with an interval of 5 minutes between drops (Fengchao et al., 2022). One week following cycloplegic refraction, the eye movement recordings were conducted with fully corrected refractive error. Participants were classified into either the anisometropic group or the control group according to the spherical equivalent calculated from the cycloplegic refraction results.

Eye movement recordings

All eye movement assessments were conducted binocularly using the Tobii Pro Fusion-120Hz eye tracker (Tobii Pro AB, Danderyd, Sweden). This eye tracker operates at a sampling frequency of 120 Hz, which enables the recording of fixation and smooth pursuit of eye movements. The device was mounted on an AOC display monitor (Model: 22B2HN) with a refresh rate of 75 Hz. The eye tracker is equipped with dark and bright pupil illumination modules, eye sensor modules, Tobii Eyechip™, and two cameras. These components enable video-based recording of pupil and corneal reflections under various lighting conditions and capture stereo images of both eyes, improving the accuracy of gaze and eye position measurements (Tobii AB, 2022)

To start the eye movement recordings, the participant was positioned 60 cm from the display monitor, with their head stabilised on the head and chin rest throughout the recordings (Figure 1). The IIUM EyeGaze application (Copyright Number: CRLY2022W05581) and Tobii Prolab software were utilised to generate and present dynamic stimuli for the recordings of SP eye movement and fixation eye movement, respectively.

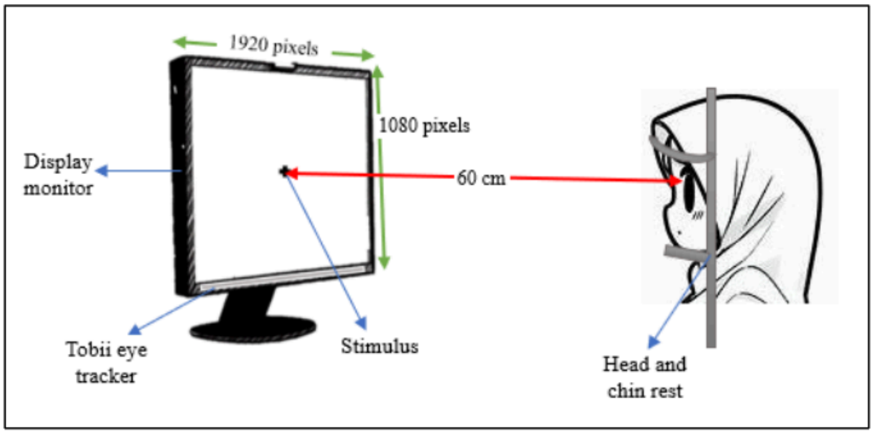

Figure 1: Participant set-up during eye movement recording

This study implemented the dynamic stimulus through the MATLAB-based eye tracking app, IIUM EyeGaze application, integrated with the Tobii Pro Fusion eye tracker that offers flexibility in the type and frequency of the stimulus motion. The stimulus moves horizontally across the display area at an average velocity of approximately 14.8°/sec and was rendered in high resolution for smooth visual tracking. For this application, eye movement data was collected in real-time, capturing the gaze coordinates for both eyes in a constant number of cycles (4 complete cycles per trial).

SP recording began with a 5-point-calibration test to ensure data reliability and accuracy. After calibration, a dynamic black cross subtending a visual angle of 0.53° was presented to the participant. The cross target moved laterally from left to right (amplitude of ± 22° horizontally from the primary position) and vice versa, following the sinusoidal wave. The participant was instructed to follow the movement of the stimulus as quickly and accurately as possible, without moving their head. The stimulus amplitudes, gaze amplitudes for each eye and timestamp were stored in MATLAB software for further analysis. SP gain (ratio of eye movement velocity to stimulus velocity) and RMSE (deviation between eye movements and target) were calculated to quantify the SP performance.

