Near addition lenses as a tool to investigate vergence adaptation in myopic children

by

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A thesis
presented to the University of Waterloo
in fulfillment of the
thesis requirement for the degree of
Doctor of Philosophy
in
Vision Science

Waterloo, Ontario, Canada, 2011

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

Accommodation and vergence are two interacting ocular motor systems that function to maintain clear and single vision across a wide range of distances. Sustained fixation results in the adaptation of these ocular motor systems and has been widely investigated in adults but not in children. Moreover, limited reports have measured adaptation to disparities induced by ophthalmic lenses. This thesis used near addition lenses as a means to investigate binocular adaptation in children. The specific aims of this thesis were three-fold. First, the thesis aimed to gain insight into the mechanism of changes to accommodation and vergence during binocular adaptation in children. The second objective was to determine the role of vergence-bias category (eso/exo/normals) on adaptation. Lastly, this thesis evaluated the influence of myopia on binocular adaptation.

Thirty- eight myopic and 38 emmetropic children between 7-14 years of age were examined for the purpose of this thesis. A series of studies were performed to evaluate adaptation using varying demands for accommodation and vergence, stimulated by binocular fixation at near (33 cm), through the addition of +2D and -2D over corrective lenses (closed loop accommodation) and using 10 base-out prisms (open-loop accommodation at 4M). In each closed-loop condition, measures of binocular and monocular accommodation (PowerRefractor, Multichannel systems) and near phoria (modified Thorington technique) were recorded at frequent intervals when children binocularly fixated a high contrast near target (33 cm) for 20 min. For the open-loop condition (obtained using 0.5 mm pinhole pupils), binocular accommodation and tonic vergence (distance heterophoria through pinhole pupils) were determined at frequent intervals when binocular fixation was sustained at 4M for 20 min. For all conditions, tonic accommodation was measured before and after the near task to measure accommodative adaptation.

The results of this thesis make three major contributions to the literature. First, it outlines that the addition of +2D and -2D lenses alters both accommodation and near phoria during sustained binocular fixation, which can be explained based on the models of accommodation and vergence. Second, it shows that the direction of phoria influences the pattern of binocular vs. monocular accommodation in closed-loop conditions and alters the degree of vergence adaptation in both closed and open-loop accommodation. These changes have been primarily attributed to the varying demands on fusional vergence. Lastly, this thesis demonstrates that myopic children show reduced vergence adaptation when fusional convergence was initiated through plus adds or base-out prisms but not when fusional divergence was initiated through minus addition lenses. Further, myopic children also showed variations in other ocular motor parameters such as higher accommodative lags, greater variability of accommodative response, larger accommodative after-effects, and higher AV/A ratios compared to emmetropes.

Consistent with the models of accommodation and vergence, the thesis highlights that it is necessary to measure changes to both accommodation and vergence when evaluating the response of the ocular motor system. The direction of phoria and type of refractive error play a significant role in determining binocular adaptation in children. Future studies should differentiate these parameters when evaluating adaptation of the ocular motor system.

Acknowledgements

I would like to gratefully and sincerely thank my supervisors Prof William R Bobier and Prof Elizabeth L Irving for their continued guidance, understanding, patience and invaluable suggestions throughout the course of my graduate studies. I am deeply indebted to them forever for providing me the opportunity to develop my individuality and grow as a self-sufficient researcher. Thank you from the bottom of my heart!

I would like to thank my committee members Prof Vasudevan Lakshminarayanan and Prof Trefford Simpson for their helpful comments and suggestions. I am also grateful to my external examiner Prof Clifton Schor (University of Berkeley, California) and internal external examiner Dr Richard Staines (Department of Kinesiology, UW) for reviewing my thesis.

I would like to extend my deep appreciation to all the child participants and their parents for volunteering their time and for their kind cooperation throughout the study. Special thanks to Tonia To and Sinthujah Jeyerasalingam for help in monitoring the children's attention and assistance in data collection.

My sincere acknowledgements to past and current members of Bobier and Irving lab for offering immediate help whenever needed.

I am thankful to Dr Debbie Jones (former clinic director) and the clinic staff Rosemary Morrison, Mary-Ann Robertson and Jennifer Oliveira for help with participant recruitment/ re-filing clinic files and directing participants to the study area.

Thanks to Robin Jones and Andrew Nowinski for technical support; Jim Davidson and Chris Mathers for computing support.

Many thanks to the former (Dr Jeff Hovis and Dr Tom Singer) and current Graduate officers (Dr Natalie Hutchings and Dr Trefford Simpson) and graduate coordinators (Krista Parsons and Kim-Tremblay Swan) for all their help and for keeping me on track.

I thank all past and current GIVS members, staff and faculty of the school of Optometry for providing a pleasant work environment.

I am very grateful to my good friends, Sruthi Srinivasan and Lakshman Subbaraman for their moral support and understanding during the most difficult days.

This research was supported by Natural Sciences and Engineering Research Council of Canada (WRB, ELI), Canada Research Chair (ELI) and Canadian Optometric Education Trust Fund (VS, WRB, ELI). I would also like to thank the American Optometric Foundation, Vistakon and Bausch and Lomb for supporting me with the William C Ezell fellowship for the years 2009-2010 and 2010-2011.

Dedication

This work is graciously dedicated

To all my gurus for giving me the gift of knowledge

To my loving parents (Lalitha and Sreenivasan) for their many sacrifices, unconditional love and tremendous support of my education

To my sister (Deepa), brother-in-law (Ram) and brother (Naresh) for their encouraging words, immense love, and support

I would not have come this far without you!

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1 Literature review

1.1 Fundamentals of accommodation, vergence and their interactions

When binocular fixation is transferred from one distance to another, changes in the refractive power of the eye and in the relative position of visual axes are required to maintain clear and single vision. The synkinetic association of accommodation, convergence and pupillary constriction has been termed the “near triad” [1-3]. The subsequent sections of this chapter will outline the fundamentals of human accommodation and vergence (horizontal) in the context of this thesis.

1.1.1 Accommodation

Ocular accommodation can be defined as the ability of the eye to change its dioptric power to bring an object of regard coincident with the retina. Human accommodation is achieved by altering the curvature of the crystalline lens with the aid of the ciliary muscle and the suspensory zonules. Together these structures form the accommodative apparatus. The classical theory or the Helmholtz theory of accommodation [4] (later modified by Fincham [5]) is the most widely accepted theory that describes the mechanism of accommodation and has been empirically supported in primates [6]. In the unaccommodated state (i.e. far fixation), the fibers of the ciliary muscle relax causing increased tension on the zonules, which flattens the lens and holds it in its conoid shape. When viewing a near object, the ciliary muscle contracts and releases the tension on the zonular fibers allowing the elastic forces of the crystalline lens to mold it into a spherical shape. Along with these changes, there is a decrease in the lens equatorial diameter, an increase in lens axial thickness, and the lens anterior and posterior central surfaces undergo an increase in curvature resulting in an increase in the refractive power.

Accommodation is primarily stimulated by a blurred retinal image [7-10]. The afferent pathway commences with the stimulation of the retinal receptors by this retinal defocus. The blur signals pass through the visual pathway (optic nerve- chiasm-optic tract- lateral geniculate body) and are transmitted to area V1 (visual cortex) for further processing. The neural signal is then transformed into a motor command at the Edinger-Westphal nucleus in the midbrain [11]. Input to the Edinger-Westphal nucleus could be derived from several areas in the cortex, midbrain and cerebellum, which have been identified to control both accommodation and vergence movements (reviewed by Gamlin 2002[12]). Evidence from neurophysiological studies on monkeys indicate that near response cells in the mesencephalic reticular formation, located dorsal to the oculomotor nucleus, may provide commands to Edinger-Westphal and the medial rectus moto-neurons for ocular accommodation and vergence respectively [11-14]. Although several studies provide valuable information about the neural pathways of accommodation, there are still unanswered questions relating to the functional role of neural innervations in controlling accommodation, and how sensory signals (like blur, disparity, proximal cues) are precisely processed and transformed into a motor output.

The efferent pathway of accommodation involves transmission of the motor commands via the oculomotor nerve, the ciliary ganglion and the short ciliary nerves. Anatomical evidence for the synapse in ciliary ganglion is controversial with some studies showing no synapse [15] and others showing evidence for a possible synapse in the ciliary ganglion [16]. The efferent pathway ends at the ciliary muscle wherein a change in the state of contraction alters the refractive power of the crystalline lens and facilitates an in-focus image on the retina.

Accommodation is composed of mutually-antagonistic, dual innervations from the autonomic nervous system. The motor innervation is composed primarily of a parasympathetic component but also receives innervation from the sympathetic system [17, 18]. The parasympathetic system is mediated by the muscaranic receptors, whose stimulation results in increased accommodation, while the sympathetic system is mediated by the β- adrenergic receptors, characterized to be primarily inhibitory and provides relatively small response magnitude (less than 2D) [17, 19, 20].

1.1.1.1 Stimulus-response properties of accommodation

Accommodation is measured in diopters (D), which is defined as the reciprocal of the linear value of the viewing distance in meters. The stimulus to accommodation (AS) is the theoretical amount of accommodation required at a particular distance while accommodative response (AR) refers to the actual amount of accommodation exerted by the eye at that target distance. The difference between the stimulus and response accommodation is called the accommodative error. Focusing errors that result from insufficient accommodation (AR<AS) are termed lag of accommodation and place the conjugate focus behind the retina. In contrast, errors that result from excessive accommodation (AR>AS) are termed lead of accommodation and place the conjugate focus in front of the retina.

The relationship between stimulus of accommodation and its response is often represented by the stimulus–response curve [2, 21, 22]. This can be generated by altering optical vergence of the target either by varying target distance in physical space, varying target position (for e.g. within a Badal optical system) or with spherical lenses placed in front of the eyes. Figure 1-1 shows a typical stimulus- response curve with the dashed line indicating a perfect (1:1) relationship between the stimulus and the response. Empirical measures (solid line) typically show a pattern that can be divided into three different zones [22].

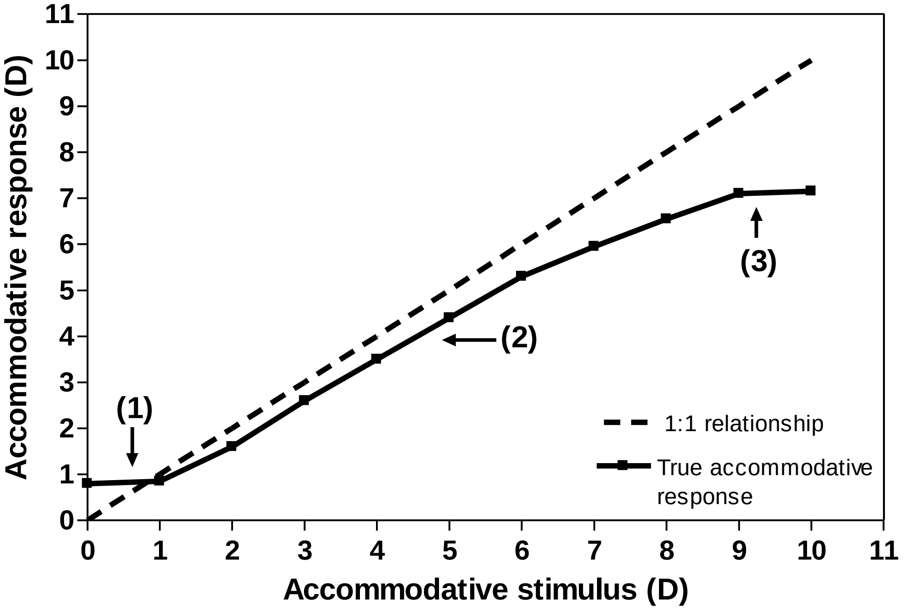


Figure 1-1: Accommodative Stimulus-response curve (adapted from Ciuffreda & Kenyon., 1983) [22]

Zone (1) represents the region exhibiting a lead in accommodation for lower stimulus levels. This response reflects the bias induced by the tonicity of the ciliary muscle (tonic accommodation) [22]. Zone (2) indicates a lag of accommodation for intermediate stimulus levels with progressively increasing lags for higher stimulus demands. The slope of the stimulus-response curve at the intermediate stimulus levels is less than unity in young adults [23]. With further increase in the stimulus to accommodation, the accommodative response saturates (Zone 3) due to age related changes in the crystalline lens, indicating that the maximum amplitude of accommodation has been reached.

1.1.1.2 Components of accommodation

Heath [8] proposed the total accommodative response to be composed of contributions from tonic, reflex, vergence, and proximal accommodation, similar to the classification proposed by Maddox [24].

1.1.1.2.1 Tonic accommodation

In the absence of an adequate accommodative (blur) stimulus, the accommodative response adopts an intermediate resting position, which is believed to reflect the tonicity of the ciliary muscle [10, 18, 25]. The terms dark focus, resting state of accommodation and tonic accommodation, have all been used to describe this refractive state of the eye when visual feedback has been rendered ineffective [26]. Toates [18] suggested that this resting position represents the balance in tonicity between the sympathetic and parasympathetic innervations. Measurements of tonic accommodation in stimulus-free conditions (such as bright empty field [27, 28], darkened room [28-30], low spatial frequency difference of Gaussian target [31] or 0.5 mm pinhole pupils [28, 32]) reveals a mean value of 1.5D in adults [8, 10, 25]. Several factors such as the method used to open the accommodative loop [28, 33-35], refractive type [33, 36-38], cognitive demand and surround proximity [30] influence the magnitude of TA [39].

1.1.1.2.2 Reflex (blur-driven) accommodation

Blur-driven accommodation, as the name suggests is a component of the accommodative response that occurs in response to a defocused retinal image. Blur or retinal defocus is considered a primary stimulus to drive the accommodative response in adults [7-9]. Reflex accommodation is responsive to relatively smaller amounts of blur, up to approximately 2.0D [9]. This component of accommodation is constrained by the depth of focus of the eye, which represents the dioptric extent to which an image may be focused away from the retina and still be perceived clearly. Typical values range around 0.3D for a 3mm pupil [40]. Several parameters such as the pupil size, target luminance and target spectral composition influence the magnitude of the depth of focus [40].

1.1.1.2.3 Vergence accommodation

Convergence (or vergence) driven accommodation is the synkinetic change in accommodation driven by disparity vergence [1, 31, 41, 42]. VA/V (commonly CA/C) ratio quantifies the strength of the vergence accommodation cross-link and describes the change in accommodation produced by a unit change in vergence. This cross-link is measured by using a non-accommodative target (to eliminate input from blur-driven accommodation) while vergence changes are induced through changes in disparity such as the addition of prisms. The cross-link ratio can be represented as a *"response"* ratio, where the denominator or the unit change in vergence is quantified along with the measurement of accommodation or as a *"stimulus"* ratio, where the unit change in vergence is not measured and is assumed to represent the stimulus demand. In adults, the VA/V ratio ranges between 0.02 – 0.16D/Δ [1, 31, 41-43]. The difference between the stimulus and response VA/V is small because the error in the vergence response is small (5 to 10 minutes of an arc) [44].

1.1.1.2.4 Proximal accommodation

Proximal accommodation is a term used to define the input of higher centers such as perceived distance or knowledge of the apparent nearness of an object [45-47]. Cues such as apparent size and distance [48, 49], voluntary effort [50], awareness of surround [30] have been used to determine the perceptual higher order influence on accommodation, typically under the absence of dioptric stimulus to accommodation. Cognition (i.e. testing instructions or mental effort needed to focus the targets) has also been found to influence the magnitude of accommodative response [51, 52]. Further, the role of perceived distance (proximal) on the cross-coupling interactions suggested that accommodation is directly controlled through voluntary effort while the vergence response is driven through the accommodative vergence cross-link [50].

1.1.2 Vergence

Vergence refers to the disjunctive (opposite) movement of the two eyes, which brings the images of a target onto corresponding retinal points of each eye thereby providing single binocular vision [53]. Generally, vergence responses can be described selectively with respect to foveal imagery. Convergence occurs in response to a crossed retinal disparity. In this case the object of regard lies in front of the intersection of the primary lines of sight and its image lies on the temporal retina of each eye. A convergence response rotates the primary lines of sights to intersect at the object of regard which is now imaged approximately bifoveally. On the other hand, divergence responds to the presence of uncrossed disparities resulting from an object set beyond point of fixation such that it is imaged on the nasal retina.

Neuro-physiological observations in primates provide evidence for the presence of disparity sensitive cells in the primary visual cortex (area V1), extra-striate areas, V3 & V4, middle temporal area and medial superior temporal area [54]. A precise vergence center for humans is still under investigation. Research from non-human primates (monkey) has found evidence of such a loci in the midbrain [12, 13, 55, 56]. These mid brain neurons are located in the mesencephalic reticular formation, close to the oculomotor nucleus, in a region called the supraoculomotor area [55, 56]. Three types of neural cells, the vergence burst neurons, vergence tonic neurons and vergence burst-tonic neurons have been identified to play an important role in overall vergence control [55, 56]. The neural control of vergence eye movements is believed to follow the pulse-step design as is found in the more highly investigated saccades. The magnitude of the vergence response is coded in a pulse of innervation which is then integrated to a “step” reflecting increased tonic activity needed to hold the eyes in the new position of gaze [56].

1.1.2.1 Units of measurement of vergence

Vergence can be expressed in two units: Meter angle (MA) and prism diopters (ΔD). A meter angle is numerically the reciprocal of the fixation distance in meters and analogous to the diopter. For example, a target at 33 cm would require 3MA of convergence just as it would require 3D of accommodation. Meter angles allows a rapid comparison between accommodative and vergence responses. The prism diopter on the other hand defines the actual rotation of the eyes and thus is a function of the individuals' interpupillary distance in cm in addition to the fixation distance in meters. It can be calculated by multiplying MA of convergence with the pupillary distance of the individual. For example, the stimulus to convergence for an adult with an interocular separation of 6 cm viewing a target at 33cm would be 18 ΔD. The prism diopter is conventionally used when prism powers are defined.

