Gait kinematics during walking in children with amblyopia

by

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Author’s Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners. I understand that my thesis may be made electronically available to the public.

Abstract

Introduction: Coordination between the eyes and body is important for navigating the environment. Children with amblyopia score lower for walking on standardized tests of motor ability. However, standardized tests do not assess gait kinematics during walking. Here, I investigated the development of gait kinematics during walking under natural binocular viewing conditions in children with amblyopia compared to controls.

Methods: A total of 21 children ages 7-13 years with amblyogenic factors (14 anisometropia, 7 strabismus) were enrolled in the ‘amblyopia’ group (15/21 had current amblyopia). An age-similar group of 27 controls were also enrolled. While viewing binocularly, children walked the length of a GAITRite pressure-sensitive walkway and completed 3 conditions of varying complexity: 1) Straight Walk (SW): walk on mat, 2) Isolated Target Walk (IT): walk and step on two-dimensional targets, and 3) Distractor Target Walk (DT): walk and step on two-dimensional targets while avoiding two-dimensional distractors. Gait kinematics were temporal outcomes of normalized velocity (leg lengths/second), cadence (spm), step time (msecs), and stance time, and spatial outcomes of (msecs), step length (cm), step width (cm) and accuracy (%) of stepping on targets or avoiding distractors. Variability in gait kinematics was also examined using the coefficient of variation (COV, %).

Results: Temporal and spatial outcomes of gait kinematics did not differ between children with amblyopia and controls. However, the amblyopia group was less accurate at stepping on targets overall than controls (amblyopia, mean±SD=90.8±8.5% vs control, 96.9±3.8%, p=0.003), with less accuracy found in the IT condition (89.7±9.7% vs 96.5±5.3%, p=0.005), and for the far T2 target (87.4±13.9% vs 97.2±5.4%, p=0.001). Lastly, the amblyopia group showed increased variability (i.e., higher COV) for temporal measures, including normalized velocity (8.9±3.0% vs 6.4±3.0%; p=0.007), stance time (5.7±1.8 % vs 4.7±1.8%; p=0.049), cadence (5.0±2.4 % vs 3.3±1.7 % p=0.005) and step time (4.9±2.5% vs 3.5±2.1%; p=0.040), and for spatial measures, including step length (8.0±2.4% vs 6.4±2.4%; p=0.024) and step width (7.7±2.2% vs 6.11±2.2%; p=0.014). In the amblyopia group, spatial outcomes were correlated with amblyopic eye visual acuity and temporal measures were correlated with stereoacuity.

Conclusions: This thesis shows that unbalanced visual input early in life from pediatric eye conditions that cause amblyopia results in variable and inaccurate walking patterns compared to children with age-typical visual development. This pattern of findings is similar to younger children, indicating that the typical development of gait is delayed in children with amblyopia, especially when they have poor binocularity outcomes. These findings point to the importance of typical binocular vision for the development of walking.

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List of Abbreviations

ANOVA – Analysis of Variance

Arcsec – Arc seconds

BCVA – best-corrected visual acuity

BOTMP – the Bruininks-Oseretsky Test for Motor Proficiency

COV – Coefficient of Variation

D1 – Distractor 1

D2 – Distractor 2

DT – Distractor Target condition

DT-1 – Distractor Target Trial Type 1, Target 1 on right, Distractor 1 on the left, Target 2 on left, Distractor 2 in the center

DT-2 – Distractor Target Trial Type 2, Target 1 on left, Distractor 1 in the center, Target 2 on right, Distractor 2 on the left

e-ETDRS – the Electronic Early Treatment Diabetic Retinopathy Study

IT – Isolated Target condition

IT-1 – Isolated target Trial Type 1, Target 1 on right, Target 2 on left

IT-2 – Isolated target Trial Type 2, Target 1 on left, Target 2 on right

LogMAR – Logarithm of the Minimum Angle of Resolution

Movement ABC – Movement Assessment Battery for Children

MT+– Middle Temporal Visual Area

PVAT – Precision Vision®, Inc

SW – Straight Walk condition

T1 – Target 1

T2 – Target 2

V1 – Primary Visual Cortex

V2 – Secondary Visual cortex

3D – Three Dimensional

Chapter 1

Background and Rationale

1.1 Typical Visual Development

1.1.1 Sensory Development

Our visual system is not fully developed at birth.[1–3] In general, rapid development of this system is seen from birth to 6 months of age followed by slower development during childhood until we reach the age of 7 years where a plateau occurs for many visual functions such as visual acuity, binocularity, and ocular motor function.[1–3] Visual acuity is the ability of the visual system to see our environment in sharp, fine detail.[4,5] Visual acuity is dependent on the health of the visual pathways and its development relies on balanced binocular input early in life.[6,7] During the first year of life, visual acuity improves from 1.5 logMAR (20/640) at 1 month old to 0.5 logMAR (20/60) by 1 year old. Acuity continues to improve with age reaching 0.2 logMAR (20/30) by 3 years of age to finally an adult-like level of 0.0 logMAR (20/20) by 6-7 years of age.[1,7–10] This ongoing improvement reflects the continued maturation of the eyes and visual pathways.

Along with visual acuity, binocular vision develops rapidly during childhood. Our two eyes create different images of the world because of disparity.[7] Binocularity is our brain's ability to combine these two images to see one image, allowing for depth perception. This is accomplished by fusion and stereopsis. Fusion is controlled by motor (i.e., vergence) and sensory mechanisms that interact to provide normal single binocular vison and depth perception.[7,11] The emergence of fusion occurs between 3-5 months of age, with continued development throughout childhood.[12,13] At the same time, stereopsis emerges.[14,15] Stereopsis is the ability to perceive depth in three dimensions (3D) based on the slight disparities in visual images between our eyes. Stereopsis is measured by assessing stereoacuity, which is the smallest detectable difference in disparity that can be perceived. Stereopsis has an onset around 3-4 months old,[1,7,9,12,14–17] with improvements in stereoacuity found from 370 arcsec at 1 year of age, 100 arcsec at age 3 years, 60 arcsec by age 5 years, and adult-levels of 40 arcsec by age 7 years.[9,12,13,16,17]

1.1.2 Ocular Motor Development

The ocular motor system is a proactive system that anticipates and helps us plan our actions by gathering visual information through eye movements including fixation stability, saccades, smooth pursuits, and vergence. While some aspects of ocular motor function are present from birth, there is a long developmental period that follows until the ocular motor system is mature. Fixation stability is our ability to maintain steady and stable gaze patterns.[7,11] Fixation stability is present at birth but is immature, becoming more refined during the first 6 months of life and maturing alongside visual acuity, reaching adult-levels at around the age of 10 years.[7,18–20] Saccades are fast, eye movements that align our central vision and focus the eyes on a specific point of interest or targets based on the environment and the motor task being performed.[21–23] Studies suggest that saccades are present at birth but continue to improve into childhood, becoming fully developed during adolescence and young adulthood between the ages of 12 to 20 years old.[24–26] Smooth pursuits are the way we track moving objects in our environment, by estimating the velocity of the moving target.[7] Smooth pursuits are present in newborns but are only sensitive to large slow-moving targets.[27] Smooth pursuits develop quickly within the first 6 months of life but does not reach full maturity till the ages of 14-17 years.[28–30]

Vergence is the movement of our eyes in opposite directions to either converge (eyes move towards the nose) or diverge (eyes move towards the temples).[7] Fusional vergence is sensory and is driven by disparity; accommodative vergence is motor and is driven by blur and proximal vergence.[31] Newborns can make vergence movements but only are able to use proximal cues (i.e., cues that indicate nearness of the object) until the ages of 3-6 months when they have developed the ability to use disparity, accommodation, and proximal cues equally.[32] Latency of vergence movements are larger in children compared to adults, reaching adult levels by 10 years old.[33] In general, studies suggest ocular motor function is not mature at birth and emerging as eyes begin to work and move together around 4 months old and continues to improve into childhood, becoming fully developed during adolescence and young adulthood.[19,25,26,34–36]

1.1.3 Cortical Development

The progression of sensory and ocular motor visual functions depend largely on the development of the visual pathways, in particular primary visual cortex (V1) and higher-order visual areas from V2 – V5/MT+ and beyond. V1 undergoes a series of neurobiological changes across the lifespan that align with the development and maturation of some of our main visual functions.[3] From birth to 1 year old, the mechanisms responsible for excitatory inhibitory signals are established.[3,37,38] Rapid improvements in visual acuity are observed along with emergence of binocular fusion and stereoacuity at around 3-4 months old.[3,12,39] From the ages of 1 to 4 years old, V1 enters a stage of heighted variability, which is accompanied by continued experience-driven improvements in visual acuity, contrast sensitivity, and motion perception.[3,40–42] By 5 to 11 years old, mechanisms that support plasticity are at their peak and are signaling for stabilization in the cortical circuits and the end of the critical period for ocular dominance plasticity.[3,43–47] At the same time, visual acuity and fusion are now reaching adult-like levels.[1,7–10,12,13] From 12 years old into adulthood, V1 continues to undergo structural and molecular fine tuning allowing for the continued enhancement of higher order visual functions.[3,43,47] In parallel to V1, higher-order visual areas are also maturing, including area V5/MT+ which is responsible for processing binocular functions such depth and motion.[48–52]

1.2 Typical Motor Development

1.2.1 Postural Balance

Starting from birth until we learn to stand, muscle control of our head and its connections to the lower body emerges.[53–55] By age 6 years, we master the coordination of both our upper and lower body, using ascending organization of balance control from the feet to the head during static balance (balancing while standing still) and from the hips to the head during dynamic balance (walking).[53–56] From age 7 years to adolescence, refinement in head stabilization in space is observed during balance control in dynamic balance.[53–57] Some research shows that from the ages of 7-10 years children show adultlike postural responses during static balance.[58] Balance control parameters such as sway speed, sway path length, and variability decrease significantly in childhood through to adulthood.[53,54,56,59,60]

1.2.2 Walking

Alongside the development of postural balance, there are age-related changes observed in locomotor ability.[61] Children typically walk unaided by 13-14 months, however walking at this age is not adult-like.[62] While we are learning to walk, our gait parameters change. A significant interaction is found between cadence (speed of walking measured in steps per minute) and age, with a decrease in cadence observed with age. Following this decrease, velocity of walking increases from age 3.5-4 years.[55,61,63–66] Stride length increases quickly until we reach the age of 4 years where it continues to increase at a slower rate.[55,64–67] During these years, stabilization of gait continues to mature until we reach age 4 years, after this time any changes in gait are found in the time and distance parameters which are correlated with leg length and height. [68–70] Children and young adolescents take longer, wider, and more frequent steps than older adolescents and adults, allowing them to keep adult-like velocities while covering less ground.[69,70] Walking stability is based on stride width, stride length, and variability.[69] Variability in gait parameters is important for the typical development and movement in children.[64] Younger children exhibit a larger percentage of abnormal strides than older children, showing an overall more variable gait pattern during walking.[69,71] Consistency in gait speed and gait speed variability might develop around the age of 8 years old.[66,72]

Children use visual information about their environment to plan ahead in complex environments just like adults.[73] However, children use different strategies when coming across obstacles in their path, using avoidance to increase their stability since they do not prepare for crossing a second obstacle until they have cleared the first.[73,74] Children are more cautious, variable and have increased toe clearance but also tend to touch obstacles more often than adults.[73,74] Variability is useful to explore new pathways and find the most efficient or useful way to accomplish motor goals.[73] Children aged 3-5 years old accommodate for their high variability by using dynamic scaling to adjust movement patterns and maintain stability and efficiency, ensuring safe walking even when in complex environments.[73]

1.2.3 The Role of Vision in Walking

To get through life we must be able to efficiently navigate our surroundings and we predominantly make use of vision to determine where our bodies are positioned relative to our surroundings.[75] For children, vision and eye movements are the main method of learning about the world around them, assisting them in many developmental milestones such as learning to walk.[76–79] The ocular motor system is key in making this possible. Fixations, saccades, and the vestibular ocular reflex (VOR) stabilize gaze during walking by providing the correct eye movements at the correct time and by allowing the eyes to focus on specific targets to help in planning footsteps.[80,81] For example, during walking, people use slow downward saccades to track the approaching environment, then faster larger upward saccades to focus on points ahead.[82] This pattern is more prominent during more complex walking such as ascending stairs.[82] Further, the VOR makes compensatory eye movements to stabilize gaze during head movement. [83]

The pattern of eye movements that occur during walking changes developmentally. After the age of 7 years. there is a lower sensitivity to peripheral viewing during walking which is thought to be due to the re-weighting of the use of different sensory systems.[58,84] Other research has shown that with age, inputs from the somatosensory and vestibular systems are used during static and dynamic balance as well, which help to ensure upward balance and forward progression during walking.[85–89] Somatosensory input is important in walking as it provides information regarding limb placement, orientation, and velocity.[87] Vestibular inputs detect the orientation of your head relevant to gravity and the world around you, which is used to detect limb orientation relative to the ground as you walk. [88] One study suggests that between the ages of 8-11 years old, the shift to multisensory integration is complete, meaning that the brain is combining sensory information from the visual, somatosensory and vestibular systems during visuomotor tasks such as walking.[53,77,90]