The static fixation stimulus was designed using the Tobii Prolab software to ensure precise control over the stimulus presentation and accurate eye-tracking data recording. The Tobii Prolab software allows precise placements of the target, ensuring the cross-symbol target remains centrally aligned at the center of the display monitor. Dwell time percentage, which is the duration of eye fixation at the area of interest (AOI), was calculated to assess the fixation stability. After the SP recording, calibration was conducted before the fixation task. A static cross symbol (1.05° visual angle) was presented at the center of the display monitor. The participant was instructed to fixate precisely at the center of the black cross target and maintain a steady fixation as accurately as possible for a fixed duration of 30 seconds (Shafee, 2021).

During the fixation period, binocular gaze data at a sampling rate of 120 Hz was recorded to capture the participant's eye position. The gaze coordinates were tracked in real-time with the cross symbol as the reference point. Additionally, Tobii Prolab provides a real-time display of gaze points, allowing the examiner to review the data while the participant performs the fixation task. The built-in analysis tools in Tobii Prolab were used to evaluate fixation stability and calculate the participant's average gaze on the AOI. This software provides various metrics for comprehensively analysing fixation behavior, but for this study, only one metric; total fixation duration (dwell time) was noted to measure how well the participant maintained stable fixation.

Data analysis

All collected data were analysed using the Statistical Package for Social Science Software (version 28, Statistical Package for Social Sciences; SPSS Inc., IBM Corp., Armonk, NY, USA). Normality testing was performed based on the skewness and kurtosis tests (Kim, 2013). The differences in SP performance (SP gain and RMSE) were examined using an independent sample T-test, while the Mann-Whitney test was employed to compare the dwell time percentage between the anisometropia and control groups. The significance level was set at p-value < 0.05.

Results

For analysis, RMSE was used as an indicator of tracking accuracy. Lower RMSE indicates smaller deviations of eye movements from the target, suggesting more precise SP eye movements. For fixation analysis, dwell time percentages were calculated as the proportion of time spent fixating on the AOI relative to the total fixation duration throughout the test. Higher dwell time percentages suggest longer periods of focus, reflecting better attention to the target stimulus.

Figures 2 and 3 show horizontal smooth pursuit recording and fixation behavior visualisations of a control and an anisometropic participant. The tracing of SP (Figure 2) showed notable deviations at certain points for the anisometropic participant, indicating inaccurate eye tracking, while the control participant demonstrated accurate stimulus tracking. Heat map visualisation of fixation (Figure 3) showed higher fixation density within the AOI for the control participant, indicating longer fixation within the AOI compared to the anisometropic participant.