1.1.2.2 Inaccuracies of the vergence system: Fixation disparity and heterophoria

When both eyes fixate a target, small vergence errors may occur without causing diplopia if they fall within the Panum's fusional area. These vergence errors have been referred by terms such as retinal slip, fixation disparity or micro-strabismus [57]. Schor proposed that the vergence system is operated by a "leaky integrator" where fixation disparity acts as a purposeful steady state-error [58] that stimulates continued vergence and maintains binocular alignment [57-59].

Heterophoria is a vergence position observed when fusional vergence is suspended, for example by occluding one eye or by presenting dissimilar targets. The dictionary of visual science [60] defines heterophoria as "the tendency of the lines of sight to deviate from the relative positions necessary to maintain single binocular vision for a given distance of fixation". Heterophoria is commonly abbreviated to phoria or sometimes referred as a latent deviation of the eye, since the deviation becomes manifest only during dissociation of the two eyes. This latent deviation is corrected by the fusional vergence mechanism such that visual axes return to the appropriate relative positions upon regaining sensory fusion.

Horizontal heterophoria can be classified based on the direction of the deviation as follows [61]: Orthophoria is a situation where the visual axes cross at the object of regard in the absence of fusional stimuli. Esophoria is present when the visual axis cross in front of the object of regard and exophoria is present when the visual axes intersect beyond the object of regard. The magnitude of phoria is expressed in prism diopters (Δ). Further, heterophoria can also be classified based on its magnitude for distance or near fixation [62] or the whether the deviation is compensated (resulting in no symptoms) or symptomatic and decompensated [61, 63].

1.1.2.3 Components of vergence

Maddox [24] proposed the aggregate vergence response to be composed of contributions from tonic, accommodative, proximal and disparity components (similar to the format described in section 1.1.1.2).

1.1.2.3.1 Tonic vergence

Similar to tonic accommodation, the vergence system assumes a convergent eye position in the absence of an adequate stimulus, which reflects the level of baseline neural innervation to the extraocular muscles [64, 65]. Tonic vergence can be measured in the absence of retinal disparity, achieved by monocular occlusion or darkness. Pinhole apertures [66], low spatial frequency difference of Gaussian targets [67] have been used to reduce blur information. The magnitude of tonic vergence ranges between 0.25 to 0.75 MA [64, 65].

1.1.2.3.2 Accommodative vergence

Accommodative vergence refers to the change in vergence initiated by changes to accommodation [68, 69]. It is quantified as the AV/A ratio (commonly AC/A), which is the amount of convergence resulting from a unit change in accommodation. AV/A cross-links are relatively easier to study than VA/V because it only requires the measurement of binocular alignment under monocular viewing conditions (to avoid any input from disparity vergence). Similar to VA/V (previous sections), this ratio can be expressed as a stimulus or response measure with the latter involving measurement of both accommodation and vergence. In normal adults, the stimulus AV/A ratio is known to 4 ± 2ΔD /1D while the response measures are usually higher than the stimulus ratios by approximately 8% due to the lag of accommodation [69]. The AC/A ratio is linear for intermediate stimuli ranging between +1 to 5D but can exhibit non-linearity at lower and higher stimulus levels [68].

1.1.2.3.3 Proximal vergence

This type of vergence is elicited by stimuli that provide the impression of being nearer in the absence of input from accommodation/disparity. Cues such as apparent size [46], apparent distance [71-73] and voluntary fixation of imaginary near targets in dark [50] evoke a change in vergence. Past studies have shown that proximal cues contribute approximately 50-70% of the stimulus demand in the absence of disparity and accommodative cues [46, 74].

1.1.2.3.4 Disparity vergence

Disparity (reflex) vergence is stimulated by retinal disparity (i.e. images falling on non-corresponding points outside Panum’s area) and has been considered to be a primary stimulus for vergence in adults [53, 75]. Since the objective of disparity vergence is to obtain retinal correspondence and subsequently fuse the images seen by two eyes, this type of vergence is also called fusional vergence. Disparity vergence is typically measured by recording changes to eye movements using a scaled, non-accommodative target to avoid accommodative and proximity cues. Disparity is then induced either by moving the target in space or by the addition of prisms. Similar to depth of focus for reflex accommodation, reflex vergence is initiated when the binocular disparity exceeds its threshold - Panum’s fusional area. The reflex vergence has been hypothesized to consist of two components: a rapid disparity driven component responds to the disparity and a slow sustained fusional component functions to maintain the fused percept [59] (discussed below).

1.1.3 Adaptation of accommodation and vergence

When the stimulus for accommodation or vergence becomes sustained over a period of time (60 sec or more), both ocular motor systems exhibit adaptation such that the initial response is directionally biased for a substantial period of time depending on the duration and magnitude of the stimulus [76-82].

The occurrence of vergence adaptation was reported as early as 1893 in Maddox's classical experiments [24] that described the components of vergence. Maddox [24] reported an increase in tonic convergence after prolonged exposure to base-out prisms. He suggested that these changes were adaptive and served to relieve the stress on the fusional vergence. Initial evidence for prism adaptation was based on changes in residual tonicity after forced duction (vergence amplitude) tests [76, 83, 84]. These alterations to the fusion-free (phoria) position persisted for long durations even after the removal of the adaptive stimulus [76, 85]. Schor [59] attributed this phenomenon to adaptive changes in tonic vergence in response to prolonged output of reflex vergence. The fusional (disparity) vergence was believed to be composed of two components: First, a fast (reflex) fusional component which aligns the eyes within 1 sec in response to retinal image disparity and has a short time constant. This is then followed and by a second, a slow fusional component that receives input from the fast and acts to maintain the alignment [59]. The slow component has a long decay time constant and it is this prolonged rate of decay that causes vergence adaptation (discussed further in sections 1.1.4). An analogous system was suggested for accommodation, such that reflex (blur-driven) accommodation provides a stimulus for the slow component of accommodation (accommodative adaptation) [78, 79]. In the accommodation system, factors such as the magnitude or duration of the adapting stimulus [78, 86-88], method used to open the accommodative loop [28] dioptric distance between baseline tonic level & the steady state accommodative response [89] and refractive state [36, 38, 90], influence the degree of accommodative adaptation.

Vergence adaptation has been reported to occur to horizontal, vertical and torsional disparities [44, 59, 77, 85, 91-96]. This thesis primarily deals with horizontal vergence adaptation which is further discussed below.

1.1.4 Vergence adaptation

1.1.4.1 Adaptation to prism-induced disparities

Vergence adaptation is used synonymously with prism adaptation or phoria adaptation. Vergence adaptation to prism induced disparities has been extensively reported in the literature[59, 77, 81, 85, 91, 92, 97-102]. These studies show that the prism- induced inaccuracies in vergence (phoria/fixation disparity) gradually reduce upon binocular fixation through the prism [76, 91, 92, 99]. Adaptive nature of the horizontal vergence system has been demonstrated with prism values up to 10 base-in and 32 base-out [85, 97]. A subsequent study by Sethi & North [100] indicated that the magnitude of prism adaptation is influenced by fusional reserves such that adaptation increased with an increase in prism value until the fusional vergence limit, after which the amount of adaptation decreased. These results agree with the models of adaptation [59, 103, 104], where slow fusional vergence (or adaptive element) receives its input from the fast vergence. Thus, an increase in the demand on the fast controller by means of larger prisms, results in greater amount of adaptation.

The magnitude of adaptation to horizontal prisms has often been reported to be asymmetrical, being greater in one base direction than the other [77, 85, 92, 101, 105]. Maximum vergence adaptation matched with the direction of lowest prism-induced fixation disparities [59, 105], suggesting that the mechanism of vergence adaptation minimizes the binocular errors of vergence and stress on the fast vergence. Schor and Horner [106] showed that binocular disorders such as convergence excess and convergence insufficiency were associated with adaptive disorders of accommodation and vergence. Reduced adaptive ability in symptomatic patients has also been demonstrated by other studies [77, 97, 99, 107-109] but orthoptic training usually improves the ability to adapt to prism-induced disparities [102, 110, 111].

Further, asymmetrical adaptation to horizontal prisms was also seen as a function of testing distance [85, 92, 101]. Henson & North [92], North et al [101] showed faster adaptation to base-out compared to base-in when viewing a distant target but almost symmetrical adaptation for base-in and base-out stimulus for near fixation [92, 101]. Mitchell and Ellerbrock [85] showed better adaptation to base-in prisms at near fixation compared to base-out prisms. The frequency with which the ocular motor system deals with a type of disparity was viewed as one possible explanation for dissimilarities in adaptation as a function of viewing distance [92].

Factors such as magnitude [85, 100] and duration of the adapting stimulus [76, 85, 112] have been found to be related to vergence adaptation. The amount of vergence adaptation to prism-induced disparities was directly proportional to the magnitude of the adapting stimulus [100] and the rate of decay of adaptation was inversely related with the stimulus duration [76, 85, 112].

1.1.4.2 Vergence adaptation to near addition lenses

Compared to prism induced disparities, limited reports exist on vergence adaptation to near addition lenses in pre-presbyopic subjects [59, 113, 114]. Ophthalmic lenses alter vergence through the accommodation vergence (AV) cross-link [69] such that plus / minus lenses reduce or increase the accommodative response, inducing exophoria / esophoria respectively, based on the strength of AV/A cross-link. Schor [59] monitored adaptation to plus lenses under binocular viewing conditions by recording vergence eye movements using an infrared monitor under conditions of closed loop accommodation and vergence. Three subjects were instructed to view a vertical line target at a distance of 50 cm through +2.00D lenses and eye movements were recorded after 5s and 60 s of binocular viewing. These lenses were reported to induce exophoria but no phoria adaptation was seen after 5 s of binocular viewing. However, after 60s of binocular viewing, the exophoria had either partly or totally reduced. The author concluded that plus lenses demonstrate partial or total vergence after-effects if they are worn during binocular viewing conditions.

North and Henson [113] measured vergence adaptation to +2D and -2D adds (placed over spectacle lenses as a bifocal) at 40 cm in four adult participants (with mixed refractive errors). Heterophoria was measured every 15 sec for the first 3.5 minutes, after 33.5 min and 66.5 minutes of binocular viewing. The most rapid reduction in lens-induced phoria occurred within 3.5 minutes of binocular viewing (Mean adaptation: +2D= 46.3%; -2D=39%) with further gradual reduction to 70% and 60% through plus and minus adds, respectively during an hour of binocular viewing. However, the authors measured changes to phoria alone and did not evaluate changes to the accommodation system which initiated the vergence adaptation through the AV cross link.

Sreenivasan, Irving & Bobier [114] evaluated the coincident time course of changes to accommodative response and near phoria when emmetropic adults with normal near phoria sustained fixation (33 cm) through +2D lenses. Plus addition lenses initially induced an exophoric shift, accompanied by a significant increase in binocular accommodation over that of monocular accommodation. This difference, (attributed to convergence accommodation), was believed to be a result of the lens-induced exophoria triggering an increase in fast reflex convergence and subsequently an increase in the output of convergence driven accommodation [103]. After several minutes of prolonged viewing, vergence adaptation occurred, concurrently reducing the exophoria and the binocular levels of accommodation while monocular levels remained constant. The reduction in the binocular accommodation was attributed to the reduced activity of VA cross-link activity upon vergence adaptation [78, 103, 115]. The constant accommodation response under monocular viewing condition indicated that the AV cross link was not significantly altered during the process.

1.1.4.3 Vergence adaptation to sustained near task

In addition to prism-induced and near addition- lens induced disparities, vergence adaptation has also been reported to prolonged viewing of a near stimulus. Ehrlich [116] reported a mean esophoric shift of 1.6 Δ and a significant correlation between pre-task phoria and adaptation after 2 hour visual search task with binocular fixation at 20 cm. However, the sample consisted primarily of exophores and the author did not measure accommodative adaptation (changes to dark focus), given the demanding near task used to induce adaptation. Differences in accommodative adaptation may influence vergence system by means of the accommodative-vergence cross-link [78, 117].

Similar convergent shifts in tonic vergence following prolonged near activity was also reported in other studies [80, 112]. None of these reports differentiated participants based on refractive error or phoria category (called vergence-bias category in this thesis). The direction of phoria may influence vergence adaptation due to varying demands on fusional vergence (discussed in section 1.1.5.2) Further, refractive error may influence vergence adaptation due to the differences observed in the attributes of accommodation and vergence in myopes compared to emmetropes (sections 1.2.3&1.2.4).

1.1.5 Factors influencing vergence adaptation to lens-induced disparities

1.1.5.1 Magnitude of adapting stimulus

The effect of varying magnitudes of prism induced disparities have been studied by researchers who report prolonged rates of adaptive decay but greater magnitudes of adaptation with larger adapting stimuli [76, 85, 100]. However, the disparity induced by the introduction of a prism is different from that induced by the addition of a near addition lens because the latter is influenced by the individuals AV/A ratio. For example, introduction of +2D lenses would result in an exophoria of 10ΔD in one individual with 5:1 AV/A ratio and only 6ΔD in a different individual with a ratio of 3:1, despite the same magnitude of lens addition.

North and Henson [113] reported an inverse relationship between the rate of adaptation and the amount of induced phoria. Individuals with larger induced phorias did not show complete adaptation even after 1 hour of binocular viewing. Similar results were also reported by Sreenivasan et al [114] where higher ratios were associated with greater magnitudes of adaptation but the lens-induced exophoria did not return to its habitual level indicating less-than complete vergence adaptation.

1.1.5.2 Relationship between heterophoria and vergence adaptation

Previous studies that measured vergence adaptation to lens-induced disparities [113, 114] were performed in participants with normal near phoria (between 0 to 4 exo) or were neutralized so that baseline position did not affect adaptation [59]. Under natural viewing conditions, the presence of large heterophoria may influence the degree of vergence adaptation. Heterophoria, observed under fusion-free state is compensated during binocular viewing by the fusional vergence mechanism. The degree and type of fusional vergence required for binocular viewing (convergence/divergence) varies in proportion to the size and the direction of phoria (exo/eso). Larger phorias would produce greater stress on the fast fusional vergence system, which may also affect the slow vergence adaptive mechanism. An individual with a large baseline (habitual) divergent phoria would require increased fusional convergence demand (increased phasic activity) through plus adds (since the habitual exophoria would be increased in response to the near add). Model of accommodation and vergence [103] suggest that the tonic element receives input from phasic controller, indicating a directly proportional relationship between the magnitude of vergence adaptation and the demand on the phasic controller. Several empirical studies have also confirmed this prediction by showing larger amounts of adaptation to higher prismatic disparities [85, 100].

Following these suggestions, an exophoric individual would be expected to show increased adaptation to plus adds. Similarly, esophores may experience less fusional vergence stress and reduced adaptation to plus adds compared to exophores. An opposite scenario could occur for fixation through minus addition lenses where exophores may show less adaptation and esophores may experience greater fusional vergence stress and greater adaptation. The role of baseline vergence-bias category on the degree of vergence adaptation to plus/minus addition lenses has not been identified.

1.1.6 Control theory- Models of accommodation and vergence

Control theory plays a unique explanatory and predictive role in analyzing biological systems [18]. A control system consists of subsystems (e.g. controllers) and processes (plants) assembled for the purpose of obtaining a desired output from a specified input [118]. The difference between the input and the output is called the error. There are two major configurations of control systems: closed loop and open-loop, differentiated by the presence or absence of feedback. Closed-loop systems are characterized by the presence of feedback, where the output is compared with the input to maintain the accuracy of the system. Several control theory models have been used to describe the static and dynamic responses of accommodation and vergence. A simplified schematic of static accommodation and vergence is shown in Fig 1-2 [78, 119, 120].

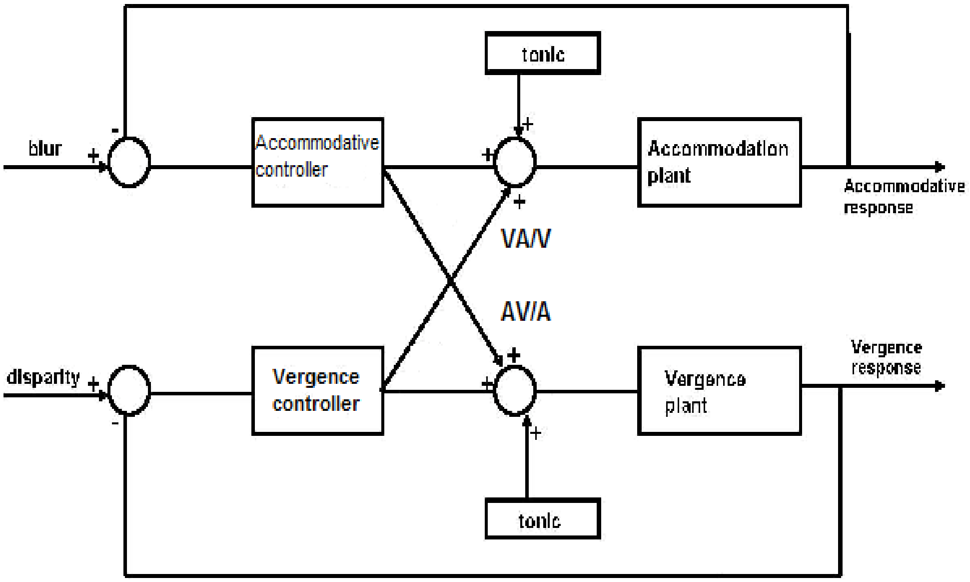


Figure 1-2: Simplified static model of accommodation and vergence showing negative feedback and cross-link interactions between accommodation and vergence

In the above model, accommodation and vergence are represented as two negative feedback driven parallel systems that interact with each other through cross-links (AV/A and VA/V). Retinal blur and disparity are the inputs to the accommodation and vergence system respectively. The inputs are neurologically processed by the controller, which responds as a reflex to the stimulus and also feeds in as an input to the cross-links AV and VA. The responses produced by the controller and the crosslinks are summed up in the summing junction where the tonic input feeds in. The combined response of each system is finally fed into the plant (crystalline lens for accommodation and extra ocular muscles for vergence) for eliciting the total accommodative or vergence responses. The error (stimulus-response) is fed back into the respective systems through the negative feedback loop in order to keep the system functioning over a prolonged period of time [58]. The responses obtained from the ocular motor systems in the presence of visual feedback (blur or retinal disparity) are termed as *closed-loop accommodative/vergence response*. On the other hand, the responses that are independent of visual feedback (feedback loop non-operational) are termed as *open-loop accommodation / vergence responses*.