Past research on the role of the ocular motor system in motor development is inconclusive.[85] However, based on what we know about the ocular motor system and its functions of examining surroundings and sending signals to the brain so the body will respond accordingly, it can be assumed that this system plays an important role in the development of walking.[85,91,92] Because ocular motor function is still developing in childhood, it could impact the efficiency of neural processes responsible for maintaining postural balance during walking. [19,25,26,34–36]

1.3 Atypical Visual Development (Amblyopia)

1.3.1 Etiology

Amblyopia ('lazy eye) is a pediatric eye condition that results from unbalanced visual experience early in life. It is the most common cause of monocular vision loss in children, affecting 1.3%-3.6% of all children.[39,93,94] Amblyopia is reduced visual acuity of at least a 2-line difference between the amblyopic eye and the fellow eye, accompanied by one or more amblyogenic factors.[39,94,95] These factors include strabismus (misaligned eyes), anisometropia (unequal refractive error), or more rarely, cataracts (blurry lens).[39,96]

Strabismic amblyopia is caused by the stimulation of non-corresponding retinal areas; to avoid seeing double the brain must adapt and suppress the eye with strabismus.[93,94] There are many types of strabismus, but the most common form that causes amblyopia is esotropia (inward turn of one or both eyes). Esotropia can be infantile (onset before 6 months of age) or accommodative (due to increased accommodative effort) with on onset typically after 2 years of age. These forms of strabismus can be constant or intermittent. [97] Anisometropic amblyopia (i.e., refractive amblyopia) is caused by the image being blurrier in one eye than the other due to unequal refractive error.[93,94] There are three types – hyperopic, myopic, and astigmatic anisometropia.[98]

Strabismus is the dominant amblyogenic factor for children under the age of 3 years, but by age 5 years anisometropia and strabismus are equally likely to cause amblyopia.[39] Even when these eye conditions are treated with glasses or eye alignment surgery, the visual deficit remains. The severity of amblyopia is determined by the degree of imbalance between the eye as well as the age of onset of the amblyogenic factor.[93] The presence of amblyogenic factors interferes with the typical development of the visual system, leading to deficits in visual acuity, reduced or complete absence of stereopsis, interocular suppression, and ocular motor dysfunction (i.e., slow saccades, fixation instability, reduced vergence).[36,94,99]

1.3.2 Sensory deficits

A host of monocular deficits are found in the amblyopic eye. The primary deficit used for diagnosis is a significant interocular difference in visual acuity where the affected eye is at least 0.2 logMAR (i.e., 2 lines) worse than the fellow eye.[100–102] This reduction in acuity is in absence of any eye pathology. Other spatial deficits, including contrast sensitivity are present in the amblyopic eye, particularly in anisometropic amblyopia.[100,101,103,104] Amblyopia is also accompanied by a large increase in the spatial extent of foveal crowding in the affected eye, but not the fellow eye, especially in those with strabismic and mixed amblyopia.[100,105]

Binocular deficits such as interocular suppression, reduced stereoacuity, and motion perception deficits are also present in amblyopia and are often quite severe. Due to the unbalanced binocular experience early in life, the brain learns to suppress the visual information from the eye with worse vision and to pay more attention to the stronger, fellow eye. The information from the suppressed eye is still available for visual processing during binocular viewing.[106,107] However, the signals received from the amblyopic eye have been found to be strongly suppressed making them weak and noisy compared to signals from the fellow eye.[107] This chronic interocular suppression is what is thought to lead to amblyopia.[98,107,108] Duration of non-preferred eye suppression is related to the interocular visual acuity difference between the amblyopic and fellow eyes, suggesting that longer suppression leads to worse visual acuity.[106] Worse visual acuity is also related to stronger suppression.[109,110] Visual acuity and stereopsis are not as tightly linked as originally thought, instead depth of suppression is the main visual limitation that influences reduced stereopsis in individuals with strabismus and amblyopia.[107,108,111] Suppression plays a primary role in both the monocular and binocular deficits that people with amblyopia have.[107]

On top of suppression, we also see deficient stereoacuity and poor motion perception in children with amblyopia, which are pervasive and often resistant to treatment. Stereoacuity is significantly worse in individuals with mixed and strabismic amblyopia compared to those with anisometropic amblyopia and controls, however, it is still present in anisometropic amblyopia.[101] Children with amblyopia have deficits in global motion perception, even in the fellow eye.[41,112] Children with amblyopia also show deficits in motion contrast and multiple object tracking, which can affect both the amblyopic eye and the fellow eye and are quite resistant to patching therapies.[113] These deficits persist into adulthood and are a consequence of degraded input to the binocular visual system.[114]

1.3.3 Ocular motor dysfunction

Ocular motor dysfunction in amblyopia and strabismus is well-documented. Fixation instability is found compared to controls, not only in the amblyopic eye but also the fellow eye.[99,102,115] This is accompanied by an increase in amplitude of fixational saccades and inter-saccadic drifts, and fusion maldevelopment nystagmus (FMNS).[36,116–118] Poor fixation instability and increased saccades are associated with slower reading in children with amblyopia.[119–121] Amblyopia is associated with increased saccade latency and amplitude especially when amblyopia was severe and stereoacuity was poor.[122–124] Amblyopic and strabismic individuals also produce more secondary saccades to counteract undershooting or overshooting a target.[122,123] Children with strabismus show an increase in amplitude of catchup saccades and larger disconjugacy of pursuit compared to controls.[125] Adolescents and adults with amblyogenic factors showed unequal vergence amplitudes between the eyes and an increase of corrective saccades to make up for the smaller vergence eye movements.[126]

1.3.4 Critical periods

The critical period of amblyopia – when deprivation can have the greatest effect – is from birth to age 3 years.[39] Up to age 10 years, children are still susceptible to visual deprivation, but the damage is less severe.[39] Parts of the visual system that take longer to develop (i.e., cortical regions) are more vulnerable to disruption from amblyopia.[41] In the monkey model, early visual deprivation causes disruptions in signals to V1, although there is evidence that early visual processing remains intact despite the presence of amblyopia.[127,128] The feedforward network from V1 to V2 remains unchanged. However, deficits found downstream in V2 impose limitations on visual sensitivity in amblyopia,[127,128] suggesting that cortical dysfunction caused by amblyopia is caused by weaking of synapses or the alteration of functional processing in the brain rather than an anatomical disconnection.[127] Neurons in both V1 and V2 display strong interocular suppression, with the degree of suppression in V2 being correlated with the severity of amblyopia.[128] While weaker responses and reduced spatial resolution in V1 and V2 are reported, they are insufficient to explain all of the sensory and ocular motor deficits in amblyopia.

In human studies, amblyopia causes a shift in the neural substrate for motion processing from MT to other regions of the brain such as pulvinar and V3.[129] Monocular deprivation during the critical period induced deficits in binocular vision beginning in the thalamus.[130] V1 has been noted to change substantially under amblyopic conditions including spatial acuity impairments and shifts of ocular dominance which could account for deficits in both acuity and stero-vision.[100,130–132]

1.3.5 Amblyopia Treatment

For many children with amblyopia, the first step in treatment is refractive correction, where up to 30% of children will resolve their amblyopia.[133–137] For those whose amblyopia persists, then occlusion (e.g. patching) of the fellow good eye is prescribed to the child.[133–135] This forces the use of the amblyopic eye to help strengthen its connections to the brain.[133–135] Occlusion improves amblyopic eye visual acuity in up to 90% of children. However, up to 50% never receive age-typical visual acuity following treatment and for those that do, up to 50% will have reoccurring amblyopia.[138,139] Stereoacuity can improve with occlusion,[102] but treatment does not fully remove the stereoacuity deficits and residual deficits persist into adulthood.[104,111] Recently, newer binocular treatments have emerged with the goal of alleviating not only the visual acuity deficit, but also the residual binocular deficits caused by amblyopia.[140,141] Despite the current treatment methods, permanent deficits in visual acuity, depth perception, and suppression persist into adulthood, which can impact the development of other maturing systems such as the motor system.

1.4 Atypical Motor Development

Because amblyopia typically occurs during the critical developmental period for many functions that depend on vision, its presence is likely to have an impact on visuomotor development, including fine and gross motor skills.

1.4.1 Fine Motor Impairments

Fine motor impairments are found during natural binocular viewing conditions in children with childhood eye conditions such as amblyopia and strabismus when assessed using standardized tests for motor ability. Past research using the Movement Assessment Battery for Children (Movement -ABC) and the Bruininks-Oseretsky Test for Motor Proficiency (BOTMP) showed that children with amblyopia and strabismus scored significantly lower overall compared to their peers, putting them in the at-risk category for having total motor impairments. [142–146] Differences in performance on the motor tasks were linked to lack of binocularity and suppression, but not to visual acuity, angle of deviation, age of onset or type/severity of amblyopia.[142,144,145] Another study by Webber et al[146] showed that following 5 weeks of binocular amblyopia treatment, improvements were seen in fine motor skill scores reaching the level of their peers with normal vision. Outside of standardized testing, recent studies found that children with amblyopia had impaired kinematic measures (i.e., longer grasp duration, larger grasp aperture) during fine motor skills with the severity of deficits being correlated with poor stereoacuity but not severity of amblyopia.[147–149]

1.4.2 Gross Motor Impairments

While there has been extensive research on fine motor impairments, there is a little research investigating the impact of amblyopia on gross motor development. Using standardized tests for motor ability while binocularly viewing, postural balance in children with amblyopia and strabismus has been examined. Results from previous studies show that strabismus and anisometropia, both amblyogenic factors, result in below average scores for the static balance subtask (e.g., standing on one or both feet on the floor or a board) of the Movement ABC and BOTMP (e.g. standing on one foot on the floor or on a beam), leaving these children in the at-risk category according to their scores.[142,144,150,151] For the most part, the extent of the motor impairment was based mainly on the binocularity impairment i.e., the lack of stereopsis and extent of suppression, rather than visual acuity, etiology, or the angle of deviation.[142,144] However, one study did mention that amblyopia severity did affect performance with only children with moderate and severe amblyopia experiencing balance deficits compared to mild amblyopia. [144] A recent study by Kelly et al 2023, showed that children with amblyopia had increased sway and a decrease in postural stability during static balance compared to controls, even when both eyes were open.[152]

For dynamic balance, walking in children with impaired vision during childhood caused by strabismus and amblyopia has been paid little attention in the literature. One study reported that children with amblyopia had lower motor performance compared to controls for balance, walking, and jumping tasks. [144] Correlations were observed in this study between balance and both severity of amblyopia and poor stereoacuity.[144] Another study using the Movement ABC saw that children with strabismus performed poorer on a walking tasks with heels raised when compared to controls, the performance on this task improved following corrective surgery.[143] Lastly, another study saw that children with amblyopia performed poorer than their peers during running tasks and had lower scores in stability and locomotor components of the Motor Competence Assessment Battery.[151]

1.5 Research Gap

Amblyopia is a prevalent eye condition, seen in approximately 2-4% of children world-wide. Evidence from previous research shows that amblyopia can impact many aspects of a child's day-to-day life, including motor skills. Fine motor impairments in children with amblyopia are well-documented, with studies finding impaired kinematic measures during reaching and grasping tasks. Recent research is now uncovering evidence of gross motor impairments in amblyopia as well. However, most of this research has used standardized tests for motor ability that only tell us that there is an impairment, rather than describing what their body kinematics are as they perform gross motor tasks such as balance and walking. My research examined gait kinematics during walking in children with amblyopia compared to controls – with the goal of determining if the presence of amblyopia impacts walking in children and whether the impact increased during more complex tasks (i.e., if targets and distractors are placed in the path). I also examined whether clinical (age of onset, amblyopia type) and sensory factors (amblyopic eye visual acuity, stereoacuity, and suppression) were associated with performance.

Chapter 2

Purpose and Hypotheses

2.1 Purpose

This research will provide insight into the effects of pediatric eye conditions that cause amblyopia (i.e., strabismus and anisometropia) on the development of walking by examining gait parameters using a pressure-sensitive mat that can detect footfalls. Exploring gait parameters in children with amblyopia will reveal the role of normal binocular vision during the development of visuomotor abilities, will elucidate the interaction between the visual and motor systems during development, and will shed light on whether deficits arise due to challenges in visual information processing, planning of the movement or both. Findings can be used to help develop targeted interventions and programs to help children with amblyopia succeed physically, socially, and academically in their daily lives.

2.2 Aims

The overall objective of this research is to determine the impact of amblyopia on the development of walking during natural binocular viewing conditions. More specifically, the main aims are to examine whether amblyopia impacts spatial and temporal gait parameters in children (**AIM 1)**, to determine if increasing task complexity will increase any deficits found **(AIM 2),** and to explore whether clinical factors (age of onset, etiology) and sensory factors (amblyopic eye visual acuity, stereoacuity, and suppression) are associated with performance **(AIM 3)**.

2.3 Hypotheses

Hypothesis 1: Compared to controls, children with amblyopia will have impaired gait parameters (e.g. slower pace while walking, shorter stride lengths, less step accuracy) during walking.

Hypothesis 2. Children with amblyopia will perform poorer compared to controls during more complex tasks where they encounter targets and avoid distractors.

Hypothesis 3. Deficits will be correlated to sensory factors, especially those related to binocular function including stereoacuity and suppression of the amblyopic eye.