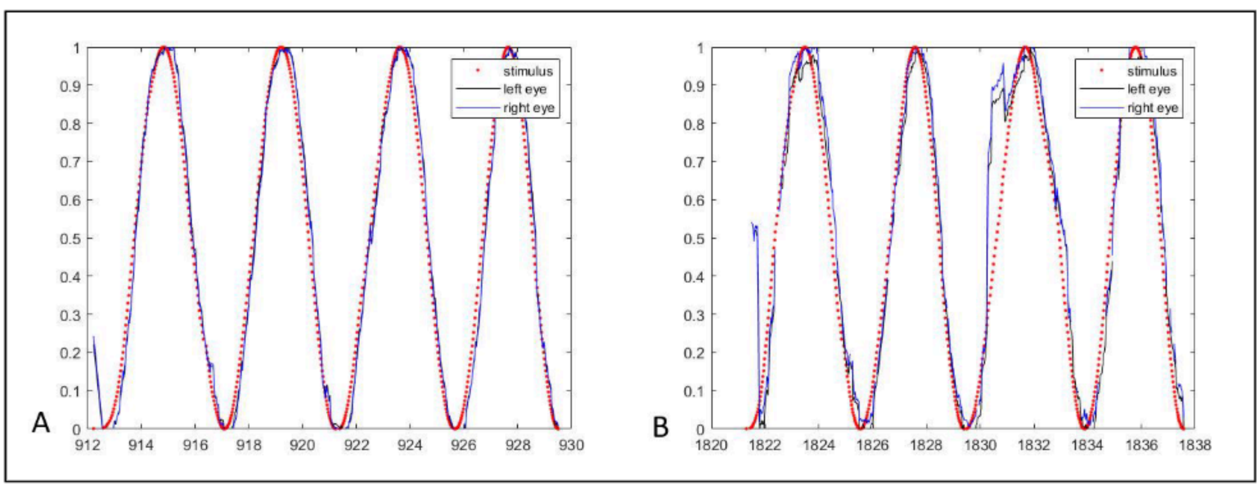

Figure 2: A sample of a live trace of smooth pursuit eye movements with four complete cycles of sinusoidal waveform performed by (A) a non-anisometropic participant and (B) an anisometropic participant in this study.

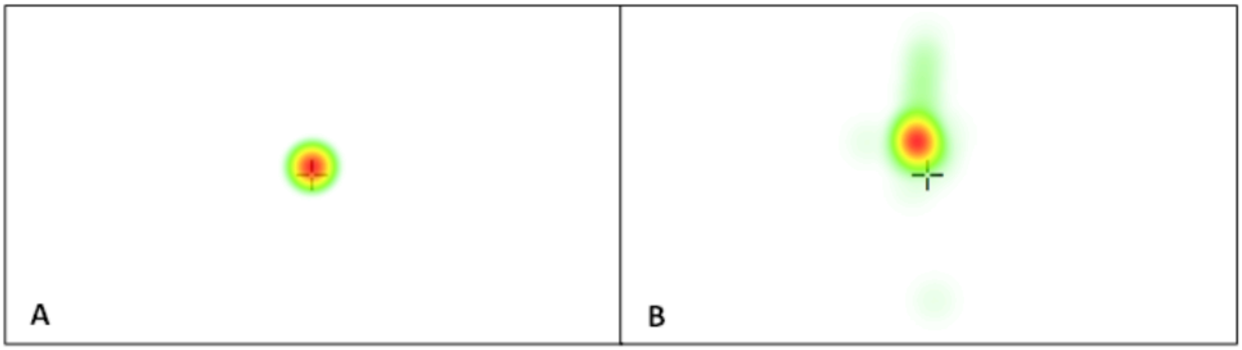

Figure 3: Heat map visualisation of fixation from (A) a non-anisometropic participant and (B) an anisometropic participant. Red/dark shade indicates a high density of fixation and green/light shade indicates a low density of fixation.

The study revealed a significant difference in SP RMSE (p<0.001) between the control (1.803 ± 0.149) and anisometropia (2.266 ± 0.318) groups. However, the calculated SP gain was comparable between these two groups (p=0.793). The findings indicated that although anisometropic children exhibit similar eye movement velocities during target tracking, their tracking accuracy was less precise compared to the control group. The results for both SP gain and RMSE are summarised in Table 1.

Table 1: Comparison of the smooth pursuit gain and RMSE between the control and anisometropic groups

Smooth pursuit (SP) performance	Non-anisometropia Mean (SD) (n=15)	Anisometropia Mean (SD) (n=15)	p-value*
SP Gain	0.980 ± 0.046	0.973 ± 0.082	p=0.793
SP RMSE (°)	1.803 ± 0.149	2.266 ± 0.318	p<0.001

*p-value analysed using an independent sample t-test

A comparison of the dwell time percentages showed a significant finding (p=0.004) between the control and anisometropic groups. The Mann-Whitney test indicated that control children maintain fixation within the AOI longer than anisometropic children, as shown in Table 2.

Table 2: Comparison of dwell time percentage between the control and anisometropic groups

Fixation stability	Non-anisometropia Mean rank	Anisometropia Mean rank	Z-value	p-value[ɫ]

	(n=15)	(n=15)		
Dwell time (%)	20.03	10.97	-2.83	0.004

[1]p-value analysed using the Mann-Whitney test

Discussion

This study observed SP performance and fixation stability in non-amblyopic anisometropic children, comparing their eye movement characteristics with the normal control group. Regarding SP performance, the study demonstrated that anisometropia predominantly influenced precision (higher RMSE values) rather than eye movement velocity (SP gain).