Several dynamic models have been proposed to describe the adaptive patterns observed in the accommodation and vergence systems during sustained fixation [103, 104, 121, 122]. The current quantitative models [103, 104] differ in their approach of defining the process of adaptation and in identifying the effect of controller adaptation on their respective cross-links. Figure 1-3 shows the dynamic model of accommodation and vergence proposed by Schor [78, 103]. Two parallel leaky integrators were used to represent the fast (phasic) and the slow (tonic) component with short and long time constants respectively. The phasic component is responsible for the initial response to a change in accommodation/ vergence stimulus and its output feeds into the tonic component (Fig 1-4). The tonic element is in a parallel feed-forward loop such that the total system response equals the sum of activity of phasic and tonic components. When accommodative or vergence stimuli are viewed for an extended period of time, the tonic component with a longer decay time constant takes over the majority of the response. Opening the feedback loop at this point would exhibit directionally biased responses that demonstrate the adaptation effects of either system.

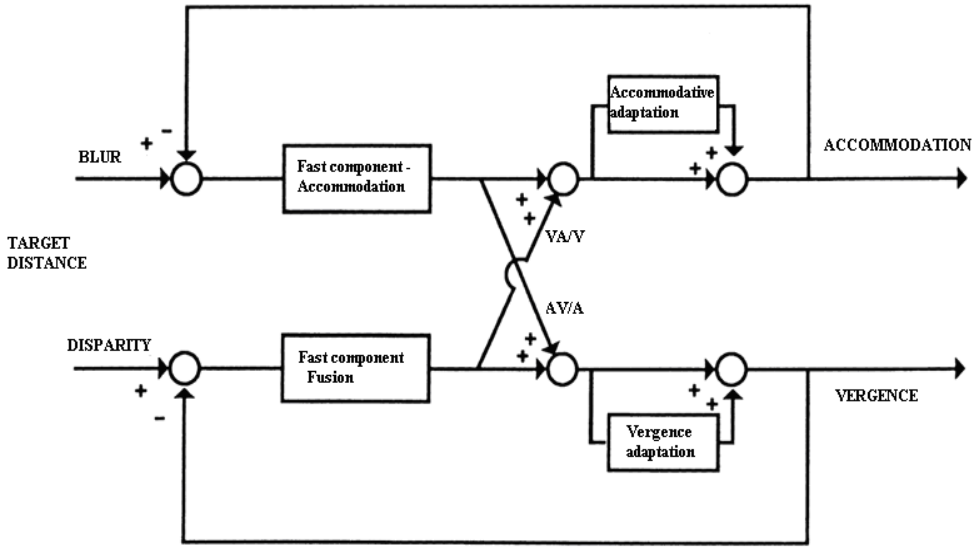


Figure 1-3: Simplified dynamic model of accommodation and vergence that suggests reduction of cross-link activity with adaptation

(Reprinted with permission from Schor (1992) [103]; A dynamic model of cross-coupling between accommodation and convergence: Simulations of step and frequency responses. Optom Vis Sci Apr 1992;69(4):258-69 © Wolters Kluwer Health).

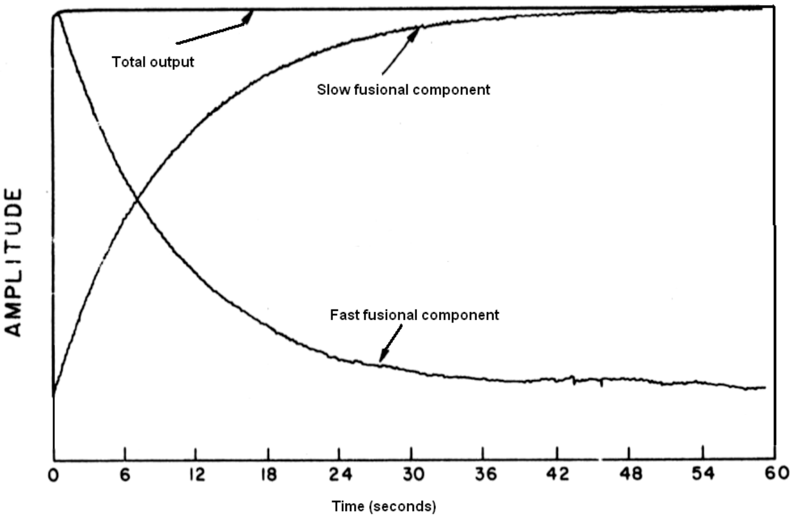


Figure 1-4: Illustration of complete prism adaptation and the relationship between fast and slow components

The above figure shows the respective outputs of fast and slow fusional components over time.
The output of slow fusional component can be seen to increase over time with a subsequent reduction in the output of fast fusional component yet maintaining a constant aggregate response. (Reprinted with permission from Schor (1979a)[59]; Relationship between vergence eye movements and fixation disparity, Vision Research 19(12} 1979 © Elsevier).

The other quantitative model of accommodation and vergence adaptation proposed by Hung [104] was an extension of the static dual-interactive feedback model [119]. This model (Fig 1-5) has an accommodative/vergence controller in the forward loop whose output drives the adaptive component. The distinctive feature of this model is that the time constant of the controller is modified by the output of the adaptive component. Thus, with increased effort or sustained fixation, the output of the controller increases the output of the adaptive element, which in turn increases the time constant of the controller. When the feedback loop is opened at this point, the controller response will take a longer time to decay and becomes manifest as accommodative/vergence adaptation.

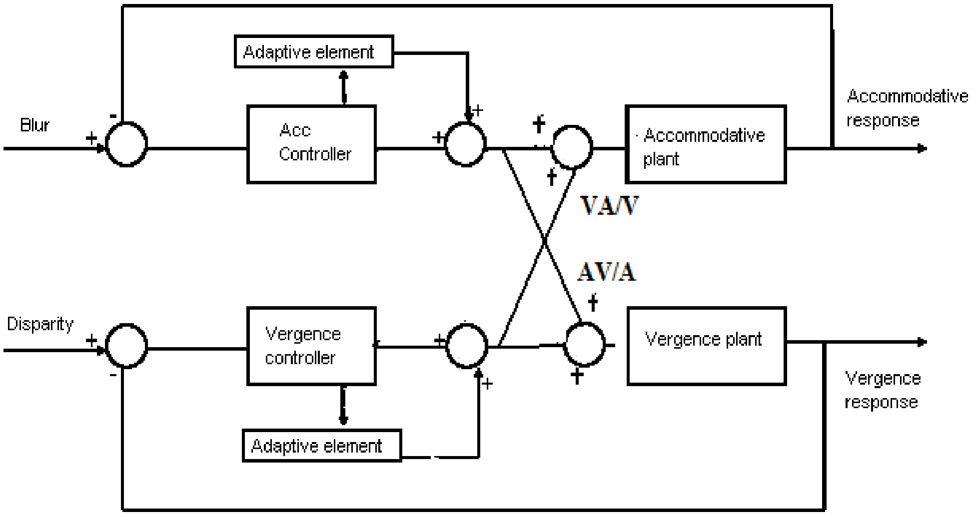


Figure 1-5: Simplified adaptation model of accommodation and vergence that suggests constancy of cross-link interactions

(Reprinted with permission from Hung [104]. Adaptation model of accommodation and vergence. Ophthal Physiol Opt 1992;12(July):319-26© John Wiley and Sons).

Although the two models discussed above [103, 104] differ in their approach of defining adaptation, they agree that the tonic (or adaptive) element receives input from phasic (or accommodative/vergence) controller, and suggest a directly proportional relationship between the magnitude of vergence adaptation and the demand on the phasic controller.

It is the position of the cross-links (AV and VA) or the effect of accommodative/vergence adaptation on their respective cross-link outputs that differs between the two models. Schor's adaptation model [79, 103] places the cross-links in-between the two leaky integrators (Fig 1-3) such that the phasic (fast) element provides input for the cross-links interactions. Adaptation of either system will increase the output of the tonic component and decrease the phasic output, thereby reducing the output of their respective cross-link interactions. On the other hand, in Hung's model of accommodative and vergence adaptation [104], the cross-link interactions AV and VA receive inputs from their respective controllers (Fig 1-5) whose output remains constant during sustained closed-loop conditions. Thus, this model suggests constancy of cross-link interactions after adaptation of either system. Similar constancy of cross-link with adaptation was previously suggested by Ebenholtz and Fisher [122]. This model of accommodation and vergence consisted of two components: a reflex (fast fusional component) and adaptive (slow fusional component) but differed from Schor's model [79, 103] with respect to the position of cross-links. In this model [122], both reflex and adaptive components contribute to the cross-link input in such a way that the output of CA remains constant even after vergence adaptation.

Evidence for the placement of cross-link between the phasic and tonic controllers [79, 103]comes from studies which indicate that accommodation and vergence can be adapted to stimuli from opposite cross-link despite the absence of direct stimulation (i.e) accommodation can be adapted through vergence accommodation in the absence of blur, and vergence can be adapted through AV cross-link in the absence of disparity. Jiang [117] confirmed this finding by demonstrating an exophoric shift with accommodation adaptation in the absence of disparity. Hence the author concluded that cross-links (AV/A) must be placed between the fast and the slow controllers.

On the other hand, empirical investigation by Rosenfield and Gilmartin [123] measured the pre and post task heterophoria and vergence-accommodation over a period of 3 minutes of viewing through 0 & 6 Δ under open-looped accommodation. Their results showed a change in phoria indicative of vergence adaptation but showed no significant change in the output of VA after prism adaptation. This investigation supported the Ebenholtz and Fisher model of accommodation and vergence [122]. However, the authors did not measure accommodative adaptation , which could have resulted in the constancy of VA observed in their study[124].

In light of these mixed results, experiments designed in this thesis measured changes to both accommodation and vergence during sustained activity to enhance our understanding of the model that best supports experimental data.

1.2 Myopia

Myopia is a form of refractive error, where parallel rays of light from a distant target are focused in front of the retina when accommodation is at rest. The word “myopia” was derived from the Greek word mūopia, signifying “closing” or “contracting the eyes”, attributes which describe the typical facial behavior of a myope [125]. Among refractive errors, myopia has attracted considerable attention over the last century. For instance, a keyword search for refractive errors in Pubmed database from the year 1900 shows the highest citations for myopia (14595), followed by astigmatism (7517), and the least for hyperopia (3142). Myopia can be classified based upon refractive error (low = -

0.5D to -3D; moderate= -3D to -6D; high>-6 D), based on the age of onset (early or juvenile onset between 6-15 years and late onset >15 years), congenital vs. acquired or based on pathology (simple or pathological) [126].

The VISION 2020 (Right to Sight) initiative by the World Health Organization included refractive error (with myopia) as one of its top priorities to eliminate preventable blindness in the world by the year 2020 [127]. Myopia is a vastly researched area compared to other refractive errors, probably due to the enormous cost to the society for eye examinations and correction procedures (spectacles, contact lenses, refractive surgery) [128] and the increasing prevalence of the refractive condition [129]. Further, high myopia is associated with a higher incidence of sight-threatening complications such as chorioretinal degeneration, retinal detachment, open-angle glaucoma and cataracts [130-132].

The prevalence of myopia has been increasing over the recent decades such that 41.6% of individuals in the United States between the ages of 12-54 were myopic during 1999-2004, compared to a previous estimate of 25% during 1971-1972 [129]. In school-aged children, the prevalence of myopia reached approximately 60-70% in Chinese and Canadian-Chinese children between 12-15 years [133], compared to 40% in Caucasian population between 12-17 years [129]. Higher percentages have been reported in Taiwanese children with the prevalence of myopia increasing from 20% at 7 years to 84% at the age of 16 [134]. Further, studies have shown that the myopia is often a progressive condition at least in school age years (until 15 years of age) with mean rate of yearly progression ranging between 0.40D to 0.6 D [135, 136]. Higher rates of myopia progression were associated with earlier onset age [137, 138], near work variables such as time spent on reading and shorter reading distance [139-142], less time spent outdoors [141] and esophoria at near [143, 144].

1.2.1 Etiology of myopia

The nature versus nurture question of myopia development has been studied for centuries; however, the exact nature and the relative contributions of environmental factors or the precise genes that play a role remain unanswered questions. Support for genetic predisposition comes from studies that show greater myopic prevalence in individuals with myopic parents [145-147]. The prevalence of myopia in children with two myopic parents is 30% to 40%, decreasing to 20% to 25% in children with one myopic parent to less than 10% in children with no myopic parents [145-147]. Further, Pacella and colleagues [148], showed that children with two myopic parents were 6.42 times more likely to become myopic compared to children with one or no myopia parents. However, the increasing prevalence of myopia [134, 129, 149, 150] over the last few decades cannot be solely attributed to genes since the genetic pool would not be expected to have changed dramatically during this period. Most likely myopia should not be seen as a nature or nurture issue but rather one in which environmental factors act upon genetically defined susceptibility [151].

1.2.1.1 Environmental risk-factors (associations) for myopia

Near work has been linked to myopia for more than a century. Evidence for environmental influence on myopia comes from epidemiological studies that show associations between attributes of near work and myopia [139-142, 152, 153]. The prevalence of myopia is high in occupations demanding near work such as 70% in British microscopists [154], 80% in orthodox Jewish school boys who underwent extensive training [155] and 90% in Singaporean medical students [156]. Myopes show increased intelligence quotient and higher scholastic success [139, 157-159], greater amount of hours spent studying [140] / reading for pleasure [159] and closer reading distance [160] compared to non-myopes.

Another environmental factor studied of late is outdoor activity. Several studies of different ethnic groups found that the time spent outdoor may be an important risk factor for the onset of myopia since myopic children (or those who become myopic) spend less time outdoors compared to emmetropes [161-163]. Higher myopic refraction were observed in children who combined high levels of near work with low levels of outdoor activity [141].

1.2.2 Theories of myopia development

1.2.2.1 Older theories

The biological-statistical theory and the use-abuse theory were two major (older) theories proposed for the development of myopia [164] Sorsby's biological theory (cited in [164] postulated that refractive errors were genetically determined and were due to the abnormal correlation between refractive components (axial length, corneal power, lens power and anterior chamber depth).

The use-abuse theory suggests that myopia develops due to the abuse of eye during prolonged near work (attributed to Cohn, 1886 cited by [164]). The theory is based on epidemiological evidence that suggests greater prevalence of myopia in occupations demanding near work. Young (1977) [165] postulated that myopia developed due to the inability of the eyes to relax accommodation to the far point after excessive near work. Since near work increases accommodation and convergence, various mechanisms for the near-work induced development of myopia were proposed. These include myopia development due to an increase in intra-ocular pressure with increased accommodation (Ware 1813, cited in [125]), increase in vitreous chamber depth producing myopia with increase in accommodation and tension in extraocular muscles leading to increased intra ocular pressure and myopia development [166]. However, recent evidence strongly suggests that myopia arises from growth of the vitreal chamber which exceeds the focal length of the eye. Experiments on a wide range of species has given insight into a possible mechanism [167, 168] whereby reduced retinal imagery leads to uncontrolled axial growth.

1.2.2.2 Ocular response to visual input: Animal models of myopia

According to this theory, reduced retinal imagery is the key environmental factor that underlies the mechanism of refractive development [125]. Several animal models have been used to study the evidence for an active vision guided growth of the eye [167, 168]. Two major approaches have been used to study development of myopia in animals: form-deprivation myopia and spectacle-lens compensation. Form-deprivation myopia is produced by suturing the eye-lid [169] or by placing a translucent diffuser over the eye, all of these serve to reduce the contrast of the retinal image.

Furthermore, the direction of defocused retinal imagery created by plus or minus lenses was found to dictate the direction of axial growth [170-172]. Concave lenses shift the plane of focus behind the retina, producing a hyperopic defocus on the retina (for an emmetropic eye). Similarly, positive lenses shift the plane of focus in front of the retina, resulting in markedly decreased rates of eye growth in animals. Compensatory axial elongation has been observed in many animal species such as monkeys [172], chicks [170, 171], tree-shrews [173], fish [174]. The effect is limited by a critical period where the effects can be somewhat reversed by the removal of the lens. Myopic defocus may be stronger than hyperopic defocus since brief periods of myopic defocus through positive lenses, prevented the daylong effect produced by minus lenses [175]. The ability of the eye to grow in both directions indicates that the visual system is capable of detecting the sign of defocus and adjusts the rate of eye growth accordingly. However, efforts to determine how the eye responds to the sign of the inducing lens have shown that compensation can still occur if potential cues such as accommodation, chromatic aberration, and image magnification/minification are eliminated [176]. Visual deprivation leads to myopia even when the optic nerve is sectioned [177], after the destruction of Edinger-Westphal nucleus [178] or when the ganglion cell action potentials are blocked [179]. The precise mechanism for detection of the sign of defocus is still unresolved.