Chapter 3

Methods

3.1 Participants

The majority of participants were recruited by examining medical records for eligible participants via VisualEyes, the electronic patient database at the School of Optometry clinic at the University of Waterloo. For additional recruitment, I advertised via postcards handed out to eligible participants at their clinic appointment with their optometrist and via word of mouth for recruiting children of family, friends, and colleagues.

3.1.1 Amblyopia Group

A group of participants aged 7 to 13 years were enrolled who were diagnosed with strabismus (esotropia), anisometropia, or both. Each child's diagnosis was confirmed through medical records. Amblyopia was defined as 0.2 logMAR or worse (≥20/32) best-corrected visual acuity (BCVA) in their amblyopic eye, 0.1 logMAR or better (≤20/25) BCVA in their fellow eye, with a ≥2 line visual acuity difference between their eyes. Participants with strabismus had esotropia (infantile or accommodative) with distance ocular misalignment of <10 prism diopters; misalignments >10 diopters are known to prevent proper development of binocular vision and decrease the chance of the child getting some binocular vision function back following treatment.[144,153] Exclusion criteria were preterm birth (<36 weeks), ocular misalignment >10 prisms diopters, co-existing ocular or systemic disease, congenital infection/malformations, or neurological, motor and developmental delays. Amblyopic group characteristics are shown in **Table 3**. See **Appendix A** for individual patient information.

3.1.2 Control Group

A group of age-similar participants with age-typical vision were also enrolled. Inclusion criteria for controls was a monocular BCVA of 0.0 logMAR (20/20) or better for both the left and right eyes, stereoacuity of 1.78 log arcsec or better, and fusion at the farthest distance tested (3 meters) using the Worth 4-dot test. Exclusion criteria were preterm birth (<36 weeks), no ocular misalignment (i.e., orthotropia), co-existing ocular or systemic disease, congenital infection/malformations, or neurological, motor and developmental delays. Control group characteristics are shown in **Table 3.**

3.2 Procedures

3.2.1 Ethics

A parent or legal guardian provided written informed consent after reading the information letter and after explanation of the project and its risks by the experimenter. Each child was given an age-appropriate assent form. For participants <10 years, the form was read to them, and they provided verbal assent to participate in the study. Participants ≥10 years read an assent form themselves and provided written assent.

Before consent/assent was given, the experimenter addressed any questions that either the child or the parent had about the study. This study was reviewed and received ethics clearance through the University of Waterloo Research Ethics Board (#45607) in accordance with the Declaration of Helsinki. Upon completion of the study, participants were given $50, a toy prize and sticker as appreciation for their time.

3.2.2 Vision Assessment

A brief in-lab vision assessment was performed for each child with their habitual refractive error (if required).

1. Monocular crowded best-corrected visual acuity (BCVA): Using the Precision Vision Visual Acuity Testing software (PVAT; Precision Vision®, Inc; Illinois, USA) the Electronic Early Treatment Diabetic Retinopathy Study (e-ETDRS) protocol was used. [154] Monocular BCVA was tested at 3 meters. Participants were asked to identify the letter they saw inside the four crowding lines on the display screen.[154] Results were determined by recording the smallest letter size reliably seen by the participant. Testing began with the amblyopic eye (or right eye for controls), with an adhesive patch placed over the other eye. Then the patch was moved over to the nonamblyopic (or left eye for controls), and the process was repeated.
2. Randot® Preschool Stereoacuity: Stereoacuity was measured at a distance of 40 cm using the Randot® Preschool Stereoacuity (stereoacuity range = 800 – 20 arc seconds) and Stereo Butterfly Tests (stereoacuity range = 2000 – 700 arc seconds

(Stereo Optical, Inc; Illinois, USA).[155] Testing was conducted following the manufacturer's instructions. For each test, participants were asked to identify any images that 'pop out from the book' while wearing polarized glasses overtop of their habitual refractive error. Results were determined by recording the smallest disparity the participant could reliably see.

3. Worth 4-Dot fusion: Fusion or the extent of suppression scotoma was assessed using the Worth 4-Dot test (Bernell® Corporation; Indiana, USA) at 7 different distances (range 0.16 m to 3 m) from the participant.[156] The participant wore red-green glasses over their habitual refractive error. The Worth 4- Dot flashlight was presented at eye level, and the child was asked to indicate how many lights they saw and their colors at the various distances. Results were determined by recording the farthest distance up to 3 meters where the child was able to report seeing 4 lights on the flashlight. This test was conducted to determine the degree at which a participant's eyes are working together otherwise known as fusion.

3.2.3 Walking

To assess gait parameters during walking under binocular viewing conditions, the GAITRite® 17-foot Electronic Walkway (CIR Systems Inc. Sparta, New Jersey, USA) was used. This walkway is pressure-sensitive and measures temporal and spatial parameters during walking by detecting footfalls using 32,000 individual sensors.

Sensor data can be visualized, processed, and exported using the GAITRite® custom software (**Figure 1**).

Figure 1. GAITRite® footfall data visualization example for one walking trial of a child walking from left to right. Purple = Right foot, Teal = Left foot.

The GAITRite® mat was placed on the floor with 2 yellow X's at a distance of 3 feet from both ends of the mat (total walking distance = 23 feet), indicating where the participant was to start and stop **(Figure 2)**. The X's allowed enough room for at least two steps before the active area to reach typical stride pattern and speed before they hit the mat, as well as room to slow down after they have stepped off the mat.[157,158]

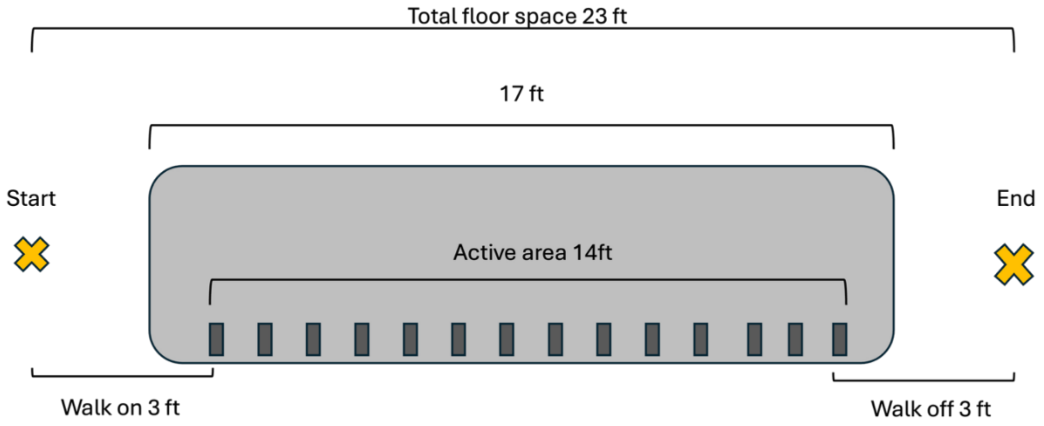

Figure 2. GAITRite® mat setup on the floor. The yellow X's indicate start and end locations for participants, allowing for 3 meters on either side of the active mat area for proper walk on and

walk off distances. During each trial, the participant walked 23 feet in total (17 feet on the mat) with 14 feet of actual active area where footfall data was recorded. The dark grey rectangles are the control panels for the sensors inside the mat.

Following the vision assessment, leg length (cm) was measured from the hip bone to the bottom of the shoe using a soft measuring tape, as required by the GAITRite® protocol to calculate gait measures and as described in previous studies.[159–163] Each child walked the length of the walkway under 3 separate conditions (**Table 1**) that were pseudorandomized and counterbalanced: 1) *Straight Walk (*SW): the participant was asked to walk the length of the walkway at their normal pace with nothing on the mat, 2) *Isolated Target Walk (IT)*: the participant was asked to walk the length of the walkway at their normal pace while stepping on two targets placed in their path on the mat, 3) *Distractor Target Walk (DT)*: the participant was asked to walk the length of the walkway at their normal pace while stepping on two targets and avoiding two distractors placed in their path on the mat (**Figure 3**).

Table 1. Task description per experimental condition (straight walk [SW], isolated target walk [IT], distractor target walk [DT]).

Condition	Task Description
Straight Walk (SW)	Walk the length of the walkway
Isolated Target Walk (IT)	Walk the length of the walkway and step on 2 targets (turtle) placed on the walkway 
Distractor Target Walk (DT)	Walk the length of the walkway and step on 2 targets (turtle) while avoiding 2 distractors (fish) placed on the walkway  

Targets (turtle) and distractors (fish) were 15 cm x 15 cm 2-dimensional laminated paper circles with a rubber backing to prevent slipping that contained well-known characters from the cartoon Disney Pixar movie ‘Finding Nemo’. The targets were white circles with Squirt the turtle and the distractors were blue circles with Nemo the fish. In the SW condition, no targets or distractors were placed on the mat (**Figure 3A**). In the IT and DT conditions (**Figure 3B & C**), two targets were placed on the walkway 158 cm (Target, T1) and 378 cm (Target 2, T2) from the beginning of the mat. Targets were placed on either the right side (39.5 cm from the edge of the mat) or on the left side (65 cm from the edge of the mat) of the mat. The vertical distance between targets was 220 cm, which was calculated based on twice the average stride length of

8-12 years olds (110cm).[159–163] In the DT condition (**Figure 3C**), distractors were placed on the walkway 97 cm (Distractor 1, D1) and 317 cm (Distractor 2, D2) from the start of the mat. They were placed either to the left side (65 cm from the edge of the mat) or in the center (52.2 cm from the edge of the mat). The distractors were placed 220 cm apart and were 60 cm away from the closest target.

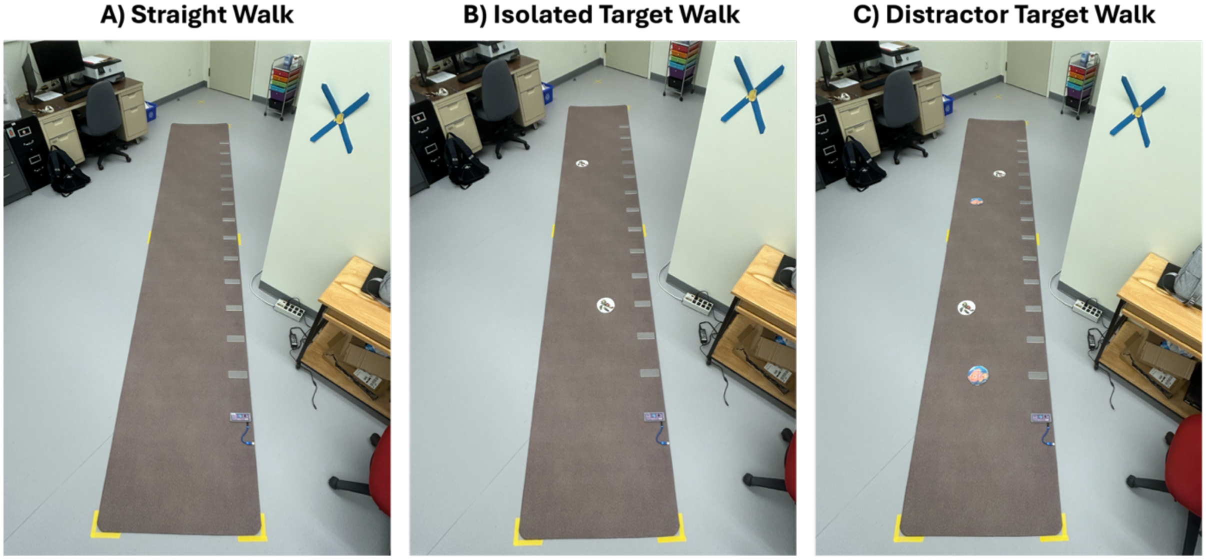
A) Straight Walk
B) Isolated Target Walk
C) Distractor Target Walk

Figure 3. Examples of the setup of each of the three conditions. A) straight walk (SW), B) isolated target walk (IT) with 2 targets on the walkway, C) distractor target walk (DT) with the 2 targets and 2 distractors on the walkway. The blue cross on the wall is the fixation target that participants looked at prior to starting each trial.

Prior to walking, the experimenter gave verbal instructions and physically demonstrated each condition to the participant. While viewing binocularly, participants were instructed to walk at their normal pace and to not run, jump, or step off of the mat and to make sure they do not look at anyone in the room as they completed the walk. Participants were instructed to try and step on each target with as much of their foot as possible, and to not step on the distractors. For each trial, participants were instructed to stand on a yellow X on the floor 3 feet away from the start of the GAITRite® walkway. While here, they were asked to fixate on a yellow fish (bubbles from finding nemo) in the middle of a blue fixation cross on the wall at eye level (See **Figure 3**). Participants were instructed to continue fixating on the cross until they heard the experimenter say the word “GO”, and then to look at the mat and begin their walk.

Participants completed 1 practice trial of each of the three conditions (3 practice trials in total) to ensure they understood the task. Feedback was given if the child did not step on the target properly or if they stepped off the mat. Following practice trials, each participant completed 10 experimental trials per condition (30 experimental trials in total). Participants were given an opportunity to take a 10-minute break after the 18th trial if they were feeling tired. Two experimenters were always present during testing – one to set up targets and distractors and carefully observe while taking notes as the child completed each trial, and one to operate the GAITRite® and instruct the child when to begin each trial, along with observing the child walk.