Although the SP gain in the anisometropic group is similar to those executed by the normal group, their tracking accuracy showed a significant difference, evidenced by higher RMSE values. The variation in RMSE values in the anisometropic group might be due to asymmetrical SP eye movements between the anisometropic and fellow eye, contributing to binocular inaccuracy when tracking a moving target. Previous studies suggested that differences in refractive error can lead to the different positions of the center of ocular rotation (COR), as it is related to axial length (Grolman, 1963; Ohlendorf et al., 2022). A possible explanation is that, in anisomyopia for example, the eye with a higher refractive error (longer axial length) may exhibit a shifting in COR, affecting precise target tracking and increasing tracking errors. Besides, the differences in refractive errors in anisometropia may interfere with binocular synchronisation, resulting in instability during dynamic visual activities (Hopp & Fuchs, 2004; Lemij & Collewijn, 1991).

The study revealed no significant differences in SP gain, indicating that eye velocity while tracking the moving target was comparable in both groups. This finding aligns with the previous study which demonstrated that even in amblyopic anisometropia, the SP gain was not affected (Raashid et al., 2016). This may be related to the catch-up saccades (CUS), the corrective response during pursuit eye movements that realigns the eyes with the target (Shafee, 2021). A higher frequency of CUS may interrupt and delay eye movement velocity, resulting in slower eye tracking during SP. However, the frequency of CUS in anisometropia was close to the one executed by normal individuals, indicating that eye movement velocity when pursuing the target is not affected in anisometropia (Raashid et al., 2016).

In terms of fixation stability, the anisometropic group demonstrated a shorter duration of fixation within the AOI, as indicated by a lower dwell time percentage. This finding was in line with a previous study among treated anisometropic amblyopic children, which reported greater fixation instability during binocular viewing compared to age-matched controls (Kelly et al., 2018). The authors explained that fixation instability in anisometropic children was due to discordant binocular visual experiences during visual development, which interferes with ocular motor control between the two eyes (Kelly et al., 2018). On the other hand, Mompart-Martínez et al. (2023) speculated that interocular asymmetry in anatomical and functional parameters might also contribute to fixation instability in anisometropia.

This study provides valuable insight into the effects of anisometropia (without amblyopia) on dynamic visual functions, specifically SP and fixation eye movements, which to our knowledge, have not been reported before. These findings offer valuable information for both clinicians and educators. For clinicians, clinical evaluation of anisometropic children should not only focus on visual acuity but also the assessment of eye movements, as accurate and stable eye movement is essential for reading and other learning activities (Kelly et al., 2017). Early detection of anisometropia and related eye movement problems can lead to prompt interventions, potentially enhancing academic achievement and reducing the risk of learning difficulties. As for educators, the results emphasised the visual challenges that may be faced by anisometropic children in the classroom. Thus, educators may consider adapting their teaching strategies, particularly for anisometropic children with poor academic performance, who may struggle in visual tasks and require additional support to succeed.

With promising results from this study on SP and fixation eye movements, future studies may further investigate the broader implications of anisometropia, specifically on the saccadic eye movements, another important parameter in evaluating eye movement control. Besides, future studies should consider using a larger sample size with different types of refractive error (i.e. myopia, hyperopia or astigmatism) and varying magnitudes of anisometropia to provide a more comprehensive analysis of eye movement patterns in non-amblyopic anisometropic children.

Conclusion

Although a comparable velocity of eye movement when tracking a moving target was observed between both normal and anisometropic groups, a greater deviation between eye movement and the target was observed in the anisometropic group. The results from this study reflect the difficulty in accurately tracking and sustaining steady eye fixation among anisometropic children. This suggests that anisometropia, even without amblyopia, affects fixation stability, which could impact activities requiring precise visual tracking.

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