Based on the results of animal studies, the analogy for human myopia development would be presence of hyperopic defocus on the retina. Researchers [180, 181] have hypothesized that excessive accommodative lags may produce hyperopic defocus on the retina, similar to the effect of negative lenses in animal studies, inducing axial elongation.

1.2.3 Myopia, accommodation and retinal defocus

Ever since near work was believed to be associated with myopia, the mechanism of accommodation was suspected to be a possible link (Kepler – cited in Curtin [182]/Duke and elder[183]). Several features of accommodation such as the overall static accommodative response and individual components of accommodation (section 1.1.1.1) have been examined in an attempt to elucidate the association between accommodation and myopia development.

1.2.3.1 Static accommodative response

A number of investigators have showed that accommodative response is reduced in myopic individuals compared to emmetropes [23, 180, 181, 184]. Reduced accommodation (greater accommodative lags) has been reported in myopic individuals when accommodation was stimulated through negative lenses [180, 181, 184], with monocular real targets [185] or under binocular viewing condition through full refractive correction [186]. Based on evidence from animal models of myopia [170-172], the hyperopic retinal defocus produced by excessive accommodative lags has been proposed as a cause of myopia progression in humans. However studies that measured accommodative lag before and after the onset of myopia show conflicting results. Few studies suggest that accommodative lag is higher in children who became myopic prior to onset of myopia [187-

[189] while another report [185] shows no evidence for increased lag before myopia onset, instead suggested that myopes show larger lags after the onset of myopia. The relationship between accommodative lag and myopic progression has also been inconsistent with few studies suggesting larger accommodative lag during progression [184] while others suggest no relation between lag and myopia progression [190, 191]. As suggested by Seidemann and Schaefffel [192], studies on the magnitude of accommodative lag shows large variability even among emmetropic individuals. Several reasons may contribute to this variability. Foremost, the contribution of disparity/proximal cues to the viewing stimulus, differences in the experimental design/ instrument used to measure accommodative lags, and age of participants may be confounding factors.

1.2.3.2 Myopia and the components of accommodation

Blur driven accommodation: Myopic individuals show poor accommodative response when monocular accommodation was measured through negative lenses but not when the stimulus was altered by physically changing the target distance [180, 184]. The negative lens series was performed when participants fixated a distant target through a set of negative lenses under monocular viewing condition. In such a case, the predominant stimulus for accommodation is blur (proximal cues kept minimal and disparity eliminated) compared to the changing distance series, where proximal cues are also present. Poor accommodative response to negative lenses has been attributed to reduced blur sensitivity in myopes [193]. Adult myopes are less sensitive to defocus signals that drive accommodation compared to emmetropes [193, 194], although a study in children suggested similar blur detection thresholds in myopes compared to age matched emmetropes [195].

Vergence accommodation: The strength of synkinetic cross-link from disparity vergence measured under open-loop accommodation has been found to be similar between myopes and emmetropes [196-198].

Tonic accommodation: Tonic accommodation has been widely studied as a function of refractive error. Majority of the studies indicate that tonic accommodation is lowest in adult-onset or early-onset myopes and highest in hyperopia [33, 34, 38, 90]. Few longitudinal studies that attempted to investigate the relationship between tonic accommodation and the development of myopia have provided conflicting results. Some studies show no difference in baseline tonic accommodation with the onset of myopia [33, 199], or higher baseline tonic accommodation in emmetropes who later became myopic compared to those remained that emmetropic [197] or report a correlation between reduced tonic accommodation and higher myopia progression [200].

Comparative studies on accommodative adaptation among refractive groups reveal differences in the magnitude and rate of decay of adaptation. Late-onset myopes [36, 37], and early onset myopic children [38] show greater magnitude of accommodative adaptation after sustained near task compared to emmetropes or hyperopes. Myopes of recent onset show increased adaptation compared to individuals with long term myopia [38]. The rate of decay (regression) of adaptation has been found to be slower in late-onset myopes compared to emmetropes [201-204]. The slower rate of decay in myopes has partially be attributed to the larger accommodative after-effects in this group [201] or may reflect a deficit in the sympathetic innervation [37, 205].

Model predictions have attempted to simulate how cross-links interact with the distance heterophoria and refractive error on accommodative lag [206]. These simulations indicate that uncorrected hyperopia and esophoria increase the accommodative lag while uncorrected myopia and exophoria decrease the lag. These effects were exaggerated when AV/A and VA/V ratios were both increased or reduced but not when they were altered reciprocally. The author concluded that lag of accommodation cannot be predicted by a single factor but depends upon a combination of factors such as AV/A ratio, heterophoria, refractive error or adaptability of accommodation system [206].

1.2.4 Myopia and vergence

Von-Grafe (cited in Curtin [182]) was the earliest to postulate that the role of vergence (activity of extraocular muscles) could be myopigenic due to the compression of the eyes during periods of near work. The association between near work and myopia led several investigators to examine the role of accommodation, but vergence has been examined to a much lesser extent compared to accommodation. Uncorrected myopia is associated with exophoria [182], presumably due to the reduced output of accommodative vergence. However, several reports in corrected myopes indicate that the onset and progression of myopia is associated with a more convergent near phoria [144, 188, 189].

Accommodative vergence and myopia: Several studies have shown refractive group differences in the strength of the synkinetic cross-link from accommodation. Response AV/A ratios, which employs measures of accommodative vergence and the actual change in accommodation, were observed to be higher in myopes compared to non-myopes [197, 207-209]. These elevated ratios were observed when accommodation was altered using positive/negative lenses or due to change in fixation distance [207] and has been observed in early-onset (onset before 15 years of age-i.e. children) [207, 208] and late onset myopes (>15 years of age -usually adults) [197]. Accommodative-vergence cross link has been identified as a risk factor for the development of myopia since several studies found higher response AV/A ratios in those emmetropes that became myopic compared to those who remained emmetropic [197, 207, 208]. The greater ratios have been attributed to both reduced accommodation and enhanced accommodative vergence [207].

1.2.4.1 Vergence adaptation and myopia

Flom and Takahashi [210] measured distance and near phorias (and AV/A ratios) in 28 previously uncorrected/undercorrected myopes immediately and one week after the prescription of a new correction. The authors observed esophoria through the full refractive correction, which reduced by 2-3Δ after one week. This reduction was attributed to vergence adaptation. The authors postulated that before correction, the stimulus to accommodation was reduced by the magnitude of under correction, resulting in exophoria. In an effort to maintain binocular vision, the children may have used their reflex convergence, which may have stimulated vergence adaptation after prolonged fixation.

So far, only one investigation has experimentally evaluated vergence adaptation as a function of refractive error. North and colleagues [211] compared adaptation to 6 Δ base-in and base-out in adult groups of emmetropes, early onset and late onset myopes. Vergence adaptation was measured at distance and near. The authors reported no significant difference in the magnitude of prism adaptation between the three groups for base-in/base-out prisms [211]. However, it must be noted that this investigation was performed under closed-loop accommodation, which is controlled by an interactive negative feedback mechanism (section 1.14). Thus, any changes to accommodation (such as accommodative adaptation) may alter the fast controller, thereby influencing the vergence system through the accommodative-vergence cross-link [79, 117]. Progressing myopes show higher AV/A ratios [197, 207, 208], and greater susceptibility to accommodative adaptation [36, 38] which may produce larger changes in the vergence system compared to emmetropes. Thus, it is still unclear whether school aged myopic children (who often show greater progression of myopia[134]) exhibit differing vergence adaptive ability compared to emmetropes.

1.2.4.2 Possible link between vergence and myopia

As mentioned in the previous section, a convergent vergence posture has been found to be associated with the onset [144, 188, 189], progression [143] and higher amounts of myopia in children[212]. Two possible explanations were proposed for this esophoric deviation [213]. Firstly, esophoria could be secondary to an increased accommodative response and thereby excessive accommodative vergence. This hypothesis may not be true because myopic esophores show larger accommodative lags (or reduced accommodative response) under binocular viewing conditions compared to orthophores or exophores [213, 214]. The second hypothesis was attributed to vergence adaptation, based on studies that showed a convergent shift in phoria in response to a sustained near task [116, 215]. Goss and Rosenfield [216] speculated that esophoria due to vergence adaptation may cause increased accommodative lags under binocular conditions due to the need for reflex divergence, which may then produce hyperopic defocus on the retina and induce axial elongation. [170-172]. However, as noted earlier, there is a paucity of information regarding the role of near work on the vergence adaptive ability of myopic children.

1.2.5 Control options for myopia

The fundamental aim of myopia research lies in understanding the mechanism that leads to its development or progression so that treatment strategies can be developed to prevent or control its progression. The major control procedures for myopia include spectacle intervention using single vision or plus addition lenses [217-221], contact lenses that alter the physical shape of the cornea (orthokeratology) [222, 223] or recently, to control peripheral refractive errors [224], and pharmaceutical agents (atropine [225] or pirenzepine [226]). The majority of these studies show small treatment effects that last for a short period of time or have significant side-effects.

1.3 Common applications of near addition lenses

One of the primary applications of added plus and minus lenses in pre-presbyopic individuals includes the treatment of accommodative and binocular disorders since near addition lenses are capable of altering the demand of both accommodation and vergence systems [227]. Plus addition lenses are commonly prescribed to pre-presbyopic individuals for the treatment of convergence excess [227] and accommodative insufficiency [228-230] or also considered a form of treatment for myopia due to its relation with near work [217-221]. On the other hand, minus addition lenses have been investigated as a treatment option for strabismic divergent deviation (intermittent exotropia) [231, 232]. The role of near addition lenses as a control procedure for myopia progression will be discussed further below.

1.3.1 Near addition lenses for myopia

Plus addition lenses have been prescribed as a treatment option for several decades with the aim of inhibiting myopia progression. While the original basis for prescribing plus adds was to reduce the demand for accommodation [233-236], the recent rationale has been to eliminate the excessive accommodative lags that creates hyperopic retinal defocus [217], which may lead to axial elongation of the eye [170-172] (section 1.2.2).

The initial literature concerning the use of plus adds for myopia were in the form of case reports or retrospective studies. Oft cited retrospective studies include Roberts and Banford [236] & Oakley and Young [235], which included data obtained from patients in private practice. Both studies showed reduction in the myopic progression through bifocal lenses, but the study by Oakley and Young [235] showed a reduction of almost

0.5D/year in Caucasian children. The study has been critiqued for possible selection and examiner bias due to its retrospective nature. Later, several prospective clinical trials were conducted in order to evaluate the ability of near addition lenses (bifocals/progressive addition lenses) in slowing myopia progression. The overall results of these studies have not been consistent ranging from no success [218], limited success [217, 220, 237] and successful reduction of myopia [219].

The largest multi-center randomized, double-masked correction of myopia evaluation trail (COMET) [217] enrolled 469 children aged 6 to 11 years with baseline myopia between 1.25 and 4.50 D. The rate of progression of myopia was compared between progressive addition lenses (+2D) and single vision lenses for 3 years. The authors reported an overall adjusted 3-year treatment effect of 0.20D, which was statically significant but not clinically meaningful. However, additional analyses showed significant treatment effects in children with large lags of accommodation in combination with near esophoria, shorter reading distances (<31.2 cm), or lower baseline myopia (>-2.25D). Similar results of a modest overall effect but larger reduction in myopic esophores and children with high accommodative lags were shown by a Japanese group [220]. Several other investigators also showed that children with a convergent vergence profile (esophoria) [221, 233] display greater reduction of myopic progression through addition lenses compared to children with exo/orthophoria. Recently, the COMET [237] group performed a second investigation that only included children with large accommodative lags (<1.0D at 33 cm) and near esophoria (<2PD). The overall success rates were similar to the original COMET with 0.28D reduction in myopia through near adds compared to single vision lenses over three years. However, inspection of their data (table 3) indicates that children with larger esophoria (>5PD) and large accommodative lag (>1.50D) demonstrated greater treatment rates than the mean, similar to previous reports [238]. Given that plus addition lenses are prescribed to reduce accommodative lags and are used at near viewing distances which require accurate accommodation and vergence, it is unfortunate that clinical trials did not measure changes to accommodative lag/phoria through the plus adds. Thus, it is difficult to identify whether the elimination of accommodation/ vergence error influenced the successful reduction of myopia progression in children. It is also important to note that in majority of the clinical trials, the same add power (ranging between 1D to 2.0D) was prescribed to all children. The same add power may produce different accommodative/vergence errors through the addition lenses depending on an individual's ocular motor profile (for e.g. baseline vergence posture/strength of cross-links) and adaptation effects.

1.4 Oculomotor response to near addition lenses

1.4.1 Effect on Accommodation

A number of individual reports evaluated the accommodative response through plus addition lenses in emmetropic adults [114,192,239-241], myopic adults [241, 242] and myopic children [243, 244]. In adults, these investigations consistently showed that plus lens additions are capable of reducing the lag of accommodation at low dioptric powers (+1D) [192, 239] and even resulted in a small amount of over-focus or lead of accommodation with higher dioptric powers (+2 and +3D) [114, 192, 240]. A few of these investigations measured accommodation under both binocular and monocular viewing conditions [114, 192] and reported a greater binocular compared to monocular response through the plus addition lens. This increased binocular response may be the result of lens-induced exophoria triggering an increase in fast reflex convergence and subsequently an increase in the output of vergence driven accommodation [103, 119]. The reduction in accommodative lag through plus adds were maintained in emmetropic adults after 20 min [114] or 30 min [240] sustained fixation in monocular viewing conditions but showed small reduction (~0.25D) under binocular viewing conditions [114], which was attributed to the reduction in VA cross-link activity due to vergence adaptation [79, 115].

Two studies measured the monocular accommodative response through plus adds in myopic children [243, 244]. Both studies report reduction of accommodative lag through plus addition lenses but these studies did not evaluate the effect of sustained viewing on the accommodative response. Since myopic individuals show greater susceptibility for accommodative adaptation [36, 38] it may be possible that the reduction is not maintained in myopic children unlike emmetropic adults who showed no accommodative adaptation through plus addition lenses [114].

Compared to plus additions lenses that were evaluated for a therapeutic basis in non-strabismic myopes, minus addition lenses have primarily been employed in scientific studies as a means to estimate the accommodative stimulus-response function in myopes [180, 181, 184]. As a result, the majority of the investigations were performed under monocular viewing conditions only [181, 184, 245]. Results indicated that myopic individuals show greater accommodative lags [181, 184], possibly due to their reduced blur-sensitivity compared to emmetropes [193]. However, the results do not depict the performance of the ocular motor system under natural viewing conditions, which would include the input from disparity vergence in addition to other cues. Based on models of accommodation and vergence, [79, 103] one would predict that initial and sustained changes in vergence through minus adds would also alter binocular accommodation through vergence-accommodation cross-link (VA). The binocular response to minus addition lenses, especially in myopic individuals with reduced blur-driven accommodation needs more investigation.

1.4.2 Effect on Vergence

Although near addition lenses primarily alter the demand on accommodation, these lenses also change the vergence response through the accommodative-vergence (AV) cross-link, inducing a relative shift in near phoria [24, 68]. The effect of plus adds on the vergence system has been evaluated immediately after the addition of lenses in emmetropic adults [114], myopic adults [239] and myopic children [241] or with sustained fixation [59, 113, 114]. Adult investigations showed that sustained binocular fixation through plus adds reduced the lens-induced exophoria, which was concluded to be due to vergence adaptation [59, 113, 114]. Vergence adaptation to plus addition lenses was dependent on AV/A ratio such that larger ratios resulted in higher magnitudes but incomplete return to the baseline in emmetropic adults [114] and adults with mixed refractive error [113].

Vergence adaptation to lens-induced phorias has not been investigated as a function of refractive error. Myopic individuals, especially during progression show elevated response AV/A ratios [197, 207-209], which would result in greater lens-induced phorias and increased fusional vergence demand compared to emmetropes. This increased vergence stress may require greater levels of vergence adaptation, if the lens-induced phoria has to return to its original level. Another important reason to study vergence adaptation in myopes relates to the differential effect of vergence posture on the success of myopia prevention through plus adds. Several studies report that myopic progression was reduced to a greater extent in myopic esophores compared to myopic exophores/orthophores [217, 218, 221, 233]. Based on the models of accommodation and vergence [103] and common clinical practice [227], it would be expected that plus adds will reduce the binocular vergence stress in esophores. However, the completeness of vergence adaptation may reduce the efficacy of this correction. As mentioned earlier, the role of phoria (vergence-bias category) on vergence adaptation to near addition lens needs further investigation, in myopic children as well as emmetropes.

2 Rationale and thesis objectives

Based on the literature reviewed, it is evident that binocular adaptive changes to near adds have been not been investigated to the same extent as compared to prism-induced disparity. Although myopia is one of the most frequently researched applications for near (plus) addition lenses, there is still a clear need to improve our understanding of the binocular adaptive mechanism to these lenses, especially because greater treatment effects were reported in children with esophoria and higher accommodative lags. Do the adds actually show a greater reduction of accommodative lag in the above cases or do they provide greater binocular comfort, which perhaps increases compliance? Would the adaptive processes relieve ocular motor stress in some but not all groups? Do these factors play a role in explaining why the effect of plus adds are typically small except in those with esophoria?

Unfortunately, clinical trials that evaluated the efficacy of plus adds for myopia did not measure the changes to accommodation and vergence through the addition lenses. Individual studies that measured ocular motor response through near adds only measured response from one system (accommodation/vergence) or did not measure the effect of sustained fixation through near adds. Due to the presence of tight cross-coupling between accommodation and vergence under natural viewing conditions, it is essential to evaluate changes to both accommodation and vergence during prolonged binocular viewing conditions. Investigation of binocular motor changes to minus addition lenses, which increases the accommodative demand and necessitates fusional divergence, would further enhance the understanding of adaptive changes that occur when fixating through near addition lenses in children.