For IT and DT trials, T1 and T2 were placed on the right and left, respectively, for 50% of trials and vice versa for the remaining 50% of trials. For DT trials, D1 and D2 were placed on the left and center, respectively, for 50% of trials and vice versa for the remaining 50% of trials. Thus, there were 5 different trial types – 1 SW, 2 IT, and 2 DT (shown in **Figure 4)**. All target-distractor placement combinations were pseudo-randomized.

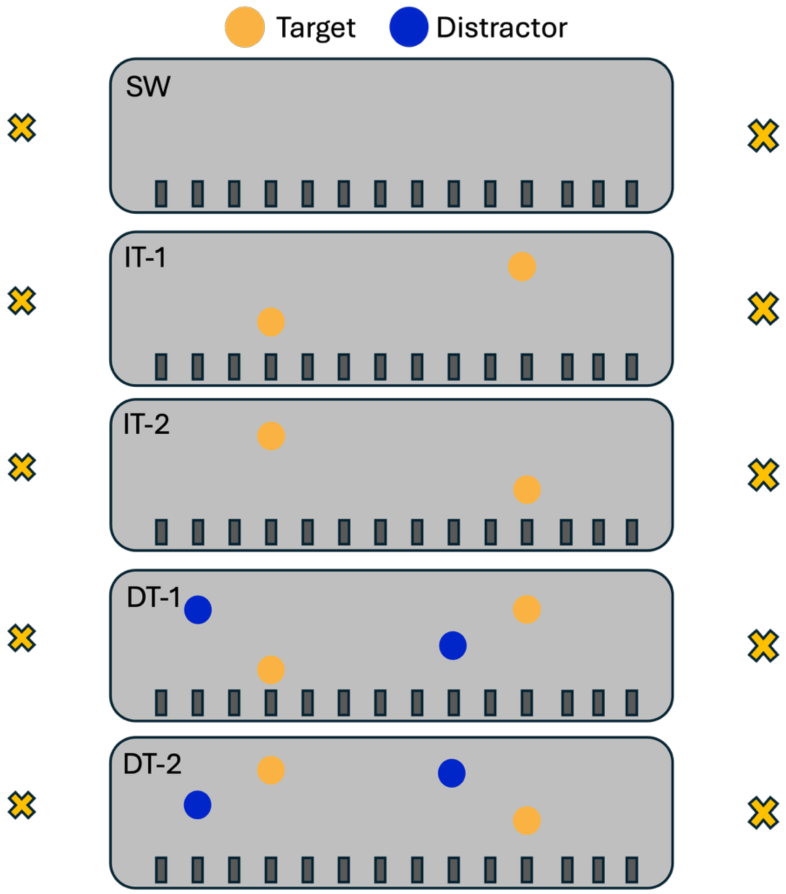

Figure 4. Schematic of the mat setup for all 5 trial types showing the placement of targets (orange circles) and distractors (blue circles) for the straight walk (SW), isolated target walk (IT), and distractor target walk (DT) conditions.

3.3 Outcome Measures

Gait parameters were calculated from the GAITRite® program and included both temporal and spatial outcomes commonly studied (see **Table 2**). Temporal outcomes include; 1) *Normalized Velocity*: walking speed, calculated by dividing the velocity by leg length and is expressed in units of leg lengths per second (LL/sec), 2) *Cadence*: step frequency, which tells us the pace of walking measured in units of steps per minute (SPM), 3) *Step Time*: time from first contact of one foot to first contact of the opposite foot on the mat, measured in milliseconds (msec). 4) *Stance Time*: time between the first contact of the heel and the last contact of the toe of the same foot, which tells us the ground contact time of steps, measured in msec. Spatial outcomes include; 1) *Step Length*: distance from the center of the heel of the footstep to the center of the heel of the next footstep from the opposite foot, measured in centimeters (cms), 2) *Step Width*: distance from the midline midpoint of the current footstep to the midline midpoint of the next footstep of the opposite foot, measured in cms, 3) *Step Accuracy*: accuracy of stepping on targets and avoiding distractors, measured as a percentage (%). I also examined variability in each participant's gait pattern by calculating the coefficient of variation (COV) for each outcome measure, which is the standard deviation divided by the mean of the gait parameter multiplied by 100 (SD/X*100), expressed as a percent. Higher COV represents more variability (i.e., less consistency between trials).

Table 2. Temporal and spatial outcome measures.

Outcome Measure	**Description**
Temporal	
Normalized Velocity	Speed of walking (leg lengths per second, LL/sec)
Cadence	Step frequency (steps per minute, SPM)
Step Time	Time between footfalls (msec)
Stance time	Duration of time a foot remains on the mat (msec)
Spatial	
Step Length	Distance between footfalls (cms)
Step Width	Distance between midline of opposite feet (cms)
Step Accuracy	Accuracy of stepping on targets/avoiding distractors (%)

The GAITRite® data analysis program is unable to confirm whether the participant stepped on the targets or avoided the distractors. To account for this, the lab built a custom program to visualize and process the accuracy data using Visual Studio Code, Version 1.101.2 (Microsoft Corporation, 2015). Target and distractor locations were first calibrated using the GAITRite® by pressing on individual sensors around each circle corresponding to the top, bottom, left, and right (4 sensors in total per circle) to provide X,Y locations. This information was used to provide target/distractor locations to the custom code program and allowed us to determine whether targets or distractors were stepped on, which was used to calculate step accuracy. A visualization of each condition using this custom program is shown in **Figure 5**. Accuracy was determined by whether there was an intersection of the footfall and a target circle or distractor circle in the program. This intersection was based on whether there was any overlap in the x and y coordinates of the footfall and the x and y coordinates of the target and distractor placement.

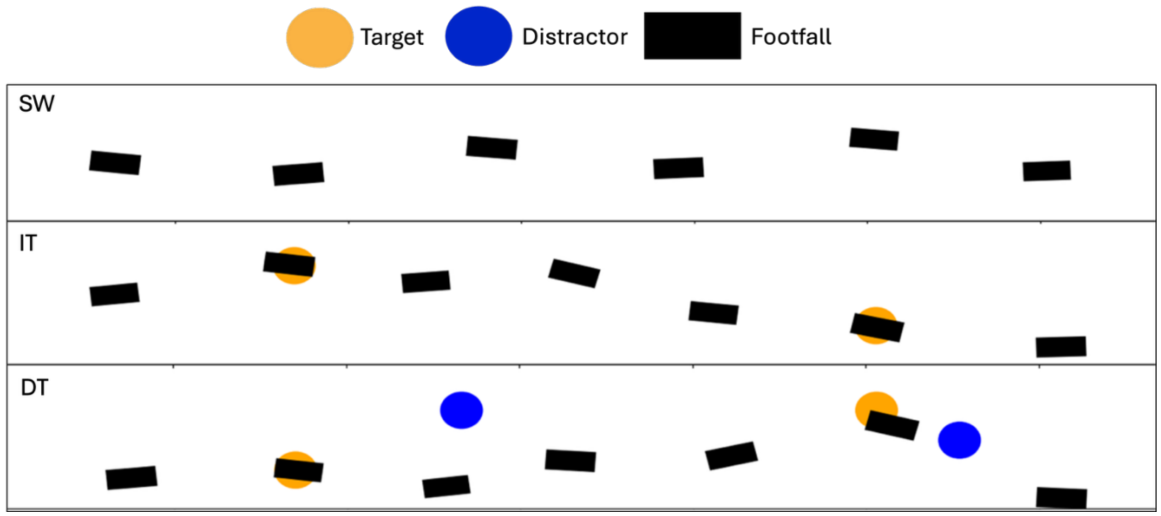

Figure 5. Examples of trials from one participant using the custom-built data visualization program to determine accuracy for each of the three conditions (SW. straight walk; IT, isolated target; DT, distractor target). The black rectangles are the participant's footfalls. The participant successfully stepped on all targets (orange circles) and avoided all distractors (blue circles).

3.4 Sample Size and Power Calculation

This study is cross-sectional. A sample size of 15 per group (amblyopic and control) was calculated to detect group differences of 15% with $a=0.05$ and $1-B=0.2$. The sample size was determined based on a previous study that examined gait parameters in stereodeficient individuals.[164] To account for unusable data and secondary analyses, my goal was to enroll a total of 40 children (20 per group).

3.5 Data Analysis

Independent t-tests and mixed model analysis of variance (ANOVAs) with Bonferroni post hocs to adjust for multiple comparisons were completed to determine group differences in walking outcomes between the amblyopic group and controls for all variables. Normality was tested using Kolmogorov-Smirnov test. Mauchly's test for sphericity was conducted for all variables tested with ANOVA's and if sphericity had been violated the degrees of freedom were corrected using Greenhouse-Geisser. Mann Whitney U tests were used to examine group differences in step accuracy, and Wilcoxon signed ranks tests were used to examine differences in accuracy between conditions per group. A secondary analysis was conducted to determine the impact of sensory and clinical factors on performance of children with amblyopia using independent t-tests and Pearson r bivariate correlations controlling for leg length.

Chapter 4

Results

4.1 Group Characteristics

A total of 48 participants were enrolled, with 21 children in the amblyopia group (12 female), and 27 children in the control group (15 female). The amblyopia group included children with amblyogenic factors of strabismus (n=7; 6 accommodative esotropia, 1 infantile esotropia) and anisometropia (n=14; 10 hyperopic anisometropia, 3 astigmatic anisometropia, 1 myopic anisometropia), with 15/21 (71%) having current amblyopia. A total of 6 (29%) of children with strabismus (n=5) or anisometropia (n=1) that were enrolled did not have amblyopia at the time of testing but were included in the analysis in the 'amblyopia' group because they still had impaired binocularity. The amblyopia and control groups did not differ in age (amblyopia, mean age ± standard deviation [SD] = 9.6±1.9 years vs control, 10.4 ± 1.8 years, t_{46}=1.61, p=0.12) or leg length (amblyopia, mean leg length ± SD = 82±10 cms vs control, 86 ± 9 cms, t_{46}=1.46, p=0. 15). See **Table 3** for group characteristics.

Table 3. Group characteristics.

	Amblyopia (n=21)	**Control (n=27)**	**Amblyopia VS Control**
Sex: F, n (%)	12 (57)	15 (55)	*p*=0.91
Etiology, n (%)			
Strabismus[a],	7 (33)	n/a	n/a
Anisometropia[b]	14 (67)	n/a	n/a
Age, Mean±SD[c] years	9.6±1.9	10.4±1.8	*p*=0.12
(range)	(7.0 to 13.6)	(7.5 to 13.3)	
Leg Length, Mean±SD cms[d]	82±10	86±9	*p*=0.15
(range)	(69 to 99)	(72 to 101)	
AE[e] BCVA,[f] Mean±SD logMAR[g]	0.4±0.3	0.0±0.1	*p*<0.001
(Snellen equivalent)	(20/40±3 lines)	(20/20±1 lines)	
(range)	(−0.1 to 1.0)	(−0.2 to 0.2)	
FE[h] BCVA, Mean±SD logMAR	0.0±0.1	−0.1±0.1	*p*=0.113
(Snellen equivalent)	(20/20±1 lines)	(20/16±1 lines)	
(range)	(−0.2 to 0.2)	(−0.1 to 0.2)	
Stereoacuity, Mean±SD log arcsec	2.6±0.7	1.6±0.0	*p*<0.001
(range)	(1.8 to 4)	(1.6 to 1.8)	
Worth 4-dot Fusion, Mean±SD log deg	0.2±0.4	−0.1±0.0	*p*<0.001
(range)	(−0.2 to 1.2)	(−0.2 to 0.0)	

a. All esotropic (infantile = 1, accommodative = 6)
b. 10 hyperopic anisometropia, 3 astigmatic anisometropia, 1 myopic anisometropia
c. SD, standard deviation
d. cms, centimeters
e. AE, amblyopic eye. For control children, the right eye is listed for amblyopic eye best-corrected visual acuity
f. BCVA, best corrective visual acuity
g. logMAR, logarithm of the minimum angle of resolution
h. FE, fellow eye. For control children, the left eye is listed for fellow eye best-corrected visual acuity

4.2 Temporal Measures

4.2.1 Normalized Velocity

There was no significant group x condition interaction for normalized velocity ($F_{1.3,\ 60.4} = 2.63$, $p=0.10$, $\eta^2= 0.05$). While there was no significant main effect of group for normalized velocity ($F_{1,46} = 0.54$, $p=0.47$, $\eta^2= 0.01$), there was a significant main effect of condition ($F_{1.3,60.4} = 32.99$, $p<0.001$, $\eta^2= 0.42$). Collapsed across group (**Figure 6**), posthoc pairwise comparisons showed a decrease in normalized velocity (i.e. became slower) as the walking conditions got more complex (SW, mean±SD = 1.59±0.28 LL/sec; IT, 1.51±0.26 LL/sec; DT, 1.45±0.25 LL/sec; all p's ≤ 0.001).