Accordingly, this thesis employed plus and minus near-addition lenses as a tool to investigate binocular adaptation in children. The major aims of this thesis were three-fold:

(1) To gain insight into the mechanism of changes to accommodation and vergence through near addition lenses in children

(2) To evaluate the effect of phoria (vergence-bias) category on adaptation

(3) To evaluate the effect of myopia on binocular adaptation

The following questions and hypotheses were proposed based on the literature reviewed:

1. Will myopic children with normal near phoria exhibit reduced adaptation to plus addition lenses compared to emmetropes?
    a. Based on the results from a previous study in emmetropic adults that showed reduced vergence adaptation in individuals with larger AV/A ratios, it was hypothesized that myopes may show reduced adaptive behavior due to the greater AV/A ratios in myopic children compared to emmetropes.

2. Will the pattern of adaptation in myopes vs. emmetropes differ through minus addition lenses?

    a. Since minus adds increase the demand on accommodation, it was proposed that adaptation to these lenses may be different compared to emmetropes, given the greater accommodative lags observed through minus lenses in myopes.

3. Will the category of vergence-bias (eso/exo) influence binocular adaptation to plus/ minus addition lenses in emmetropic vs. myopic children?
    a. Based on the model of accommodation and vergence, it was hypothesized that esophores may exhibit reduced adaptation to plus adds, compared to exophores as a result of reduced fusional vergence demand. On the other hand, the reversal of fusional vergence demand for minus adds may produce opposite patterns of adaptation in children with eso and exo misalignment.

4. Will myopes continue to show reduced adaptation to disparities necessitating reflex convergence (base-out prism) when accommodative feedback loop is open?
    a. The majority of studies reviewed in the previous sections indicate that myopes show differences in the characteristics of accommodative behavior compared to emmetropes. If accommodation is one of the important causes for differences in the binocular adaptive behavior to near adds, then myopes may not show reduced adaptation when accommodation is not directly stimulated under open-loop accommodation.

3 Methods and instrumentation

3.1 Study protocol

To test the hypotheses formulated in the previous section (Chapter 2), accommodation and vergence were measured under three stimulus conditions during sustained binocular viewing in a group of myopic and emmetropic children between 7-15 years of age.

- Stimulus condition # 1: Binocular fixation with habitual corrective lenses at 33 cm, where stimulus for accommodation = 3D (Chapter 5)
- Stimulus condition # 2: Binocular fixation through +2D only (Chapter 4) and +2D and -2D add over correction, where stimulus for accommodation = 1D and 5D respectively (Chapter 6)
- Stimulus condition # 3: Binocular fixation through 10Δ BO (open-loop accommodation) at 4M, where stimulus for accommodation=0 (Chapter 7)

3.2 Study participants

Participants were recruited from the clinic database at the School of Optometry, University of Waterloo. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the procedures involved in the study. This work received approval from the Office of Research Ethics at the University of Waterloo (ORE #14817). All subjects were treated in accordance with the tenets of the Declaration of Helsinki.

A total of 78 participants were recruited for the purpose of this thesis. Twenty-three children were enrolled in an initial study (Chapter 4) and a different set of 55 children participated in all subsequent studies (Chapters 5-8). Two out of 55 children discontinued from the study due to lack of time. Table 3-1 shows the number of emmetropes and myopes recruited. It must be noted that the total number of children included for analysis in each study was dependent on the specific criteria/type of protocol and are listed in the relevant chapter.

Table 3-1: List of participants in the various studies.

Study	***Number of emmetropes recruited***	***Number of myopes recruited***
Preliminary study- Chapter 4	13	10
Chapter 5- Habitual lenses	25	28
Chapter 6- Add condition	25	28
Chapter 7- Prism condition	25	28
Chapter 8-Variability study	25	28

3.3 Measurement of Accommodation

3.3.1 PowerRefractor and its operating principle

In the current investigation, accommodative responses were measured using an eccentric infra-red (IR) photorefractor, (PowerRefractor, MultiChannelSystems, Reutlingen, Germany) as shown in Figure 3-1) [1, 2]. The PowerRefractor is an infra-red optometer that works on the principal of eccentric photorefraction [3-6]. The advantages of this technique over most autorefractors is its ability to obtain measurements simultaneously from the two eyes, provide information about pupil size, faster sampling rate - 25 Hz (25 measurements per second) and a remote testing distance (1 Meter) due to its photographic nature.[1]

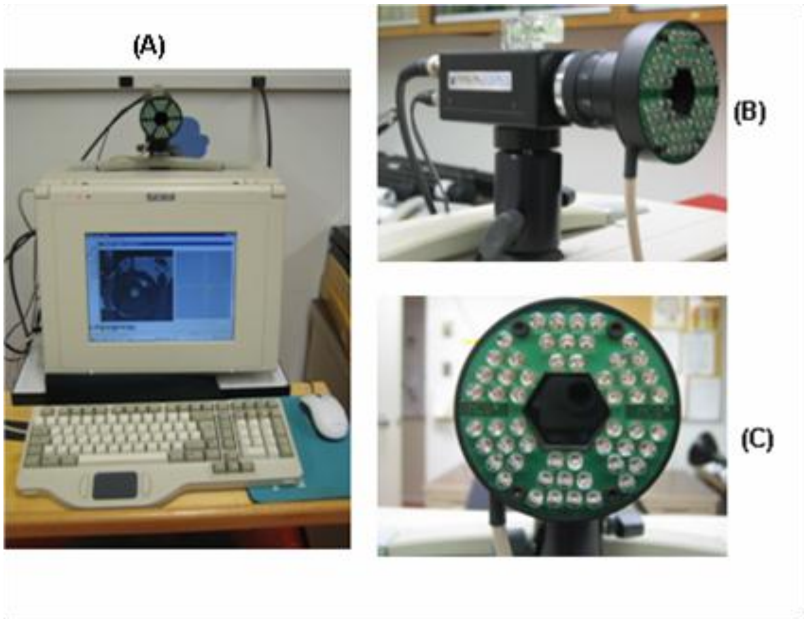


Figure 3-1: Picture of the PowerRefractor (Multichannel Co, Reutlingen, Germany)

The Power Refractor (Figure 3-1a) consists of a triangular array of six light emitting diodes (LED) segments (Figure 3-1c) each containing nine infra-red LED's arranged around a closed circuit device (CCD) camera (Figure 3-1b), connected to a portable personal computer. This extended source arrangement of LED's has been shown to increase the working range of the instrument (between +4D to -6D with respect to infinity) [1]. In this technique, infra-red light from the eccentric light source returns back to the CCD camera after reflection from the eye. The estimate of optical defocus is determined from the intensity profile across the pupil obtained in the image of the camera [3]. The slope of the intensity profile across the pupil varies with the eye's defocus and this information is converted into refractive error or accommodation based on an inbuilt calibration equation [1,6]. However, both relative and absolute measures of individual response require calibration due to inbuilt adjustment for tonic accommodation [7] and variations in fundal reflectance [6]. In the PowerRefractor, the favorable signal-noise ratios are achieved for pupil szies greater than 4 mm. Smaller pupil sizes reduces the signal-noise ratio and affects its precision due to the loss of individual pixel values required to accurately calculate the slope [1].

3.3.2 Measurement modes of the Power Refractor

The PowerRefractor has a sampling rate of 25 Hz (can measure accommodation every 0.04sec) and functions in five different measurement modes: binocular, monocular, fast-screening, complete refraction and 3D reconstruction. Continuous measures of accommodation are possible through the binocular and monocular test modes. Both settings provide information on the accommodative response along the vertical ocular meridian coupled with measures of pupil diameter and gaze deviation. Measurements of pupil size and estimates of gaze position are made using a contrast detection algorithm to locate the pupils and the first Purkinje image (Hirschberg ratio). Deviations in gaze position are identified using a Hirschberg ratio of 11.82 (i.e. 1 mm displacement of corneal reflex is produced when the eye rotates by 11.82 degrees) [1].

In the current study, *monocular mode* was used to measure accommodation in all participants. A screen dump of the "monocular mode" is shown in Figure 3-2. This mode was preferred over the binocular mode because it provides the advantage of tracking the participants gaze while recording the measurements (Figure 3-2-Section 1). The binocular mode provides the same information about gaze deviation, but only after data collection. This feature of the *monocular mode* is extremely useful to ensure proper fixation at the target especially in children due to their limited attention span. The sensitivity of PowerRefractor to detect binocular gaze misalignment was tested by Suryakumar and Bobier [8] using varying magnitudes of prism. The authors reported that the sensitivity of PowerRefractor to detect binocular misalignment was 5Δ (2.85 degrees).

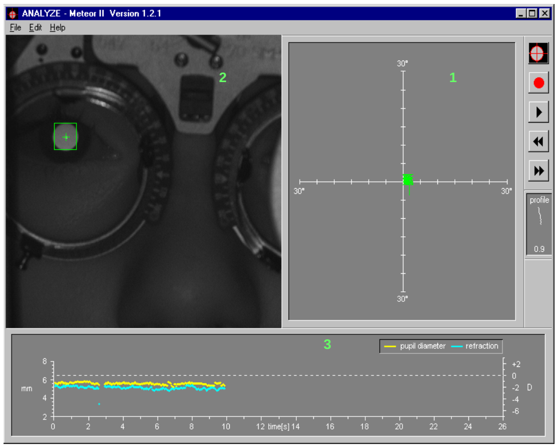


Figure 3-2: PowerRefractor interface using a Monocular measurement mode.

Section 1 (outlined on top right corner) represents the gaze tracker which identifies deviation in gaze positions up to 30 degrees with 5 deg separation. Section 2 shows the measured pupillary region whose intensity profile is converted into accommodation response. Section 3 illustrates the accommodation response measured along the vertical ocular meridian coupled with measures of pupil diameter over a 10 sec period.

3.3.3 Calibration of PowerRefractor

As mentioned earlier, the PowerRefractor converts the slope of the intensity profile into refractive information based on an inbuilt calibration equation obtained from adult participants [1, 2]. However individual calibration from each participant is necessary because the individual differences in fundal reflectance characteristics affect the gradient of light distribution in the retina, thus producing variability between individuals [6].

A two-step calibration process was conducted, similar to previous studies [7, 9, 10] to ensure accuracy of accommodative response obtained from the PowerRefractor:

- Relative accuracy to calibrate the gradient of a series of photorefractive outputs with known changes in ocular focus to estimate whether PowerRefractor provides a 1:1 relationship when the magnitude of stimulus is changed.
- Absolute ocular calibration where photorefractor output is calibrated to a specific dioptric amount. The former allow accurate measures of accommodative change while the latter ensures accurate measures of accommodative error.

Step 1: Relative Calibration

Since photorefractive measures are dependent upon pupil size, calibrations had to be conducted with natural pupils and nullified the use of cycloplegics. Participants wore corrective lenses (determined using retinoscopy and subjective refraction) that provided a visual acuity of at least 6/6 in each eye and were instructed to view a high contrast target (placed at 4m) with their left eye. An infrared (IR) filter (Kodak 87B, IR filter, Rochester, NY) was placed in front of the right eye which blocked visible light but permitted the IR light source of the PowerRefractor to obtain measurement. The accommodative response of the unfiltered eye was stabilized to a high contrast target set at 4M, viewed through the participants' corrective lenses. A series of positive and negative ophthalmic lenses (+5D to -1D in 1D step) were then added over the IR filter to induce refractive errors (accommodative responses) ranging from -5 to +1D. This range was chosen upon consideration of the stimulus demands (maximum =5D stimulated by minus add) tested in this thesis. The resulting PowerRefractor measure (Y) was assessed for each lens and was plotted as a function of induced refractive error (X ranging from -5 to +1D induced by lenses ranging from +5D to -1D). Linear regression analysis was performed to estimate the relationship between induced and measured refraction obtained using the PowerRefractor.

Step 2: Absolute Calibration

In order to evaluate the absolute accuracy of PowerRefractor, accommodative responses obtained with the PowerRefractor were compared with those obtained with dynamic retinoscopy (vertical meridian) [7, 11] at two stimulus conditions (3D and 2D), created by viewing a near target at 33 cm with and without +1D lenses.

Accommodative responses were calibrated using individual calibration functions for all participants. The results of the individual functions are shown in Appendix A.

3.3.4 Targets for measuring and sustaining closed loop accommodation

Two high contrast and colorful targets near targets were used to sustain and measure closed-loop accommodation. The latter, termed the measuring target (presented using a laptop computer) was a color cartoon slide, chosen because it can sustain the attention of the young participants better than a standard high contrast text. All accommodative measures were taken from this cartoon slide as it was necessary to maintain the same stimulus characteristics for each accommodative measure. The target measured approximately 5.5 mm with good contrast (85%) and a target luminance of 15 cd/m^2. In a previous publication from the group [10], this target was compared to high contrast (92%) text in 11 participants, and showed non-significant differences in the accommodative response between the two targets (Cartoon: -2.24 ± 0.22D; Text: -2.35 ±0.32D; $P>0.05$). Similar cartoon targets have been used to measure accommodation in infants [12, 13].

The current study protocol necessitated repeated measurements of accommodation in the same participants on three different days for the no add/plus add/minus add conditions (Chapters 5, 6, 7). Thus, repeatability of accommodation was assessed by comparing monocular responses obtained through habitual corrective lenses on the various days. Pooled data for all participants (both refractive groups) showed similar monocular responses on all three days (Figure 3-3 (a) RM-ANOVA; $P=0.38$) and the co-efficient of repeatability between visits (Fig 3-3 -b) was found to 0.8D.

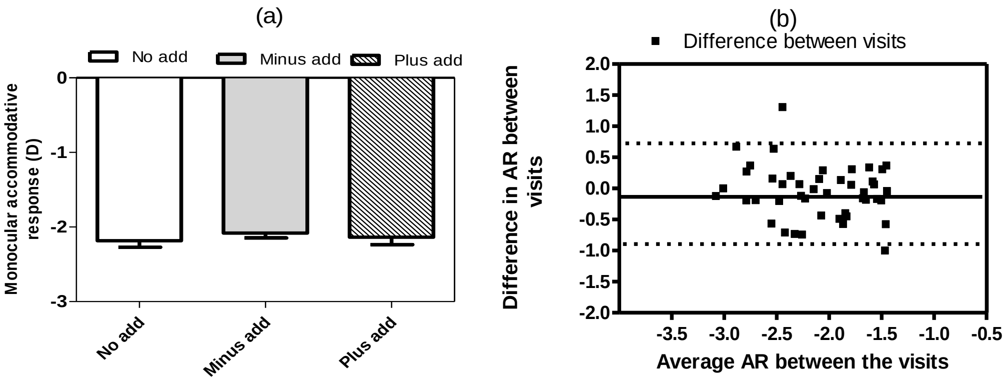


Figure 3-3 (A) Comparison of monocular accommodative response through habitual corrective lenses on three different days. (B)Bland-Altman plot showing the average and mean differences in AR determined on different visits .The COR was found to be ±0.8D. Error bars indicate mean ± SEM

The “sustaining target” was a cartoon movie displayed using a digital video disc (DVD). Again, this target was preferred to a high contrast reading text in view of the shorter attention span anticipated in young children. Similar near fixation tasks other than high contrast text have been used in previous studies to test the effects of near work on accommodation (for e.g. video game-[14])

Information from the two near displays (DVD player and Laptop computer) were sent to a custom-designed control box (Control Box, Fig. 3.6) whose output consisted of a miniature liquid crystal display (LCD) monitor (Model No: LT-V18 U; Victor company of Japan) mounted onto an optical bench (Fig 3.5). The LCD monitor was 1.77″ wide and subtended 3.5 deg x 2.3 deg (H x V) which enabled the gaze deviations to be kept within 5 degrees of fixation and thus prevented any significant off axis measurements [15, 16]. The presentation of near targets (movie or cartoon slide) to the LCD monitor was controlled using a toggle-key. The synchronization of both the near targets into the control box helped maintain a constant screen size and facilitated rapid change between the targets to enable quicker measurements. The image from the monitor was then projected at a distance of 33cms through a semi-silvered mirror (SM, Fig. 1).

3.3.4.1 DOG for measurement of open-loop accommodation

A difference of Gaussian target (DOG) of center 0.2cpd spatial frequency was used to measure open loop accommodation. Lower spatial frequency DOG targets (less than 0.5 cpd) have been shown to be an insufficient stimulus to drive reflex accommodation [17]. The target was projected on a 17 inch cathode ray tube (CRT) monitor with its edges covered using a black cloth to avoid any contour information. The DOG target used in the current investigation does not stimulate accommodation when viewed through a series of negative lenses and has been used in several other studies in the laboratory [8, 10].

3.4 Measurement of Phoria – Modified Thorington Technique (MTT)

Horizontal near heterophoria was measured using the modified Thorington technique – MTT [18] and the magnitude of the phoria was quantified using a custom designed tangent scale (TS, Fig 3-5) placed at 33cm. The tangent scale consisted of a small central aperture to accommodate the light source and a horizontal row of letters/numbers on either side. The letters/numbers on scale were 3 to 4 mm high, equivalent to a Snellen fraction of approximately 6/15 (at that distance) and each letter/number was separated by 3.3 mm (1Δ apart at a distance of 33cm). The scale was illuminated using three white light emitting diodes (LED) housed inside a rectangular box providing a background luminance of 10 cd/m^2. The TS was also connected to the control box (Fig 3-6) which facilitated the measurement of the phoria by illuminating the scale and simultaneously turning off the LCD monitor to avoid stray light affecting the visibility of the tangent scale.