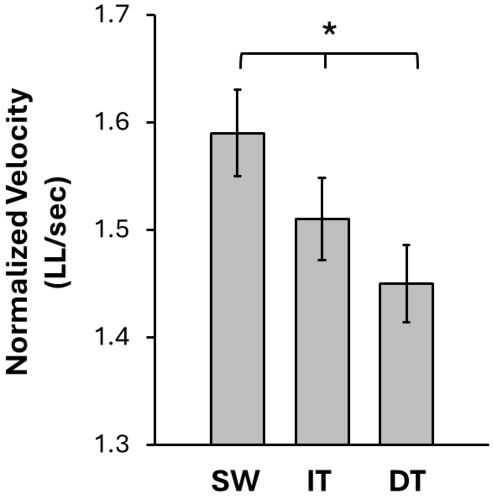

Figure 6. Bar graph depicting normalized velocity (LL/sec) collapsed across group. Normalized velocity decreased as conditions became more complex, with significant differences observed between all three conditions (SW: straight walk , IT: isolated target walk, DT: distractor target walk). Error bars represent ± standard error of the mean (SEM). *p <0.05

4.2.2 Cadence

The group x conditions interaction was significant for cadence ($F_{1.7,78.5}$= 4.12, p=0.025, η_p^2= 0.08). While there was no significant main effect of group for cadence ($F_{1,46}$= 0.16, p=0.69, η_p^2= 0.003), there was a significant main effect of condition ($F_{1.7,78.5}$= 31.0, p<0.001, η_p^2= 0.40). Simple effects analysis (**Figure 7**) indicate that while there was no group difference on any of the three conditions (all p's≥0.39), there was a significant decrease in cadence (i.e., less steps per minute) from SW to IT and DT for both the amblyopia group (SW, 125±16 spm vs IT, 120±13 spm, p<0.001, and DT 118±13 spm, p<0.001) and the control group (SW, 121±14 spm vs IT, 119±13 spm, p=0.04 and DT 118±13 spm, p=0.007). However, there was no significant difference between IT and DT for the amblyopia (p=0.21) or control (p=0.36) groups.

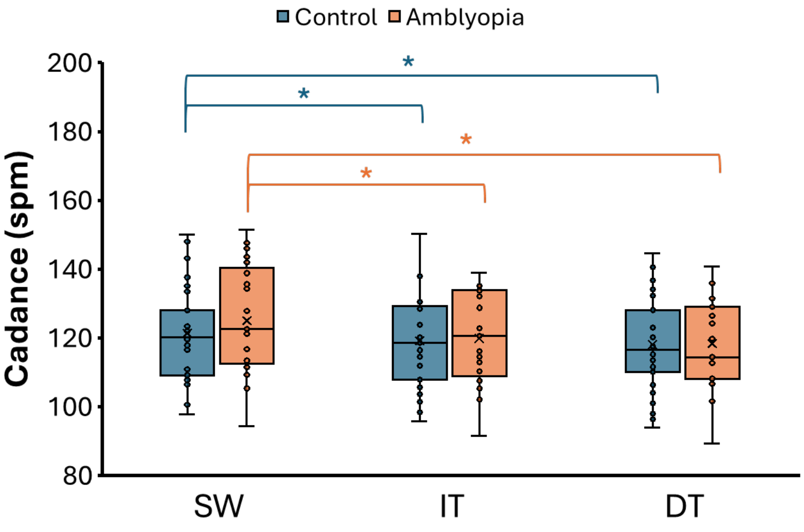

Figure 7. Box-and-whisker plots of distribution of cadence (spm) across condition (SW: straight walk, IT: isolated target walk, DT: distractor target walk) between the control group (blue) and

the amblyopia group orange). The horizontal line within each box represents the median normal control score, the boxes correspond to the 25th to 75th percentiles, and the whiskers correspond to the 5th and 95th percentiles. Individual data points for each participant are plotted (open circles). Both groups showed a decrease in cadence from SW to both IT and DT, but no difference between IT and DT. $^*p<0.05$

4.2.3 Step Time

The group x condition interaction was significant for step time ($F_{2,92}=3.35$, $p=0.039$, $\eta_p^2= 0.07$). While there was no significant main effect of group ($F_{1,46}= 0.09$, $p=0.77$, $\eta_p^2= 0.002$), the was a significant main effect of condition for step time ($F_{2,92}=37.9$, $p<0.001$, $\eta_p^2= 0.45$). Simple effects analysis (**Figure 8**) indicate there was no group difference on any of the three conditions (all p's≥0.48). However, there was a significant increase in step time from SW to IT and DT for both the amblyopia group (SW, 488±64 msec vs IT, 509±59 msec, $p<0.001$, and DT, 515±59 msec, $p<0.001$) and the control group (SW, 501±55 msec vs IT, 511±57 msec, $p=0.008$ and DT 516±60 msec, $p<0.001$). However, there was no significant difference between IT and DT for the amblyopia ($p=0.21$) or control ($p=0.25$) groups.

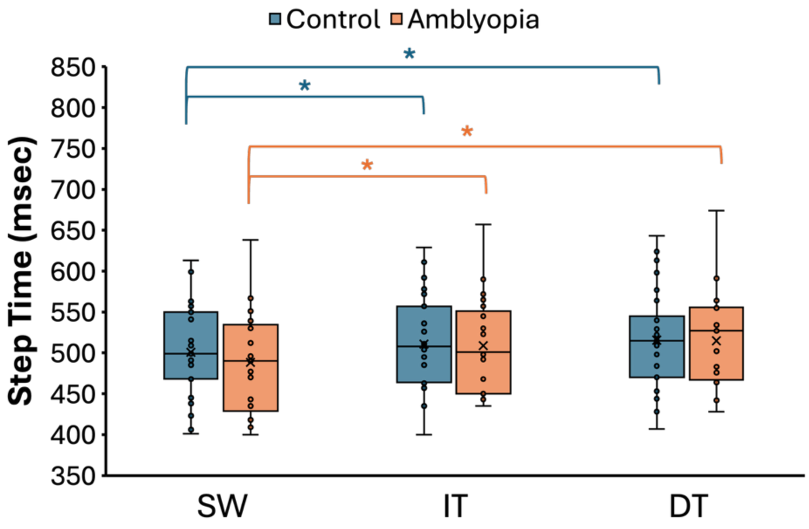

Figure 8. Box-and-whisker plots of distribution of step time (msec) across condition (SW: straight walk, IT: isolated target walk, DT: distractor target walk) between the control group (blue) and the amblyopia group (orange). The horizontal line within each box represents the median normal control score, the boxes correspond to the 25th to 75th percentiles, and the whiskers correspond to the 5th and 95th percentiles. Individual data points for each participant are plotted (open circles). Both groups showed an increase in step time from SW to both IT and DT, but no difference between IT and DT. *p<0.05

4.2.4 Stance Time

The group x condition interaction was significant for stance time ($F_{1.7, 80.2} = 4.59$, $p=0.013$, $\eta_p^2 = 0.09$). While there was no significant main effect of group on stance time ($F_{1,46}=0.03$, $p=0.86$, $\eta_p^2 = 0.001$), there was a significant main effect of condition ($F_{1.7, 80.2} = 32.9$, $p<0.001$, $\eta_p^2 = 0.42$). Simple effects analysis (**Figure 9**) indicate there was no group difference on any of the three conditions (all p's≥0.53). The amblyopia group had significantly shorter stance time from SW to IT and DT (SW, 594±87 msec vs IT, 618±80 msec, $p<0.001$, and DT, 624±79 msec, $p<0.001$), but no significant difference between IT and DT ($p=0.18$). The control group had significantly shorter stance time from SW to DT (SW, 608±77 msec vs DT, 624±81 msec, $p=0.003$) and a trend for significance between IT and DT (IT, 616±79 msec, $p=0.054$). No difference in stance time was found between SW and IT ($p=0.14$) for the control group.

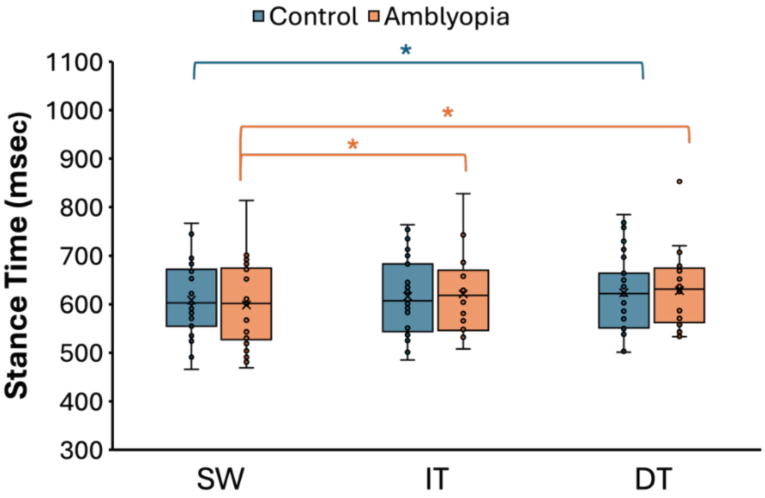

Figure 9. Box-and-whisker plots of distribution of stance time (msec) across condition (SW: straight walk , IT: isolated target walk, DT: distractor target walk) between the control group (blue) and the amblyopia group (orange). The horizontal line within each box represents the median normal control score, the boxes correspond to the 25th to 75th percentiles, and the whiskers correspond to the 5th and 95th percentiles. Individual data points for each participant are plotted (open circles). The amblyopia group had increased stance time from SW to both IT and DT, while the control group only had an increase between SW and DT. $^*p<0.05$

4.3 Spatial Measures

4.3.1 Step Length

There was no significant group x condition interaction for step length ($F_{1.4,66.3}$= 0.37, p=0.62 η_p^2= 0.008). While there was no significant main effect of group for step length ($F_{1,46}$=0.98 p=0.33, η_p^2= 0.02), there was a significant main effect of condition ($F_{1.4,66.3}$= 5.99, p=0.009, η_p^2= 0.12). Collapsed across group (**Figure 10**), posthoc pairwise comparisons showed a decrease in step length from SW to DT (p=0.027) and IT to DT (p=0.016) (SW, mean±SD = 64.4±5.8 cm; IT, 63.5±5.8 cm; DT, 62. 2±7.1 cm). No significant difference in step length between SW and IT was found (p=0.51).

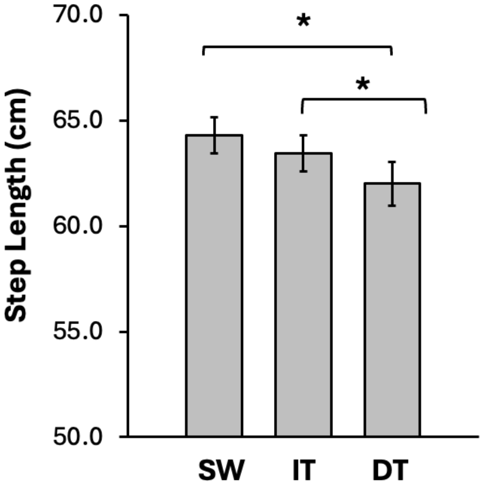

Figure 10. Bar graph depicting step length (cm) collapsed across group. Step length decreased from SW to DT and IT to DT but not from SW to IT (SW: straight walk , IT: isolated target walk, DT: distractor target walk). Error bars represent ± standard error of the mean (SEM). *p <0.05,

4.3.1 Step Width

There was no significant group x condition interaction for step width ($F_{1.4, 65.5}$= 0.27, p=0.69, η_p^2= 0.006). There was no significant main effect of group for step width ($F_{1,46}$=0.79 p=0.38, η_p^2= 0.017). There was no significant main effect of condition on step width ($F_{1.4, 65.5}$= 2.47, p=0.11 , η_p^2= 0.05).

4.4 Step Accuracy

Children with amblyopia were significantly less accurate than controls in overall target accuracy, (amblyopia, 90.8±8.5% vs control, 96.9±3.8%, U = 144, p=0.003), but not for distractor accuracy (amblyopia, 99.8±1.1% vs control, 99.3±2.7%, U = 275, p=0.67) shown in **Figure 11A**. I further probed the reduced target accuracy to determine whether it was impacted by condition (SW, IT, DT) or target placement (near T1, far T2). The amblyopia group had significantly reduced accuracy in the IT condition (amblyopia, 89.7±9.7% vs control, 96.5±5.3%, U = 155, p=0.005) and trended towards having reduced accuracy in the DT condition, but this was not significant (amblyopia, 92.1±10.3% vs control, 97.2±4.5%, U = 204, p=0.07), shown in **Figure 11B**. Further, the amblyopia group had significantly reduced accuracy for the far T2 target compared to controls (amblyopia, 87.4±13.9% vs control, 97.2±5.4%, U = 140, p=0.001), but no difference was found for the near T1 target (amblyopia, 94.3±6.6% vs control, 96.5±4.6%, U = 242, p=0.35), shown in **Figure 11C**. The amblyopia group had significantly reduced accuracy for far T2 compared to near T1 (Z = 2.09, p=0.037), but the control group did not (Z = 0.94, p=0.35), shown in **Figure 11C**.