This technique showed good validity and repeatability in previous studies [19-21], which was also confirmed for the current apparatus in adult participants. The 95% limits of agreement with cover-test were ±1.02Δ and the co-efficient of repeatability (1.96*standard deviation of difference) between measures taken on two different days was observed to be 1.98Δ [10]. This thesis measured phoria response in children only. Considering the subjective nature of the test and necessity for repeated measurements in the same participants' (for Chapters 5, 6, 7), measures of repeatability was re-assessed for this group. Fig 3.4(A) shows the comparison of mean habitual near phoria averaged across all participants' for the three closed-loop accommodation conditions. RM-ANOVA shows non-significant difference in habitual near phoria measured on the three different days. The co-efficient of repeatability was found to be 2.8 Δ for the entire group of children. The standard deviation of difference which was used to assess the co-efficient repeatability was non-significant between refractive groups (P=0.23).

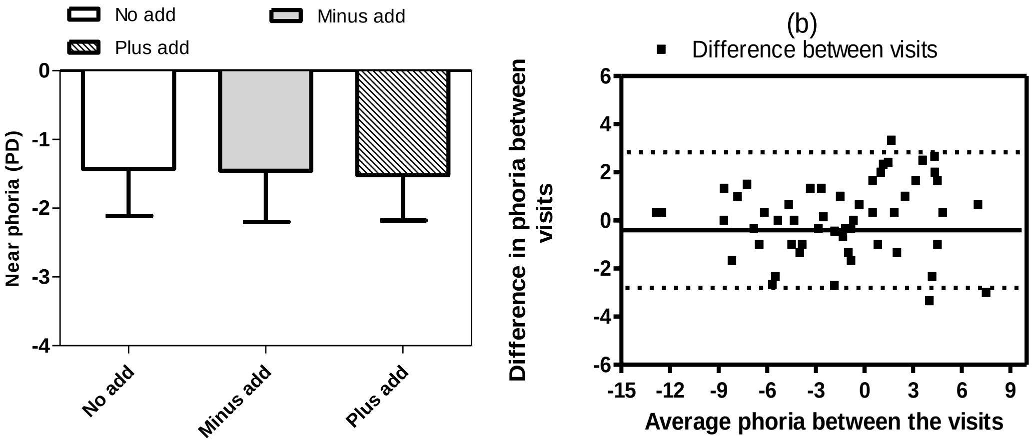


Figure 3-4: (A) Comparison of near phoria responses on three different days in children. (B) Bland-Altman plot shows a plot of average and mean differences in phoria determined on separate sessions. The coefficient of repeatability was found to be ±2.8Δ. Error bars indicate mean ± SEM

3.5 Experimental setup

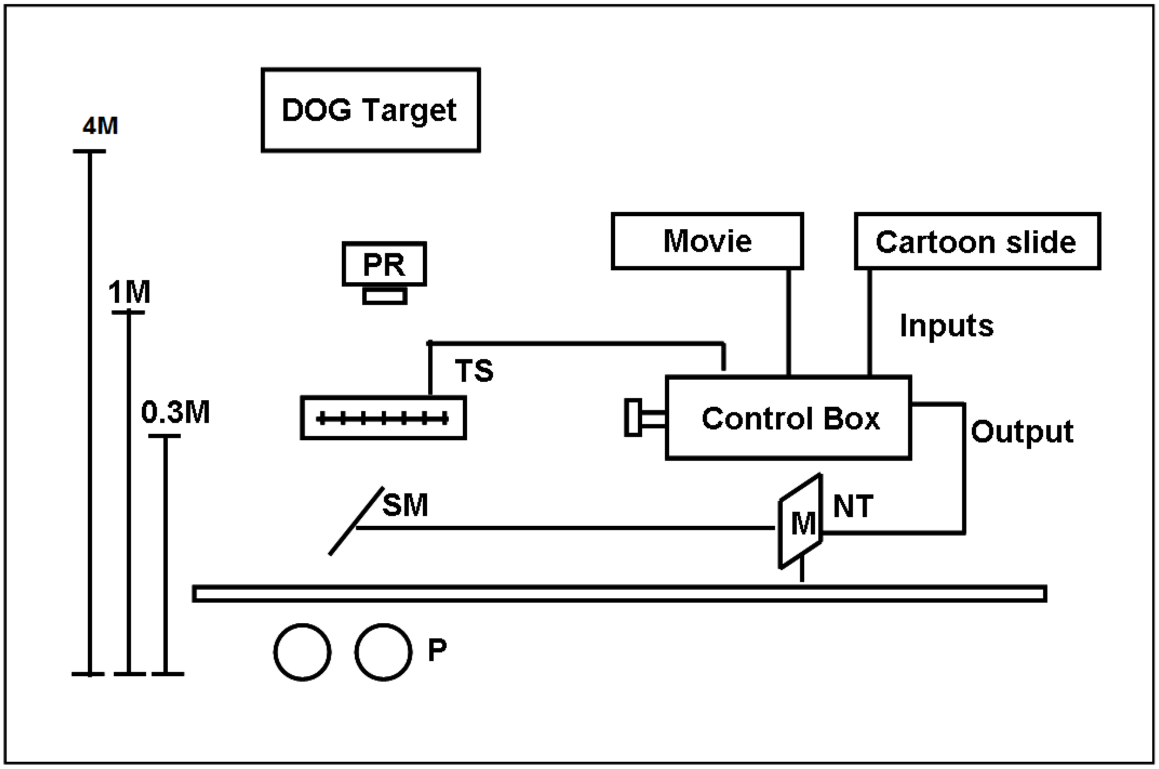


Figure 3-5: Schematic of the experimental set-up.

The participant (P) was seated at a distance of 1M from the PowerRefractor (PR). The near targets (NT) for accommodation were displayed on a miniature LCD monitor (M) that was projected at a distance of 33 cm using a semi-silvered mirror (SM). The monitor received input from either the laptop (Cartoon slide) or the DVD player (movie) and the presentation of targets were controlled using a custom designed control box. The tangent scale (TS) for the measurement of phoria was also connected to the control box for syncing with the other accommodative targets. A difference of Gaussian (DOG) target was placed at 4 M for opening the loop of accommodation.

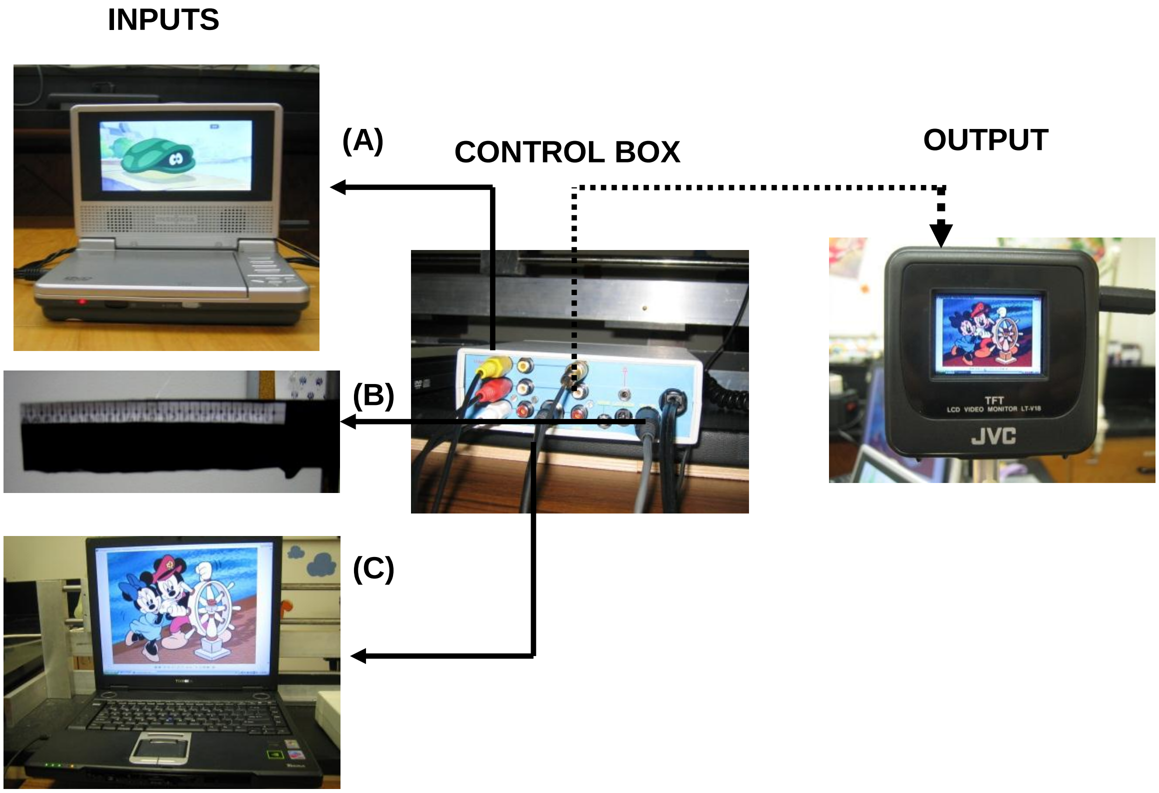


Figure 3-6: The different inputs and the output of the control box.

(A): Near fixation target- Movie played from a DVD player; (B): Tangent scale to measure near phoria; (C): Near measuring target- Coloured picture target loaded on a laptop. The output from the sources is displayed on a miniature LCD monitor.

A schematic of the experimental setup is shown in Figure 3-5. The outputs of the two near targets as well as the tangent scale were fed into the custom designed control box (Figure 3-6). This arrangement was necessary because the current investigation evaluates influence of changes in accommodation on vergence and vice-versa and it is imperative to be able to change targets for measurement of either parameter quickly. The control box was designed with a toggle key which facilitated the rapid change of targets. The order of the presentation of targets is summarized below:

By default, the LCD monitor received its input from the fixating target (movie)

- Toggle 1: The display on the LCD monitor is turned off and the tangent scale would be illuminated for measurement of heterophoria.
- Toggle 2: LCD display changed to the measuring target (colored cartoon slide) for measurement of accommodative response.
- Toggle 3: Display changed back to fixating target (movie) for sustaining accommodation under binocular viewing condition.

The time taken for one complete measurement block (measurement of phoria, binocular and monocular accommodation) ranged between 60 and 80 sec.

4 Binocular adaptation to +2D lenses in myopic and emmetropic children

This chapter is published as follows:

Vidhyapriya Sreenivasan, Elizabeth L Irving, William R Bobier. Binocular adaptation to +2D lenses in myopic and emmetropic children Optom Vis Sci. 2009 Jun; 86(6):731-40.

This study was performed as an initial investigation to determine if refractive error (myopia) shows any differential effect on binocular adaptation. Since phoria (vergence-bias) category was predicted to be an influential variable, only myopic and emmetropic children with normal near phoria were included in this study.

4.1 Summary

Purpose: To compare vergence adaptation to +2D addition lenses in myopic and emmetropic children and to evaluate the influence of the accommodative-vergence cross link (AV/A ratio) on this adaptation.

Methods: 9 myopic and 11 emmetropic children fixated a near target at a distance of 33 cm. Measures of binocular and monocular accommodation and phoria were obtained during a 20 minute near task with and without +2D lenses. Response AV/A ratios were determined from the experimental results. Vergence adaptation was quantified by the magnitude of phoria reduction and the completeness (return of adapted phoria to habitual level) after the near task.

Results: Myopic children showed significantly higher AV/A ratios which led to greater lens-induced exophoria and a greater demand for vergence adaptation. Both refractive groups showed significant vergence adaptation; however, myopes exhibited significantly reduced (P=0.010) magnitudes compared to emmetropes (Myopes= 3.95±0.15Δ, Emmetropes =4.41±0.08Δ). The mean completeness was also significantly (P< 0.001) reduced in myopes (61.02±1.57) compared to emmetropes (76.6±2.10). There was a

significant correlation between magnitude of adaptation and AV/A in both the refractive groups; however, myopes consistently showed reduced magnitudes compared to emmetropes. AV/A ratio influenced completeness in emmetropic but not myopic children. In the accommodation system, +2D lenses eliminated the accommodative lags observed in myopic children during natural viewing conditions. These lenses resulted in a small over-focus (-0.24±0.27D) at the onset of near work, which decreased during sustained viewing through the near add.

Conclusion: Myopic children demonstrate reduced magnitude and completeness of vergence adaptation to +2D lenses. The magnitude of vergence adaptation varied with AV/A in both refractive groups; however, the presence of myopia differentiated the size of adaptation. On the other hand, degree of completeness appears to be primarily associated with the type of refractive error.

4.2 Introduction

Near (plus) addition lenses have been prescribed to myopic children in an attempt to slow the progression of myopia attributed to near work [1-5.] The current basis for prescribing near (plus) adds to myopic children is to eliminate the large accommodative lags [6] that might create a hyperopic retinal defocus and possibly trigger axial elongation of the eye [7-9]. Clinical trials that evaluated the ability of these lenses to slow myopic progression provided varying results ranging from no success, [10, 11] limited success [12, 13] to clinically significant reduction of myopia [14, 15]. Several studies have shown that myopic children with esophoria display greater benefit (i.e. less progression of myopia) from wearing near adds compared to children with exo or orthophoria [13, 16, 17]. In addition, accommodative responses seemed to influence myopia progression through the plus add, with the greatest reduction of myopic progression observed in children with larger accommodative lags [13,16] and in esophoric children with higher lags of accommodation [18]. These findings suggest that the accommodative and phoria status of the child might play a significant role in the mechanism of reduction of myopic progression with plus lenses.

Several studies have evaluated the effect of near adds on the accommodative responses of emmetropic [19-22] and myopic adults [23]. These investigations consistently show that plus lens additions are capable of reducing the lag of accommodation at low dioptric powers (+1D) [19,20] and result in a small amount of over-focus or lead of accommodation with higher dioptric powers (+2 and +3D) [20- 22] Past research show evidence for greater accommodative lags in myopic children under negative-lens induced monocular viewing conditions, [6, 24] with monocular real targets [25] or under binocular viewing condition through full refractive correction [26]. However, relatively few investigations have evaluated the ability of near adds to reduce or eliminate the accommodative lags observed in myopic children.

In the vergence system, studies have evaluated the effect of near adds on adult participants, either immediately upon the addition of lenses [23] or with sustained fixation [27,28, 29]. It is known that near adds affect both accommodation and vergence through the accommodative vergence (AV) (Mueller 1826, cited in Alpern[30]) and vergence-accommodation (VA) [31] cross links. However, earlier investigations did not measure coincident changes to both systems but measured changes to either accommodation or vergence alone [19-21, 29]. A recent study from our group evaluated the coincident time course of changes to accommodative response and near phoria when emmetropic adults' sustained fixation (33 cm) through +2D lenses [22]. A consistent pattern of change was observed. Introduction of near addition lenses produced an exophoric shift, accompanied by a significant increase in binocular accommodation over that of monocular accommodation. This difference, (attributed to convergence accommodation), was believed to be a result of the lens-induced exophoria triggering an increase in fast reflex convergence and subsequently an increase in the output of convergence driven accommodation [32-34]. After several minutes of prolonged viewing, vergence adaptation occurred, concurrently reducing the exophoria and the binocular levels of accommodation while monocular levels remained constant. The degree of vergence adaptation was quantified using two parameters. The first parameter, magnitude of adaptation, represents the absolute change in phoria through +2D adds before and after the near task. The second parameter, completeness of adaptation describes the degree to which the phoria has returned to its original level prior to viewing through the near add. Past studies on prism adaptation commonly quantified adaptation as a change in induced phoria only [35-40] similar to our first parameter, the magnitude of adaptation. We found that a second term, completeness was necessary because the lens induced change in phoria was not the same for each subject but rather it depended on their AV/A. Therefore, any two individuals showing the same magnitudes of adaptation will not exhibit the same completeness of adaptation if they have different AV/A ratios. In our previous study, both magnitude and completeness of vergence adaptation were dependent on an individual's AV/A ratio [22]. Higher AV/A ratios were associated with greater magnitudes of adaptation but the lens-induced exophoria did not return to its habitual level indicating less-than complete vergence adaptation.

Past studies show higher response AV/A ratios in myopic children compared to emmetropes [41,42]. Based on the results from our adult study [22] it can be hypothesized that plus addition lenses will produce greater exophoric shift that would increase the fusional vergence demand in myopic children. This increased vergence demand requires greater levels of vergence adaptation, if the lens-induced phoria is to return to its original level. In addition, myopic children might not exhibit the same magnitude of accommodative lead seen in emmetropic adults due to the larger accommodative lags observed under binocular [26] or monocular viewing conditions [6, 24, 25]. Relatively few investigations have evaluated the changes to both accommodation and vergence response when myopic children perform near task through plus addition lenses. Recently, Cheng and co-workers evaluated the effect of various combinations of positive lens additions and base-in prisms on the accommodative lag and near phoria of progressive myopic children [43]. The authors measured the responses immediately after the addition of lenses / prisms and concluded that the combination of +2.25D lens and 6 $^{\Delta}$ base-in resulted in minimal accommodative lag and exophoria. However, as acknowledged by the authors, this investigation did not measure changes to accommodation and phoria during sustained near activity. Thus, the possibility of vergence adaptation to lenses and prisms cannot be excluded and the beneficial effect of reduced phoria and accommodative lag may not be maintained over a period of prolonged spectacle wear.

To our knowledge, vergence adaptation to near addition lenses has not been investigated in myopic children. North and colleagues compared adaptation to 6 $^{\Delta}$ base-in and base-out in adult groups of emmetropes, early onset and late onset myopes [37]. They reported no difference in the magnitude of prism adaptation between the three refractive groups. On the other hand, Rosenfield suggested that late onset myopes might have reduced vergence adaptive ability compared to emmetropes [44]. Therefore, it is still not clear whether the adaptive ability of young myopes is any different from that of emmetropes. Thus, aim of this study was to investigate the time course of changes to accommodation and vergence when myopic children perform sustained near work (20 min) through +2 D addition lenses. Based on the results of our adult study [22] and the higher AV/A ratios expected in myopic children [41, 42] we hypothesize that myopic children may show less complete adaptation to near adds compared to emmetropes. We will explore the extent to which the AV/A ratio accounts for the differences in adaptation.

4.3 Methods

4.3.1 Study participants

Twenty-three children (ten myopic and thirteen emmetropic) between the ages of 7 and 15 years were recruited from the clinic database at the School of Optometry, University of Waterloo. The protocol followed the tenets of the Declaration of Helsinki and received approval from institutional review board. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the nature and possible consequences of the study.

Participants with normal general and ocular health (determined from their clinical records) underwent preliminary examination to ensure the following: myopic refractive error between -0.75 and -6 D or emmetropic refractive error between +0.5 and +1.5 D determined using cycloplegic refraction; astigmatism < 1D; anisometropia < 0.5D; best corrected visual acuity of at least 6/6 in each eye; normal binocular vision status ensured through normal distance and near phorias [45] by prism neutralized cover test; normal amplitudes of accommodation; and that participants were not taking any medications that might influence the accommodation and vergence systems [46]. Table 4-1 lists the age and critical visual parameters of the two study groups.

Table 4-1: Critical visual parameters of myopic and emmetropic children

PARAMETER (MEAN ± SEM; AND RANGE WHERE APPLICABLE)	**EMMETROPES**	**MYOPES**
No of participants	13	11
Age	11 ± 0.65 yrs (7-14)	11 ± 0.58 yrs (7 -14)
Refractive error	0.6 ± 0.12D (0.5 to 1D)	-2.04 ± 0.48D (-0.75 to -3.75D)
Near phoria	-2.80 ± 0.87 Δ (-0.5 to -8 Δ)	-2.88 ± 0.96 (Ortho to -8 Δ)
Distance phoria	-0.45 ± 0.40 Δ (0.5 to -1 Δ)	-0.44 ± 0.43 Δ (0 to -2 Δ)

Phoria measures: Negative sign denotes exophoria

4.3.2 Instrumentation and experimental procedure

The instrumentation and the experimental setup used in this study have been described in detail elsewhere [22] (Section 3.3-3.5). Briefly, accommodative responses were obtained when children fixated a single high contrast (85%) color cartoon frame at a distance of 33cm. This target was chosen as it was expected to be more successful than conventional reading material in holding the participants' attention. Accommodative responses with and without +2D lenses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor (PowerRefractor, MultiChannelSystems, Reutlingen, Germany for description see [47, 48]*)* at a sampling rate of 25 Hz for a period of 10 sec. When tested with near addition lenses, the PowerRefractor recorded accommodative measures as a sum of the near addition lens and the accommodative response. This combination, conjugate with the participants' retina was termed *"plane of focus"*. [22] Thus, in the no add condition; the plane of focus approximates the participants' accommodative response given that myopes were corrected for their distance vision. When viewing through the near add the plane of focus would correspond to the combination of +2D lens and accommodative response through the lens. "Binocular plane of focus" was measured while both eyes fixated the target; however, responses were recorded from the right eye alone. For the measurement of "monocular plane of focus", the left eye was occluded. During the 10 sec measurement period, the accuracy of fixation was assessed using the gaze control function displayed on the PowerRefractor interface. Additionally, care was taken to ensure that the child was fixating the near target at the correct fixation distance (33 cm) while measurements were recorded. A volunteer constantly monitored the head position of the child and ensured they did not move away from the chin rest during measurement. If unsteady fixation was noticed during measurement, or when the examiner (VS) observed off axis gaze errors exceeding 5 degrees, the measures were flagged using keyboard inputs and discarded given the possibility of under or over estimation of accommodation [49-52]. In these cases, recordings were obtained for an additional 5 sec period to ensure equal data sets across subjects.

Measures of open loop accommodation (tonic accommodation) were taken by instructing participants to monocularly fixate (left eye occluded) a low spatial frequency (0.2 cpd) difference of Gaussian target placed at a distance of 3.5 meters.

Accommodative measures obtained from the PowerRefractor were calibrated using a protocol similar to previous studies [20, 22, 53]. Briefly, the output of the photorefractor was compared to actual levels of refractive error induced on each participant by the addition of ophthalmic trial lenses (-1D to +6D). From this procedure, calibration formulae were defined for each of the two groups. The absolute precision of accommodative response was then determined by comparing the PowerRefractor response with dynamic retinoscopy when participants viewed a near target (33cm). Based on the results of the calibration study all Power Refractor responses (PR) from both refractive groups were adjusted using calibration equations (see below) to define actual plane of focus response (PF)

Myopes: $PF = (PR / 1.12) - 0.22$ (1)

Emmetropes: $PF = (PR/1.07) - 0.25$ (2)

Though the two equations show slightly different slopes, this difference was small and was not found to be statistically significant ($P>0.2$). Moreover, the accommodative responses did not differ significantly when individual calibration equations were used instead of group equations in both refractive groups (Margin of error <0.10D; $P > 0.6$).

Horizontal near heterophoria (33cm) was measured using the modified Thorington technique (MTT) and the magnitude of the phoria was quantified using a custom designed tangent scale. This technique showed good validity and repeatability in previous studies [54-57]. The efficacy was also confirmed from our own experience where we have found the 95% limits of agreement with cover-test to be ±1.02Δ. The co-efficient of repeatability between measures taken on two different days was observed to be 1.98Δ (1.96*standard deviation of difference) [22]. The tangent scale used to quantify phoria consisted of a small central aperture for the light source and a horizontal row of letters/numbers on either side with each letter/number separated by 3.3 mm (1Δ apart at a distance of 33cms). A red Maddox rod was placed before the right eye and phoria was measured using a "flashing technique" similar to previous studies [22, 29]. The participants verbally reported the number/letter that was closest to the red line. The same technique was repeated thrice and near heterophoria was defined as the average of the three responses. Considering the possibility of higher variability in this age group, all children received a training session with the MTT prior to the experimental session. During the training session, picture cards were shown to facilitate better understanding of the test. Near phoria was measured 5 times and all children were able to achieve standard deviation of less than 1.5 Δ (range 0-1.25 Δ; mean = 0.51 ± 0.43). The variability of phoria response within the experimental session (i.e. the variability between the three trials obtained during a particular time point) was also determined at each time point tested in the study. The highest mean (±SD) variability was observed to be 0.50±0.53Δ in our study group.

The experimental procedure consisted of two study sessions; one session was performed with the children wearing their corrective lenses if any in a trial frame (referred to as *"no add condition"*) and the other involved measurements with +2D lenses (referred to as *"add condition"*) added over their correction (if applicable). The +2D lenses were inserted at a distance of 12 mm from the participants' eyes and the trial frame was adjusted for the participants near pupillary distance so as to reduce any prismatic effect. The two study sessions were performed on different days (separated by at least by 24hrs) and the order of testing was randomized to avoid bias. Prior to the start of the study sessions, all participants were dark adapted for 3 minutes to avoid effects of previous near work [58]. The lighting in the examination room was then reduced to approximately 10 lux to obtain sufficiently large pupil sizes (greater than 4mm as recommended by the manufacturer of PowerRefractor) for the measurement of accommodation. Each session involved measurement of pre-task tonic accommodation (open loop accommodation immediately after dark adaptation), followed by baseline measurement of phoria (vergence open loop), binocular and monocular plane of focus (closed loop accommodation). The approximate time taken for one complete measurement block (measurement of phoria, binocular and monocular focus) ranged between 1 and 1.5 min. Following the baseline measurement, participants were instructed to watch a cartoon movie that was played at a distance of 33 cm. This target was chosen to avoid boredom and to ensure sustained near fixation for the scheduled duration of the study (20 min). Subsequent measures of phoria, binocular and monocular plane of focus were then recorded after 3, 6, 9, 15 and 20 minutes of near fixation. Plane of focus measures were taken at the above mentioned time points by replacing the movie clip with the single frame (cartoon slide) used in the baseline measurement in an attempt to keep the illuminance of the target constant. Post-task tonic accommodation was finally measured after the 20 minute near task.

4.3.3 Data Analysis

The plane of focus response at each time point was estimated by averaging the data points obtained over the measurement period (normally 10 sec) similar to the method described in our previous study [22]. Briefly, each data point was screened and accepted if the following criteria were met: the pupil size was above 4mm (as per PowerRefractor manufacturer guidelines); the horizontal and vertical deviations in gaze were less than 5 degrees from the center of the camera; and the responses were free of blinks (blink artifacts removed by a method similar to our previous study [22]). To be considered for averaging and further analysis, each participant needed to have at least 200 rows of acceptable data after satisfying all of the above criteria. If the participants had more than 200 eligible data points, only the first 200 points were taken for further analysis. The data retained were averaged to obtain the plane of focus response for a particular time point. Three study participants were excluded from the averaging process since they failed to provide the minimum levels of acceptable data as a result of pupil diameters less than 4mm (1 emmetrope and 1 myope) and excessive gaze deviation (1 emmetrope). Thus the data of 11 emmetropes and 9 myopes were considered for further analysis.

In order to quantify the effect of the accommodative-vergence cross link (AV/A) on the vergence response with +2D lenses, stimulus and response AV/A ratios of all participants (N = 20) were determined from the experimental results (with +2D lenses) using the Gradient AV/A method. The change in phoria responses were then studied based on the magnitude of AV/A ratio.

Repeated measures analyses of variance (RM-ANOVA) was used to determine the effect of lens condition and time on plane of focus and vergence. In all cases, statistically significant main effects were further examined using Tukey Honestly significant differences (HSD) post-hoc tests to determine the precise time point that showed the significant difference. Differences were considered statistically significant when the likelihood of type-I error was <0.05. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Exponential curve fitting and analysis were performed using Graphpad software (Graphpad Inc, USA) to investigate the changes in near phorias through +2D lenses.

4.4 Results

4.4.1 Changes to plane of focus measures without near add and with +2D lenses

The dotted lines in Fig. 4-1 shows the plane of focus measures during the no add condition from emmetropic (Fig. 4-1A) and myopic (Fig. 4-1B) children. Myopic children exhibited significantly greater accommodative lags (denoted by negative sign) compared to emmetropes under binocular and monocular viewing conditions (binocular viewing: Emmetropes = -0.60 ±0.06D; Myopes = -1.10 ± 0.08D, monocular viewing: Emmetropes = -0.81±0.07; Myopes = -1.29±0.09, $P<0.001$). In both groups, the initial accommodative lags significantly reduced with sustained near activity (mean reduction in lag after 20 minutes of near work, binocular: Emmetropes = 0.21 ± 0.07 D: Myopes = 0.32 ± 0.08 D; monocular: Emmetropes = 0.19 ± 0.08D: Myopes = 0.28 ± 0.07D; all $P<0.050$). The binocular plane of focus showed consistently greater (i.e. more negative) response compared to the monocular plane of focus and the pattern of change in focus was similar under both viewing conditions. This pattern was also similar to previous studies with adult participants [20, 22].

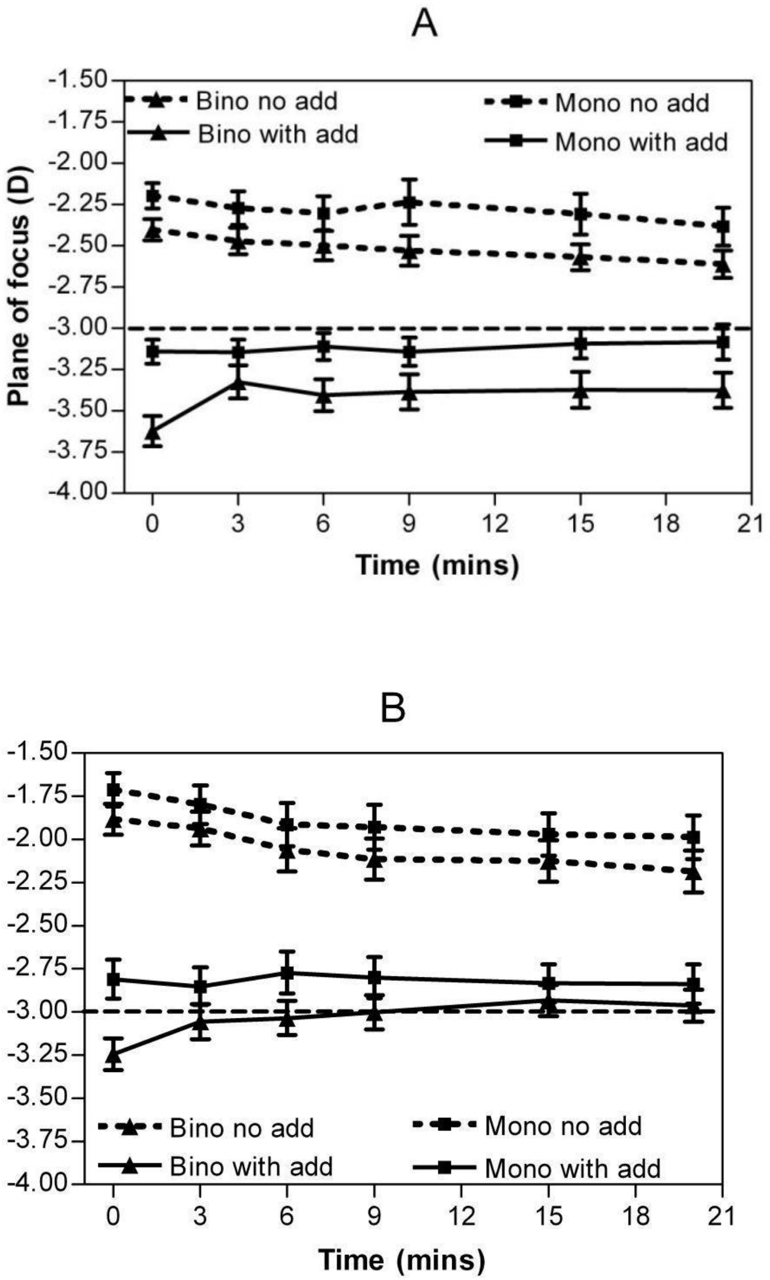


Figure 4-1 A and B: Mean plane of focus measures with and without +2D lenses in the emmetropic (Fig 1A) and myopic groups (Fig 1B).

Solid lines indicate responses with add and dotted lines represent responses without +2D lenses at 33cm (STA= 3D, dashed line in Fig) . Under both conditions, filled triangles represent binocular responses and filled squares represent monocular responses. Error bars indicate mean ± SEM

Plane of focus measures through +2D lenses (add condition) are illustrated using solid lines in Fig. 4-1 A (emmetropic) and 1B (myopic group). Addition of +2D lenses shifted the plane of focus in a myopic direction (P <0.001) compared to the no add condition under both binocular and monocular viewing states. However, the mean binocular and monocular plane of focus varied in terms of the initial response and the pattern of change over time between the two refractive conditions. In the binocular viewing condition, introduction of +2D lenses resulted in greater "*over-focus*" (term used in this study to describe lead of accommodation and denoted by a positive sign) in emmetropes (0.60 ± 0.09 D, Fig. 4-1A) compared to myopes (0.24± 0.09 D, Fig. 1B) at the onset of near work. The mean monocular plane of focus with add was close to the position of the target (33cm, dashed line in Figs.4-1 A and B) in the emmetropic group (small over-focus of 0.05 ± 0.08D, Fig 4-1A) and exhibited a small amount of accommodative lag in the myopic group (-0.15± 0.10 D; Fig. 1B). The difference in plane of focus between the binocular and monocular viewing conditions was statistically significant in both refractive groups at the onset of near work (Emmetropes = 0.48 ± 0.08D, P=0.008; Myopes= 0.44± 0.10D; P=0.005). However, this difference was not significantly different between the two refractive groups (P=0.100).

During sustained near fixation with the addition lenses, the binocular measures alone showed a significant reduction in focus after 3 minutes of near work in both refractive groups (Reduction in emmetropes = 0.30±0.09D, P=0.005, Myopes = 0.19 ±0.09D, P=0.010; Fig 4-1A and B). With continued fixation, there was no significant reduction in binocular focus in either refractive group. The reduction in binocular focus placed the mean plane of focus closer to the accommodative demand (dashed line at 3D) in the myopic group in such a way that the near target was almost exactly conjugate with the retina. The monocular plane of focus measures remained quite stable in both the groups with no significant changes throughout the 20 minute fixation period (Fig.4-1 A and B: solid line with squares; all post-hoc tests: $P<0.050$). The difference between binocular and monocular focus was not found to be statistically significant after 3 minutes of sustained viewing.

The accommodative errors (AE) through +2D lenses were compared with respect to a zero difference (relative to 3D) at all-time points in both refractive groups. The binocular AE showed significantly greater over-focus at time point 0 in both refractive groups (Emmetropes, AE = 0.60 ± 0.09D; $P<0.001$; Myopes, AE= 0.24± 0.09 D, $P<0.050$). After 3 minutes of sustained fixation, the AE in myopic group did not differ from a zero error ($P=0.70$) but emmetropes still showed significantly ($P<0.05$) greater AE (0.28± 0.09D). The monocular accommodative errors were not observed to be significantly different from zero at all-time points in both refractive groups (Emmetropes, $P=0.80$; Myopes, $P>0.1$).

4.4.2 Tonic accommodation

Fig.4-2 illustrates the differences in tonic accommodative responses (measured with the DOG target) before and after the 20 minute near task in the refractive groups during the “no add” and “the add” viewing conditions. Both refractive groups showed a significant (P<0.050) myopic shift in tonic accommodation after near work (Accommodative adaptation; Emmetropes = - 0.41 ± 0.07 D; Myopes= -0.56 ±0.15 D) in the no lens condition; however, the difference between the refractive groups was not significant (P=0.80). In the add condition, the tonic changes after prolonged fixation were not significantly different (P =0.60) from the pre-task measurements in either refractive group (Emmetropes: 0.13± 0.07D; Myopes: 0.07 ± 0.07D). Furthermore, the magnitude of accommodative adaptation with +2D lenses was significantly lower than the amount of adaptation without +2D lenses in both the refractive groups (both groups P<0.050).