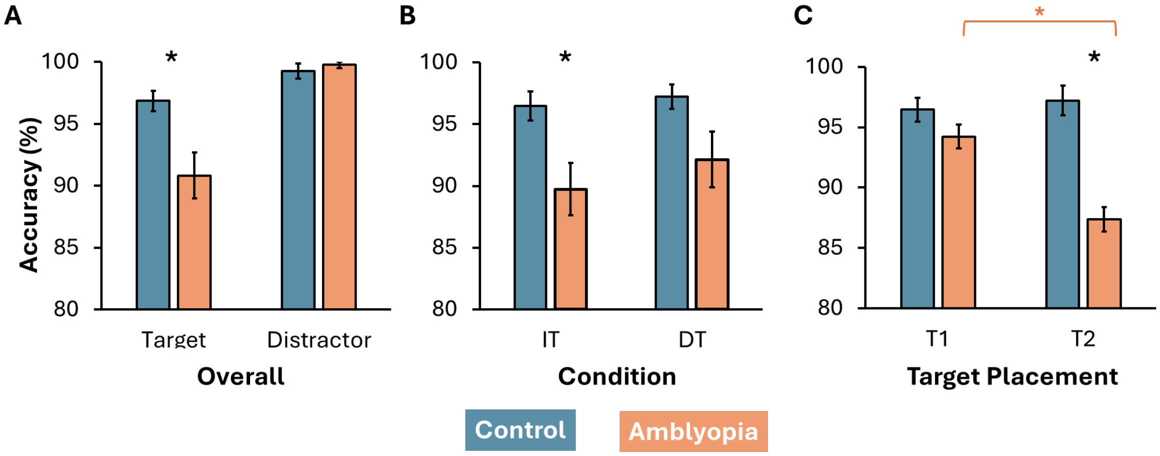

Figure 11. Bar graphs depicting step accuracy (%) between the control group (blue bars) and the amblyopia group (orange bars). Overall, the amblyopia group was less accurate than controls at stepping on targets (*Panel A)*.The amblyopia group was also less accurate than controls during the isolated target (IT) condition (*Panel B*), and at stepping on the far target 2 (T2) (*Panel C*). The amblyopia group was less accurate at stepping on T2 when compared to T1 (*Panel C*). Error bars represent ± standard error of the mean (SEM). *p <0.05,

4.5 Coefficient of Variation (COV)

4.5.1 Temporal Measures

4.5.1.1 Normalized Velocity

There was no significant group x condition interaction for normalized velocity COV ($F_{2,90}$ = 0.023, p=0.98, η^2=0.001). While there was no significant main effect of condition for normalized velocity COV ($F_{2,90}$=1.97, p=0.15, η^2= 0.04), there was a significant main effect of group ($F_{1,45}$=8.10, p=0.007, η^2=0.15). Collapsed across condition (**Figure 12**), posthoc pairwise comparisons revealed that children with amblyopia had higher COV (i.e., more variable normalized velocity) compared to controls (amblyopia mean±SD=8.9±3.0% vs control mean±SD=6.4±3.0%; p=0.007).

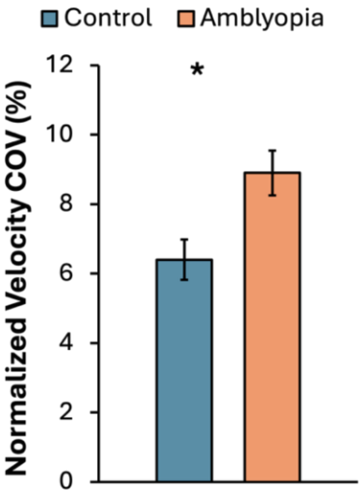

Figure 12. Bar graph depicting normalized velocity COV (%) collapsed across condition. Children with amblyopia (orange bars) were more variable in normalized velocity compared to controls (blue bars). Error bars represent ± standard error of the mean (SEM). *P <0.05,

4.5.1.2 Cadence

The interaction between group x condition was trending but did not reach significance for cadence COV ($F_{2,90}$=2.42, p= 0.095, η_p^2= 0.05). A significant main effect of group was found for cadence COV ($F_{1,45}$= 5.23, p=0.027, η_p^2= 1,04). A significant main effect of condition was seen on cadence COV ($F_{2,90}$=12.1, p<0.001, η_p^2= 0.21). Simple effects analysis **(Figure 13**). indicate that the amblyopia group had higher cadence COV (i.e., more variable cadence) than controls for SW (amblyopia mean±SD=5.04±2.42 % vs control mean±SD=3.25±1.71 % ; p=0.005), with a trend towards significance for IT (amblyopia mean±SD=6.08±2.37 % vs control mean±SD=5.00±1.63 %; p=0.071). No group differences were seen for DT (amblyopia mean±SD=5.58±2.58 % vs control mean±SD=5.15±1.52 %; p=0.48). The amblyopia group showed no significant differences in cadence COV between conditions (all p's≥0.108). However, controls showed a significant increase in cadence COV from SW to IT and DT (all ps<0.001), but not between IT to DT (p=1.00).

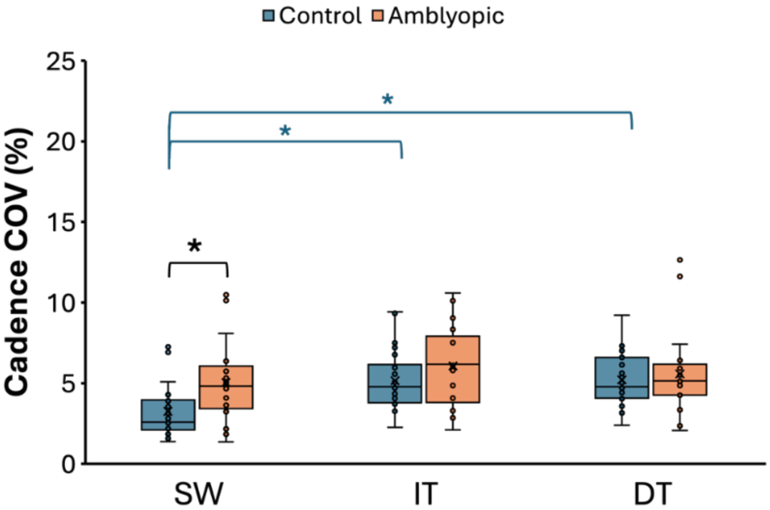

Figure 13. Box-and-whisker plots of the distribution of cadence COV (%) across condition (SW: straight walk , IT: isolated target walk, DT: distractor target walk) between the control group (blue) and amblyopia group (orange). The amblyopia group was more variable than

controls for SW only and had no within condition differences. The control group had higher COV from SW to both IT and DT, but no differences between IT and DT. The horizontal line within each box represents the median normal control score, the boxes correspond to the 25th to 75th percentiles, and the whiskers correspond to the 5th and 95th percentiles. Individual data points for each participant are plotted (open circles).

4.5.1.3 Step Time

The interaction between group x condition was significant for step time COV ($F_{2,90}$=3.19, p=0.046, η_p^2= 0.07).While there was no significant main effect of group for step time COV ($F_{1,45}$=2.10, p=0.15, η_p^2= 0.045), there was a significant main effect of condition ($F_{2,90}$=10.7, p<0.001, η_p^2= 0.19). Simple effects analysis (**Figure 14**). indicate that the amblyopia group had higher step time COV (i.e., more variable timing between steps) than controls for SW only (amblyopia mean±SD=4.90±2.54 % vs control mean±SD=3.47±2.10 %; p=0.040). No group differences were found for IT (amblyopia mean±SD=6.04±2.52 % vs control mean±SD=5.16±1.87 %; p=0.17) or DT conditions (amblyopia mean±SD=5.19±1.81 % vs control mean±SD=5.36±1.79% ; p=0.76). The amblyopia group showed no significant differences in step time COV between conditions (all p's≥0.087). However, controls showed a significant increase in step time COV from SW to IT and DT (all ps<0.001), but not between IT to DT (p=1.00).

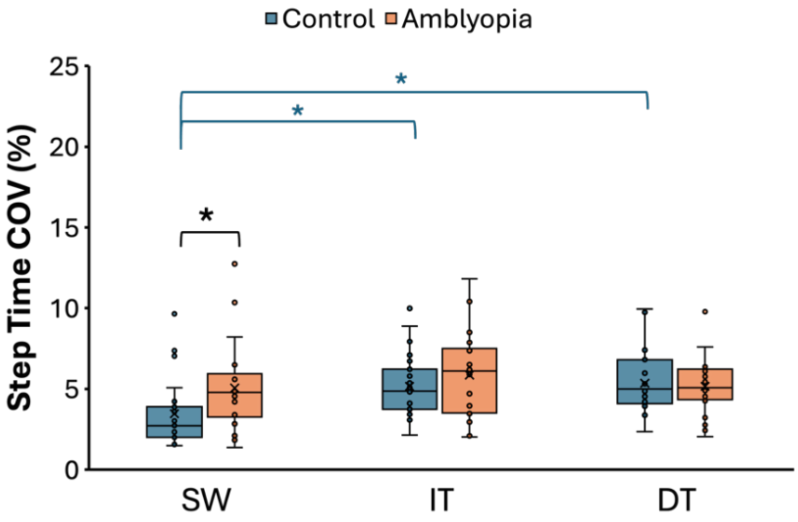

Figure 14. Box-and-whisker plots of the distribution of step time COV (%) across condition (SW: straight walk , IT: isolated target walk, DT: distractor target walk) between the control group (blue) and amblyopia group (orange). The horizontal line within each box represents the median normal control score, the boxes correspond to the 25th to 75th percentiles, and the whiskers correspond to the 5th and 95th percentiles. Individual data points for each participant are plotted (open circles). The amblyopia group was more variable than the control group for SW only and had no within condition differences. The control group had an increase in step time COV from SW to both IT and DT, but no differences between IT and DT.

4.5.1.4 Stance Time

The group x condition interaction was not significant for stance time COV ($F_{1.7,76.2}$ = 2.06, p=0.14, η_p^2= 0.04). While there was no significant main effect of condition on stance time COV ($F_{1.7,76.2}$ = 1.7, p=0.19, η_p^2= 0.04). However, there was a significant main effect of group for stance time COV ($F_{1,46}$=4.08, p=0.049, η_p^2= 0.08). Collapsed across conditions (**Figure 15**), pairwise comparisons showed that the amblyopia group had higher stance time COV (i.e., more variable ground contact time) than controls (amblyopia mean±SD=5.71±1.79 % vs control mean±SD=4.66±1.79%; p=0.049).

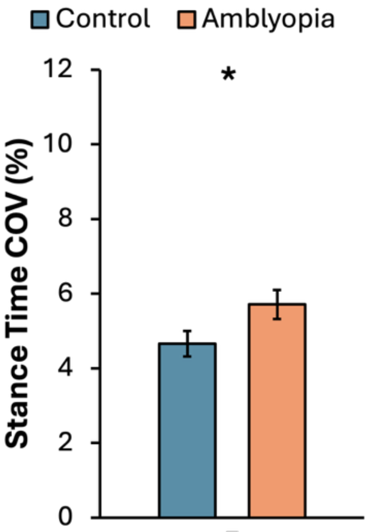

Figure 15. Bar graph depicting stance time COV (%) collapsed across condition. The amblyopia group (orange bars) was more variable in stance time compared to controls (blue bars). Error bars represent ± standard error of the mean (SEM). *p <0.05

4.5.2 Spatial Measures

4.5.2.1 Step Length

The group x condition interaction was not significant for step length COV ($F_{2,92}$ =0.06, p=0.94 η_p^2= 0.001). There was a significant main effect of group for step length COV ($F_{1,46}$=5.47, p=0.024, η_p^2= 0.11) and a significant main effect of condition ($F_{2,92}$ =

30.1, $p<0.001$, $\eta_p^2 = 0.40$). Collapsed across condition **(Figure 16A)**, posthoc pairwise comparisons revealed higher step length COV (i.e., more variable distance between steps) in the amblyopia group than controls (amblyopia mean±SD=7.99±2.38% vs control mean±SD=6.37±2.39%; p=0.024). Collapsed across groups **(Figure 16B),** posthoc pairwise comparisons showed increased step length COV from SW to IT and DT (SW, 4.9±2.4% msec vs IT, 8.3±3.6%, p<0.001, and DT, 8.1±3.3%, p<0.001). However, there was no significant difference between IT and DT (p=1.00).

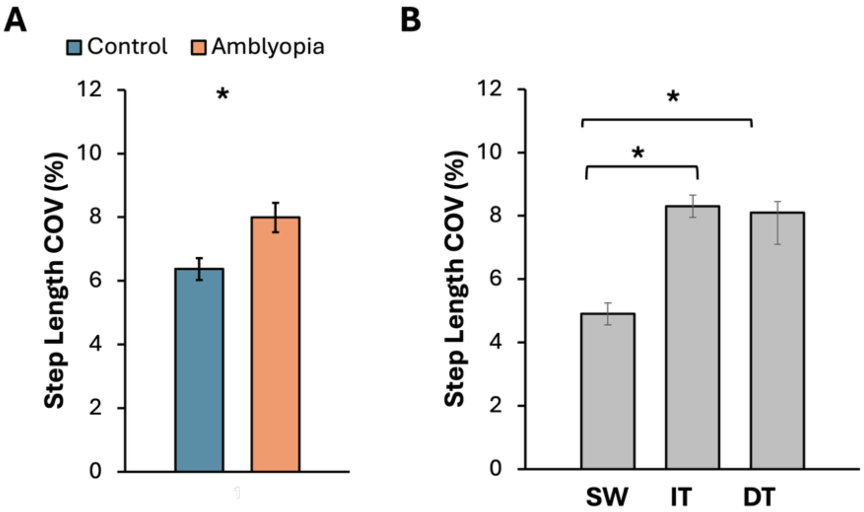

Figure 16. Bar graph depicting step length COV (%). Collapsed across condition (Panel A), the amblyopia group (orange bars) was more variable in step length compared to controls (blue bars). Collapsed across groups (Panel B), step length COV increased between SW and both IT and DT, but not between IT and DT (SW: straight walk , IT: isolated target walk, DT: distractor target walk). Error bars represent ± standard error of the mean (SEM). *p <0.05,

4.5.2.2 Step Width

The group x condition interaction was not significant for step width COV ($F_{2,92}$ = 0.003, p=0.99 η_p^2= 0.001). There was a significant main effect of group for step width COV ($F_{1,46}$=6.60, p=0.014, η_p^2= 0.13) and a significant main effect of condition ($F_{2,92}$ = 26.47, p<0.001, η_p^2= 0.37). Collapsed against conditions **(Figure 17A)**, pairwise comparisons revealed higher step width COV (i.e. more variable gait width) for the amblyopia compared to control group (amblyopia, mean±SD=7.74±2.18% vs control mean±SD=6.11±2.18%; p=0.014). Collapsed across groups **(Figure 17B)**, posthoc pairwise comparisons showed increased step width COV from SW to IT and DT (SW, mean±SD = 4.8±2.4% vs IT, 8.0±3.3 %, p<0.001 and DT, 7.7±3.1%, p<0.001). However, there was no significant difference between IT and DT (p=1.00). **Figure 18** shows examples of variability in spatial measures (i.e. both step length and step width) for a control child that has low variability between trials and for a child with amblyopia who has much more variability between trials.

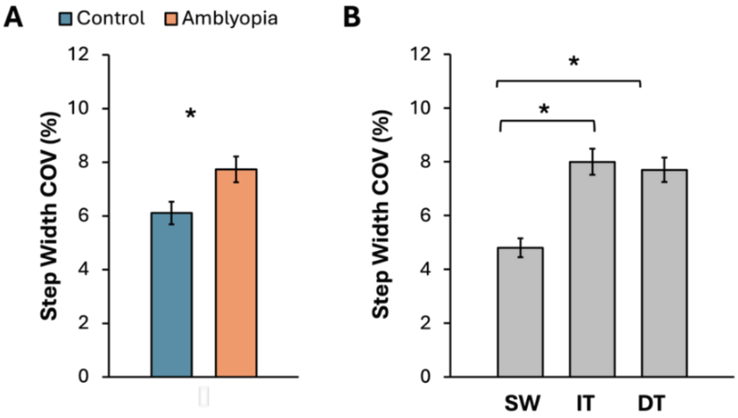

Figure 17. Bar graph depicting step width COV (%). Collapsed across condition (Panel A), the amblyopia group (orange bars) was more variable in step width compared to controls (blue bars). Collapsed across groups (Panel B), step width COV increased between SW and both IT and DT, but not between IT and DT (SW: straight walk , IT: isolated target walk, DT: distractor target walk). Error bars represent ± standard error of the mean (SEM). *p <0.05

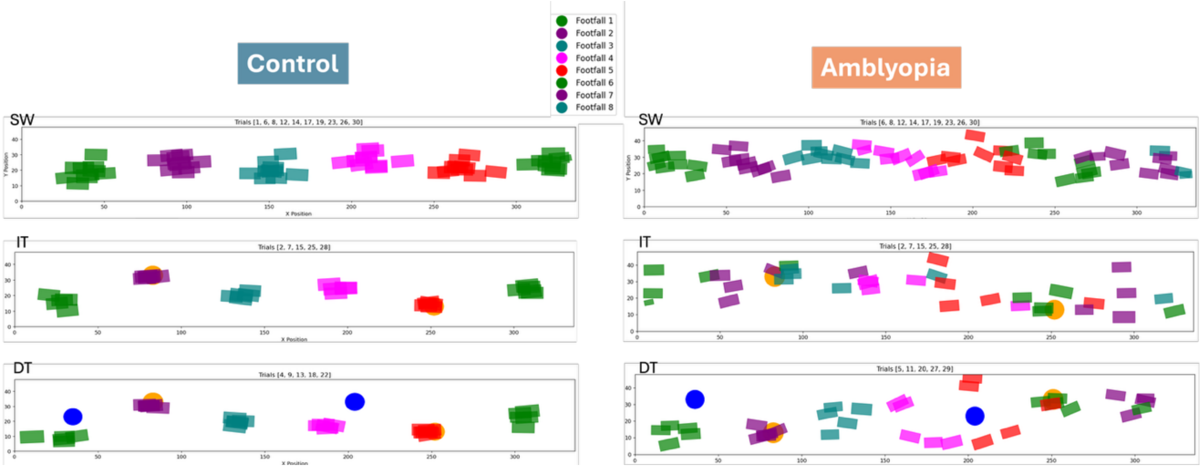

Figure 18. Examples of variability between trials of the same set up for spatial measures by condition (SW: straight walk, IT: isolated target walk, DT: distractor target walk). Each colour represents a different step number, orange circles are targets, and blue circles are distractors.

Here, increased variability in the child with amblyopia is found for all conditions. compared to the control child.

4.6 Factors Associated with Motor Performance

4.6.1 Sensory Factors

Correlations between sensory factors and gait kinematics were performed. No significant correlations with COV measures and sensory factors were found. No significant correlations were found for Worth 4-dot fusion with gait kinematics. Only variables with significant correlations are reported (**Table 4**). Worse amblyopic eye visual acuity was associated with higher IT step length and IT step width. Poorer stereoacuity was associated with decreased IT and DT normalized velocity, higher DT cadence, and shorter DT step time and DT stance time.

Table 4. Significant correlations with sensory factors.

Variable	r	95CI[a]	p
Visual Acuity			
IT Step Length	0.49	0.07 – 0.76	0.027
IT Step Width	0.44	0.01 – 0.73	0.051[b]
Stereoacuity			
IT Normalized Velocity	–0.45	–0.74 – –0.02	0.040
DT Normalized Velocity	–0.44	–0.74 – –0.01	0.048
DT Cadence	0.52	0.11 – 0.78	0.018
DT Step Time	–0.55	–0.79 – –0.16	0.012
DT Stance Time	–0.54	–0.79 – –0.14	0.015

a. 95CI, 95% confidence interval
b. trend towards significance

4.6.2 Clinical Factors

There was no significant difference between children with anisometropic amblyopia and strabismic amblyopia in leg length or age (all ps≥0.80). There were no significant group differences in gait kinematics between the 14 children with anisometropic amblyopia) and the 7 children with strabismic amblyopia (all ps≥0.081). There were no significant correlations between age of onset and any of the gait kinematics (all p's≥0.16).

Chapter 5

Discussion

5.1 Overview

Previous research has shown that children with amblyopia score lower on walking subtasks compared to controls using standardized tests for motor ability, even when both eyes are open. However, these tests do not explore gait kinematics to determine what is causing these low scores. The overall objective of this research was to evaluate the impact of amblyopia on the development of walking. This thesis used a pressure-sensitive walkway (GAITRite®) to examine temporal and spatial gait kinematics in children with amblyopia compared to controls during walking when binocularly viewing in conditions with increasing complexity, including walking in a straight line (i.e., straight walk: SW), stepping on targets (i.e., isolated target walk: IT), and stepping on targets while avoiding distractors (i.e., distractor target walk: DT). In general, the amblyopia group showed a similar pattern as controls with poorer performance as task complexity increased but had increased gait variability and less step accuracy compared to controls, especially in those with poor binocularity. These data highlight the role of balanced binocular input during motor development and shed light on the mechanisms of poor motor skills in children with amblyopia.

5.2 Gait Kinematics

The amblyopia group did not show differences compared to controls on the outcome measures traditionally studied in the research, including temporal (normalized velocity, cadence, step time, stance time) and spatial (step length and step width) gait parameters. In fact, as conditions got more complex, children with amblyopia generally followed the same trends as controls with poorer performance as the conditions got more complex. For example, both groups exhibited decreased normalized velocity when going from SW to IT to DT. Increased cadence and step time from SW to IT and DT, but no differences between IT and DT, was also found in both groups. As the conditions became more complex, all children slowed down and took more steps as they made their way down the mat. This may reflect the need to be more cautious and more intentional about where they are stepping so they could successfully complete the more complex conditions.[73,74]

Stance time was more sensitive to changes in condition for children with amblyopia but not for controls, with longer stance time for both IT and DT conditions than the SW condition. However, controls only showed an increase in stance time in the DT condition compared to the SW condition. The increase in stance time for children with amblyopia suggests that when they are encountering targets and distractors in their path, they increase their ground contact time, even in the easier IT condition, allowing for more time to plan their next step.[165–167] Controls only increase their stance time between the simplest (SW) and most complex (DT) conditions, indicating they were able to adapt faster than children with amblyopia to the IT condition and maintain their typical stance time despite targets being placed in their path.

For spatial measures, children with amblyopia had similar values compared to controls for step length and step width. Again, they followed the same pattern as controls, with both groups having decreased step length in the more complex IT and DT conditions compared to the SW condition. This pattern suggests that the targets and distractors disrupted the typical stride of participants, requiring them to take shorter steps to be able to successfully step on the targets and avoid the distractors. In contrast, there was no effect of condition on step width, showing that both groups maintained similar step widths despite the increased complexity in conditions. It is possible this lack of finding is due to the more restricted amount of space available horizontally versus vertically for stepping on targets. Thus, step length instead of step width was modified for stability during the walk.[64,69,71]

5.3 Step Accuracy

Children with amblyopia were less accurate than controls while stepping on targets in this study. The presence of amblyopia impacted the way that the children were able to adapt to a new task that they had limited life experience doing.[165] The controls picked up on the new tasks quickly and were able to accurately step on the targets almost every time. Also, the children with amblyopia have decreased visual input due to reduced visual acuity, suppression, and reduced depth perception which could play a role in the decrease accuracy in children with amblyopia.[151,168] The children with amblyopia followed the same trends as younger controls in this study, showing that they may be immature in their accuracy compared to controls.

Condition complexity mattered for target accuracy as children with amblyopia were less accurate at stepping on targets than controls when targets were isolated on the mat, but not when distractors were present. This could be explained by the limited experience having to step specific spots while walking and the children with amblyopia having trouble adapting to this new task.[165] However, it could also be because of reduced depth perception making it more challenging to accurately judge where the targets are located, may overshoot or undershoot due to visual uncertainty.[168] Another reason for more difficulty observed in the IT condition compared to DT is that in the DT condition the children are more confined in their walking pattern since the distractors are also on the mat leaving them with less places to put their feet and increasing their chances of stepping on the targets. It is important to note that although accuracy with distractors present was not significant between the control and amblyopia groups, there was trend towards significance meaning they might still be worse than controls for this condition.

Distance of the target from the start of the mat also played a factor in accuracy. Children with amblyopia were less accurate than controls for stepping on the far target (T2) but not the near target (T1). This is consistent with past research that states that children age 3-7 years tend to not plan ahead while walking, waiting until they get passed the first obstacle before working on the second.[73,74] Children with amblyopia may have waited until they finished their first task (i.e., step on T1) to start planning their second task (i.e., step on T2). However, at that point they may not have had enough time to successfully plan their movements for this second task, leading to poor accuracy.[73,74] To add to this, the accompanied visual impairments typical of amblyopia (e.g., impaired visual acuity, suppression, reduced depth perception, ocular motor dysfunction) may have disrupted any visual feedback required to accurately step on the far target. In fact, children had an extra 30 cm from the starting point to walk and plan their goal of stepping on the near target compared to the distance they had from near to far targets. Therefore, they had slightly more distance and planning time for T1 then they did for T2. Although this difference in distance and planning time did not impact the control's ability to successfully step on T2, indicating that the amblyopia group may need more distance or time for planning than controls. Unpublished data from our lab examining typical development with this protocol in controls only shows a similar trend in younger children (7 to 9 years of age) compared to older children (10-13 years of age),[169] pointing to a potential immaturity in accuracy in the children with amblyopia.

Remarkably, children with amblyopia were no different from controls in their ability to avoid the distractors in their path. Children may have less experience with stepping on targets as they do with avoiding distractors in their path. It is not very often that we are required to step on specific, small areas in our path in our daily lives. More often, they are instances where we must avoid something in our path by stepping over it or around it, similar to the distractor in this experiment. The frequent exposure to avoiding obstacles while navigating our environment could explain the lack of difference observed between the children with amblyopia and control's ability to avoid the distractors on the mat.[73,74] Alternatively, the task may have been too easy with just two distractors and more distractors may be needed to fully challenge these groups enough to find differences.

5.4 Variability in Gait Kinematics

While children with amblyopia did not differ from controls on the traditional measures of gait kinematics, they were less accurate during walking than controls suggesting a clear impairment. To further explore why children with amblyopia may be less accurate, I investigated variability in gait kinematics by calculating the coefficient of variation (COV). Overall, children with amblyopia were more variable in their gait kinematics compared to controls.

Children with amblyopia had higher variability in temporal measures of gait compared to controls, with differences observed for normalized velocity, cadence, step time, and stance time COVs. Higher variability was found overall for normalized velocity and stance time, but only for SW for both cadence and step time. Past research has shown that younger children are more variable in their gait patterns than older children and adults.[69,71,169] These data suggest that overall, gait speeds of children with amblyopia are immature compared to controls.[69,71] Because children relay mainly on vision for walking, [25,77–79,170] the decrease in visual input and stereoacuity caused by amblyopia may play a role in the presence of the immature gait kinematics.

Controls showed an increase in cadence and step time COV from the SW to IT and DT, but no differences between IT and DT. These findings support past research showing that children are more variable when encountering things in their path.[73,74] Children use variability to help them find the most efficient way to accomplish a task.[73] As children completed the IT and DT trials, they may have been exploring different walking speeds to determine the best strategy for completing the task. Children with amblyopia showed no differences in cadence and step time COV as conditions got more complex but still had higher variability than controls even in the SW condition. This suggests that it did not matter what condition the children with amblyopia were completing, they still had trouble determining the best walking strategy. This pattern of gait is similar to those of younger children.[69,71,169] Past research has shown that variability in gait speed should mature around the age of 8 years[66,72] The mean of the children with amblyopia in our study was 9.6 years. The fact that at this age, they are still showing variability in gait speed compared to controls indicates an immaturity of temporal gait patterns.[66,72]

Children with amblyopia also showed higher variability overall than controls for step length and step width, meaning they were more variable in the placement of their steps. This suggests that children with amblyopia have less gait stability and show spatial gait parameters similar to those of younger children. [64,69,71,169] Gait stability is related not only to the size of step length and width, but also to their variability. [64,69,71] Better stability is related to smaller step length and larger step width and to tighter variability.[69,171–173] Again, pointing to immature gait kinematics and the slowing down of typical gait development related to amblyopia. Although variability was higher in children with amblyopia than controls, both groups showed similar trends as conditions got more complex with increased step length COV and step width COV in both the IT and DT conditions compared to the SW condition. However, there was no difference in variability between the two complex IT and DT conditions. This supports past research showing that children are more variable when encountering things in their path compared to adults.[73,74]

Here, I found that amblyopia increases variability in both temporal and spatial gait kinematics, emulating immature gait patterns found in younger control children. However, it is unknown exactly how amblyopia increases this variability and what mechanisms are behind the delay in typical development of walking in these children. Perhaps there is a link between the sensory and clinical factors of amblyopia and motor performance in gait kinematics.

5.5 Factors Associated with Impaired Gait Kinematics

5.5.1 Sensory Factors

Poorer amblyopic eye visual acuity was related to impaired spatial measures in this study. Worse acuity was associated with longer step length and step width in the IT condition. Because children with amblyopia have overall longer stance times than controls, to keep up with their peers in gait speed, children with reduced visual acuity may need to take longer steps.[69,70] Wider step widths are related to gait stability and may be required by children with poorer visual acuity to keep their balance as they are walking.[69] One previous study did show that more severe amblyopic eye visual acuity was related to decreased scores on balance tasks on the Movement ABC.[144] However, visual acuity was not related to performance on any other measure in my study.

Instead, in my study there were more associations with stereoacuity, a binocular vision measure, which is consistent with studies that showed that children with reduced stereoacuity scored lower on balance tasks during standardized tests for motor ability.[142,144] Relationships with stereoacuity were more evident in the more complex distractor target (DT) condition. Poor stereoacuity was associated with decreased normalized velocity in both the IT and DT conditions, suggesting that children with more reduced depth perception have to slow down in the more complex conditions to help them with stepping on targets and avoiding distractors in their path. This decrease in normalized velocity may allow for more time to process changes in their surroundings and to use different cues to depth (i.e., monocular cues) as they navigate their environment. Children with poor stereoacuity also had increased cadence, and decreased step time and stance time for the DT condition, indicating that they are taking more frequent and faster steps despite the slower walking speed. Higher frequency stepping in a shorter amount of time makes it easier to maintain balance as your feet are touching the ground more often. Children with poor binocularity may be using this way of walking as a compensatory strategy to help them avoid falling.[144,151,174] Walking with slower normalized velocity and higher cadence are walking traits seen in younger children age 3.5 to 4 years.[55,61,63,64,66] Therefore, my findings suggest that reduced stereoacuity as a consequence of amblyopia is likely delaying the development of walking in children. It remains to be determined whether this continued immaturity persists beyond the age of 13 years studied in this project.

5.5.2 Clinical Factors

No differences in gait kinematics were found between children with strabismus and children with anisometropia. This finding may suggest that the amblyogenic factor does not influence performance in gait kinematics. Rather, the presence of unbalanced binocular input early in life affects the development of gait, as observed in the relationship of performance to stereoacuity. In fact, both etiologies result in this binocular imbalance and lead to poor stereoacuity.[39] This is inconsistent with past research showing that children with anisometropia score better than children with strabismus in fine and gross motor skills.[144,145] However, the lack of group difference for etiology may have been due to the small sample sizes (14 anisometropia, 7 strabismus).

There was also no relationship between age of onset and performance on gait kinematics. This is inconsistent with past research that showed that children with infantile onset had lower balance scores than children with older onset.[144] Infants start taking their first steps around 1 year of age, with walking developing rapidly up to ages 3-4 years.[68–70] This is also around the same time as the critical period of amblyopia where the greatest deficits are observed.[39] However, only 8 (38%) of the children in my study were diagnosed before they reached the age of 4 years, with over half (62%) of the participants in the amblyopia group learning to walk before their amblyopia emerged (or was diagnosed at least). These children may have had typical vision as they learned to walk, which could explain why I did not see an impact of the age of onset on gait kinematics in my group. However, my sample size was likely too small to find any effect of age of onset. An infantile diagnosis before the age of 1-year results in significantly reduced gross motor skills compared to a later onset.[144] In my study, there were only 3 (14%) children with infantile diagnoses. Therefore, to determine whether age of onset of amblyopia impacts gait development, more participants must be recruited.

5.6 Potential Limitations

While this study provides insight into the gait kinematics of children with amblyopia compared to controls, there were several potential limitations. I could not fully control where the children were looking between the trials, and it is possible that they were watching where the targets and distractors were being placed in the next trial. If so, children could have engaged in some pre-planning prior to the start of the trial. To minimize this, I had the child look at the fixation cross on the wall before the beginning of each trial which would have ensured they were not looking at the mat.

Also, I could not fully mimic normal walking as the study was completed in a lab environment with limited space on the mat. Further, the distance between targets may have disrupted normal walking patterns to varying degrees based on leg length. To minimize this, distances between targets were based on the average stride length of children 8-12 years old, which is around the same age as my participants.[159–163] The width of the mat limited the horizontal placement of the targets and the distractors. This may have impeded my ability to find a group difference in step width and step length. This is evident in the lack of between-condition differences for IT and DT trials in step width for either group, even though conditions differed in complexity. In addition, the task may have been too easy with only two targets and two distractors used, adding more obstacles on the mat may be required to see group differences.

Lastly, my sample size may have been too small to detect any group differences, especially for secondary analyses of sensory and clinical factors. Most of the amblyopia group had anisometropic amblyopia (14/21) as I was not able to recruit enough children with strabismic amblyopia (7/21) to effectively examine the impact of etiology on gait parameters. I also did not have enough children with an infantile onset (14%) to confidently determine whether onset was related to gait kinematics. This is likely because most participants were recruited from an optometry clinic only, which tend to have certain patient subtypes (refractive error, anisometropia) that are different from those that would see an ophthalmologist (strabismus). To remedy this, connecting with a local ophthalmologist will aid in recruitment of other types of amblyopia for future studies.

5.7 Future Directions

This thesis examined the gait kinematics of children with amblyopia compared to controls to learn more about how having a pediatric eye condition can impact a child’s whole life. Gait kinematics were more variable and less accurate, indicating a clear impairment and opening the path for future research into the causes of these impairments. The next logical step in this research is to determine the role of ocular motor dysfunction in any deficits found during walking by tracking the eyes with a head-mounted eye tracker. I predict that children with amblyopia will move their eyes more than controls to gather visual information to help them plan and guide their movements.

Based on the results of this study, it appears that the loss of binocular vision plays a large role in deficits in gait kinematics in children with amblyopia. Further, it is unclear how much controls are relying on binocular vision when completing this task. This can be studied by blurring one eye of controls as they walk. Testing controls with impaired binocular vision would give us insight into how much of a role normal binocular vision plays in walking. Lastly, this study only examined children’s performance when encountering two dimensional (2D) objects in their path. Increasing the complexity of the task by incorporating three-dimensional (3D) objects instead may bring out deficits that would not have been found with the easier task of stepping on 2D targets and avoiding 2D distractors. Children with amblyopia may be more cautious (i.e., slower velocity, higher toe clearance) when encountering obstacles that they must step over. It is unclear yet whether amblyopia treatment helps motor skills. Thus, there is a potential for more targeted treatments that focus on improving binocularity, which may slow down the progression or reverse the deficits in gait kinematics. Overall, future research in the field of eye-body coordination in amblyopia is promising and will answer many questions that will help these children succeed.

Chapter 6

Conclusion

Overall, during binocular viewing, children with amblyopia have immature gait kinematics and accuracy compared to children with age-typical visual development. Children with amblyopia are more variable in their gait speeds and gait stability and less accurate in their ability to step on targets compared to controls. This shows that the typical pattern of gait development is delayed in these children. The reasons for the increased variability and decreased accuracy are unknown. However, there is a link between decreased stereoacuity and gait speed, showing that children with poor depth perception are more similar to younger children. These findings point to the importance of typical binocular vision for the development of walking.

Recent research has determined that amblyopia and its causing factors impact more than just vision in individuals. Amblyopia impacts many aspects of a child's life from reading, fine motor skills, self-esteem, and gross motor skills.[94,119,144,147,174,175] This study adds to the literature on the overarching impacts of amblyopia by finding deficits in the typical development of walking. Children with amblyopia are more variable and inaccurate in their walking than controls. It is clear that impaired binocular vision results in larger deficits for the child with amblyopia, revealing that having normal binocular vision during childhood is extremely important, especially when developing visuomotor abilities. Impaired gait which may lead to problems with stability and balance when navigating challenging environments, impeding children's ability to excel in physical activity and sports, leading to changes in body composition (i.e., obesity), affecting their peer interactions and academic achievements, and ultimately affecting their whole life.[175] As we learn more about motor deficits in amblyopia, we must consider how to help. This may include a need for occupational therapies for these children to help them learn skills and strategies to help them improve their gait kinematics. My findings can be used to inform the development of targeted interventions and programs to help children with amblyopia succeed physically, socially, and academically in their daily lives.

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Appendix A

Individual Patient Information

ID	Age, years	Age of onset, years	Etiology[a]	Alignment, Distance, Near[b]	AE BCVA, logMAR[c]	FE BCVA, logMAR	RDS, log arc sec[d]	Worth 4-dot, log deg
Strab								
S1	12.1	5.1	AccET	ET14, E(T)4	0.7	0.0	2.9	1.05
S2	11.1	0.3	Inf ET	X(T)8, XT4	0.0	0.0	4.0	1.05
S3	9.0	1.5	AccET	ET14, E(T)10	-0.1	0.1	2.6	-0.15
S4	8.6	4.3	AccET	Ortho, Ortho	0.2	0.1	2.0	-0.15
S5	7.1	3.4	AccET	Ortho, Ortho	0.2	0.1	2.3	-0.15
S6	8.6	2.8	AccET	Ortho, Ortho	0.0	-0.1	2.3	0.00
S7	10.7	6.3	AccET	ET3, ET3	0.2	-0.1	3.5	-0.15
Aniso								
A1	8.3	3.2	HA	Ortho, Ortho	1.0	0.0	4.0	0.45
A2	7.7	5.9	MA	Ortho, Ortho	0.9	0.0	2.6	0.30
A3	7.9	3.9	HA	Ortho, Ortho	0.3	-0.2	2.3	-0.15
A4	10.3	4.0	AA	Ortho, Ortho	0.4	-0.1	2.3	0.00
A5	8.5	4.7	HA	Ortho, Ortho	0.4	-0.2	2.0	0.00
A6	8.0	1.8	HA	Ortho, Ortho	0.4	0.0	1.8	0.00
A7	9.1	2.8	HA	Ortho, Ortho	0.3	-0.1	1.8	-0.15
A8	8.9	6.9	AA	Ortho, Ortho	0.3	0.0	2.6	-0.15
A9	10.5	6.8	HA	Ortho, Ortho	0.4	-0.1	2.3	0.30
A10	11.5	4.0	HA	Ortho, XT13[e]’	0.8	0.0	4.0	1.20
A11	9.0	5.2	HA	Ortho, Ortho	0.3	0.0	2.3	0.30
A12	13.0	5.1	HA	Ortho, Ortho	0.2	0.0	2.3	0.30
A13	13.6	6.9	AA	Ortho, Ortho	0.4	0.1	3.3	0.30
A14	7.0	4.0	HA	Ortho, Ortho	0.2	0.1	2.6	0.30

a. AccET, Accomodative esotropia; InfET, Infantile esotropia; esotropia, ET; hyperopic anisometropia, HA; astigmatic anisometropia, AA; myopic anisometropia, MA

b. Ortho, orthotropia; ET, constant esotropia; E(T), intermittent esotropia; XT, exotropia; X(T), intermittent exotropia

c. LogMAR, logarithm of the minimum angle of resolution

d. Nil stereoacuity was assigned an arbitrary number of 4.

e. Exotropia due to sensory strabismus from having severe amblyopia