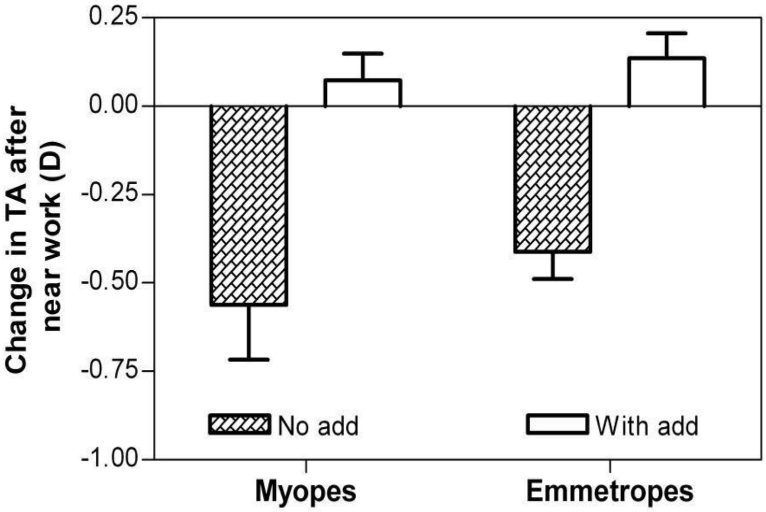


Figure 4-2: Mean tonic accommodative change (Pre task – post task) after 20 minutes of near work. Error bars indicate mean ± SE

4.4.3 Changes in near phoria without and with +2D lenses during near work in the two refractive groups

The average habitual near phoria of the emmetropic and the myopic groups were observed to be -2.80 ± 0.87Δ and -2.88 ± 0.96 Δ respectively (ranged between ortho and -8Δ in both groups with the negative sign indicating exophoria: P=0.90, Fig 4-3 and Table 4-1). Fig.4-3 compares the changes in the mean phoria when participants performed prolonged near work through their habitual correction. The mean changes in near phoria without near addition lenses were observed to be similar in both refractive groups until 9 minutes of near work. Beyond that time, the emmetropic group showed a drift towards esophoria that was statistically significant at the end of the near activity (Fig. 4-3, dashed line; difference between 9 and 20 minute time points: 1.01 ± 0.74Δ; P=0.02). The myopic group did not show any significant change in near phoria even after 20 minutes of near work through their habitual corrective lenses (Fig. 4-3, solid line; P=0.85).

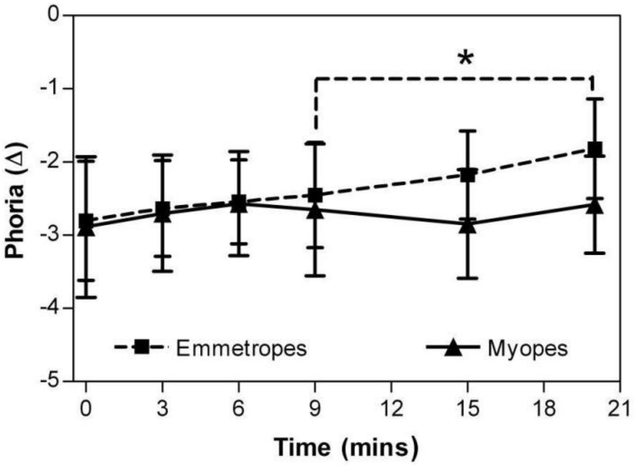


Figure 4-3: Mean phoria responses in both refractive groups in the no lens condition during 20 minutes of near fixation. Error bars indicate mean ± SEM

Fig. 4-4(A and B) shows the changes in near phoria with +2D lenses over time in the two refractive groups. Introduction of +2D lenses (Fig. 4-4 A and B, solid lines) significantly increased the mean near exophoria by 5.65 ± 0.85 Δ in the emmetropic group and 6.45 ± 0.55 Δ in the myopic group. Continued fixation resulted in a significant reduction ($P<0.001$) in phoria following 3 minutes of near viewing in both groups (Emmetropes=3.79 ± 0.65 Δ; Myopes= 3.03 ± 0.88 Δ). With extended binocular fixation, the mean exophoria in the myopic group showed a further small reduction that was approaching significance (Fig. 4-4B: Difference between 3 & 20 min time points: 1.12 ± 0.99Δ; $P = 0.059$). In both refractive groups, the pattern of reduction in exophoria significantly correlated with the reduction in the binocular plane of focus during sustained viewing through the near add (Pearson $r > 0.9$; $P=0.005$).

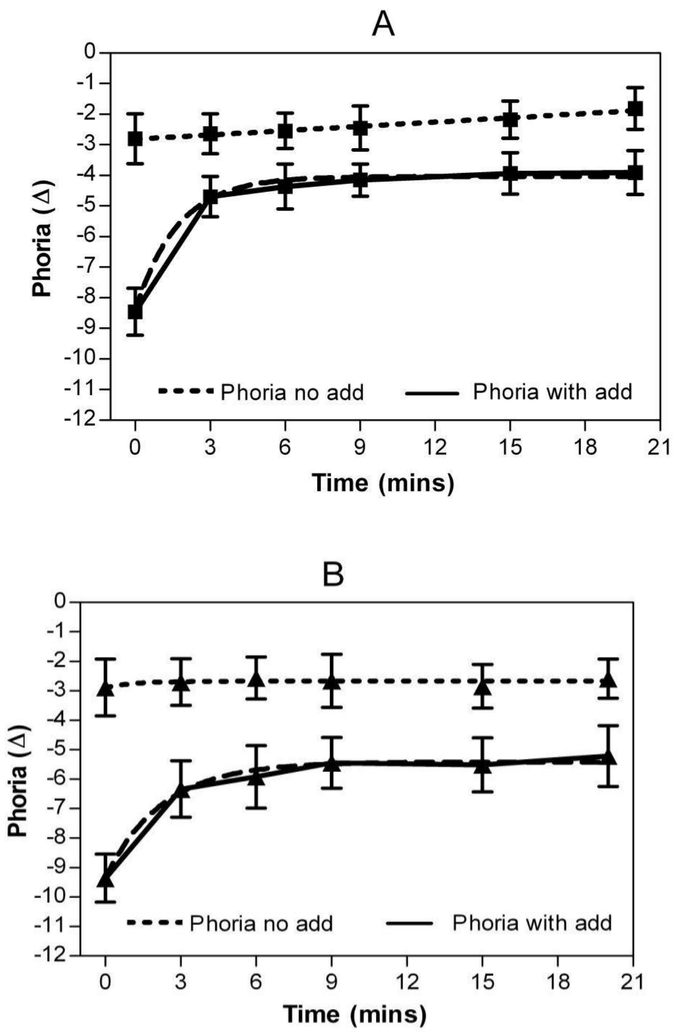


Figure 4-4 A and B: Mean phoria responses with (solid line) and without (dotted line) +2D lenses in emmetropic (Fig 4A) and myopic group (Fig 4B).

Exponential decay function for the add condition is shown as dashed line in Fig 4A (emmetropic) and 4B (myopic). Error bars indicate mean ± SEM

The changes in near phorias with +2D lenses were fit using an exponential decay function (dashed line in 4-4A and B) to compare the magnitude and percentage of completeness of adaptation between the two refractive groups. Magnitude (ΔV) refers to the total reduction in near phoria through +2D lenses upon saturation and was determined from the asymptote of the exponential function. The completeness of adaptation was calculated by dividing the amount of phoria reduced over time through +2D lenses by the initial change in phoria induced by the plus lens. We observed the completeness to be significantly lower in the myopic group (61.02 ± 1.57%) compared to emmetropes (76.6± 2.10 %; P<0.001) after 20 minutes of near viewing. The mean magnitude of the change in adaptive vergence was also significantly less in myopic (3.95 ± 0.15 Δ) compared to emmetropic children (4.41 ± 0.08 Δ; P=0.010). However, the time constant of phoria reduction (defined as the time taken to reach 63% of total reduction in exophoria) did not show any significant difference between the two refractive groups (emmetropes =1.69± 0.07 min; myopes=2.12 ± 0.08 min; P=0.35).

4.4.4 Effect of AV/A ratio on the reduction of exophoria

Myopic children showed significantly higher response AV/A (RAV/A) ratios compared to the group with emmetropic children (Emmetropes: 5.61 ± 0.61Δ; Myopes: 7.08 ± 0.9Δ, P =0.010). The stimulus AV/A measures were not significantly different between the groups.

Fig. 4-5 shows the relation between RAV/A ratio, magnitude of phoria change and completeness of adaptation in both refractive groups in the add condition. Both myopes and emmetropes showed significant positive correlations between RAV/A and magnitude of adaptation (Pearson r, Emmetropes = 0.64, P<0.05; Myopes, = 0.87, P=0.008). When magnitude was analyzed as a function of AV/A ratio, both refractive groups showed similar slopes (Bivariate regression analysis, Emmetropes = 0.41;

Myopes = 0.32; P=0.70) indicating no interaction between refractive error and AV/A ratio. However, the myopic group showed a significant offset (P<0.001) compared to emmetropes reflecting the reduced magnitude of adaptation observed in this group.

With regards to completeness of adaptation, Fig 4-5 allows comparison between the actual magnitude of adaptation through near adds (thick lines with symbols) with a reference level (thin lines and no symbols) showing complete adaptation in either refractive group. In comparison with their respective slopes of complete adaptation, the slope of actual adaptation obtained from emmetropes showed significant difference (P=0.002) as a function of AV/A ratio. Emmetropic children with low AV/A ratios showed near complete adaptation but the degree of completeness reduced with an increase in AV/A ratio (Fig 4-5). On the contrary, the slope of actual adaptation did not differ (P=0.45) from that of complete adaptation in myopes; however, the actual adaptation was significantly offset (P<0.0001; Fig 4-5) with respect to the complete adaptation, indicating less complete adaptation throughout the range of AV/A ratios observed in the study.

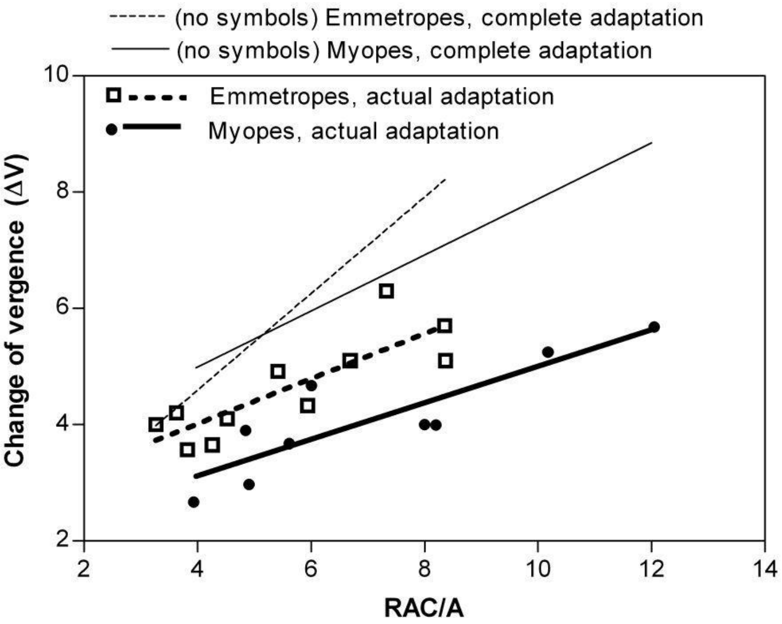


Figure 4-5: Plot showing the relation between RAV/A ratio, magnitude of phoria change and degree of completeness of adaptation in both refractive groups in the add condition.

Responses from emmetropes are shown as open squares and dashed lines while myopes are represented through solid lines and filled circles. In both refractive groups, thick lines indicate actual state of adaptation and thin lines denote complete adaptation (magnitude equivalent to the return of adapted phoria towards habitual level).

4.5 Discussion

This is the first investigation that measured changes to both accommodation and vergence responses when myopic school aged children performed sustained near activity through +2D addition lenses. The main finding of this study was that children with myopia exhibit reduced vergence adaptation to near addition lenses, both in terms of absolute change (magnitude of adaptation) and in terms of proportional change (completeness towards their habitual phoria) compared to emmetropes.

4.5.1 Influence of AV/A ratio on vergence adaptation to lenses in myopes

Irrespective of the refractive error, we observed that the magnitude of phoria adaptation increases with increasing demand of exophoria imposed by higher AV/A ratios; however, myopic children consistently showed reduced magnitudes compared to emmetropes. On the other hand, AV/A ratio influenced the completeness of adaptation in emmetropic children alone. In emmetropes, adaptation was less complete for individuals with higher AV/A ratios, similar to the results of our adult study [22]. Conversely, in the myopic group, children showed less complete adaptation at all AV/A ratios.

The higher response AV/A ratio observed in myopes (similar to previous studies [41, 42]) might be viewed as a cause for the reduced magnitude of adaptation observed in this group of children. If their AV/A ratios were the sole cause of the difference in adaptation, we would expect the absolute change in phoria to be greater in the myopic group since higher AV/A ratios result in greater amounts of induced exophoria, which would drive greater reflex convergence, and greater magnitudes of vergence adaptation [22, 29, 59]. This was not the case. In fact, the average amplitudes of adaptation were greater in our emmetropic group compared to myopes. In addition, results from this investigation indicate that myopes show deficient completeness of adaptation even at low AV/A ratios and the degree of completeness was independent of AV/A. These results suggest that the decreased adaptation found in the myopes is not solely the product of AV/A ratio, supporting the hypothesis proposed by Rosenfield [44] that the vergence adaptive property itself might be reduced in myopes.

Additionally, vergence adaptation to near addition lenses in myopes could appear incomplete if changes occurred to the AV cross-link because of accommodative adaptation [60]. The accommodative aftereffects through +2D lenses demonstrate a small positive shift indicating further accommodative relaxation; however, this change is extremely small in our sample of myopes (less than 0.1D). Furthermore, the monocular focus measures with +2D lenses was steady over time suggesting that the accommodative convergence cross link was not significantly altered during vergence adaptation.

4.5.2 Differences in vergence adaptation to sustained near work

The pattern of change in phoria following sustained near task differed between the two refractive groups when viewing through habitual corrective lenses. Emmetropic children showed a shift towards esophoria while myopes showed no change in phoria with sustained near fixation. The magnitude of esophoric shift in emmetropes

(1.01±0.74Δ), although small, is similar to previous studies. [58, 61] Ehrlich [61] reported an esophoric shift of only 1.62 Δ after sustained near fixation despite using a longer task duration (2 hour) and closer fixation distance (20 cm) compared to the current study. This smaller (1.01±0.34Δ) magnitude of adaptation compared to the add condition (4.41 ± 0.08Δ) could be attributed to the variable demand (high/low) on fusional vergence system in either (add/no add) conditions [28]. The lack of adaptive change after sustained binocular viewing through habitual lenses in myopes seems to provide additional evidence towards reduced vergence adaptive ability in this group. However, this reduced adaptation can be considered beneficial since a shift towards esophoria might further reduce the accommodative response (due to reduced output from vergence accommodation due to reflex divergence) in an eye with previously large accommodative lag.

4.5.3 Near add, vergence adaptation and accommodation

The general patterns of changes to accommodation and near phoria in both refractive groups were similar to our adult study [22] , with the emmetropic children exhibiting similar time course of adaptation compared to emmetropic adults. More specifically, the introduction of near adds eliminated the excessive lags of accommodation observed in our myopic group comparable to previous studies with myopic children [43] and myopic adults [23]. At the onset of near work, these lenses resulted in a small degree of binocular over-focus in both refractive groups similar to investigations in adults [19-22]. This over-focus was smaller in the myopes compared to emmetropes, presumably due to the large accommodative lags seen during natural viewing conditions in myopic children. Convergence accommodation, which was calculated from the difference between monocular and binocular focus through near add, was greatest at the reading onset in both the groups. This could be attributed to the lens-induced exophoria triggering an increase in reflex convergence, resulting in an immediate increase in binocular focus through the convergence accommodation crosslink [22, 31-34]. During sustained near fixation, vergence adaptation occurred in both refractive groups; however myopic children showed lower magnitude and completeness of adaptation compared to the emmetropes. Vergence adaptation resulted in reduced binocular over-focus in both refractive groups, which resulted in a plane of focus closer to the fixation target in the myopic group and a small over-focus in the emmetropic group. This position of the binocular focus appears to be a product of the monocular accommodative lags, high AV/A ratio and reduced vergence adaptation (leading to a reduced output of convergence accommodation). Based on the results of our study, it appears that +2D lens additions are beneficial for myopic children with large accommodative lags, provided vergence adaptation occurs to minimize accommodative error (over-focus). These results seem to support the findings of a recent clinical trial [13] that show greater treatment effect (i.e. reduced progression of myopia) in children with larger lags of accommodation. Additionally, based on our study results, we extrapolate that lower magnitude plus additions (such as +1D) might not be as beneficial in reducing myopic progression as +2D lenses, at least in a group of myopic children similar to our study. Though earlier studies [20] with emmetropic adults (and smaller accommodative lags) observed a best match between accommodative demand and response through +1D lenses, this magnitude might not work in our myopic study group as these children experienced large accommodative lags. Furthermore, the presence of vergence adaptation to the near addition lens might result in further reduction in the binocular accommodative response resulting in greater lag of accommodation. This increased lag through the low powered near add might possibly explain why a previous longitudinal study [14] showed better treatment effect with +2D lenses compared to +1.50D lenses.

It appears from the results of this study that differences in vergence adaptation do exist between myopes and emmetropes, at least in response to viewing through near adds for 20 minutes. Possibly this adaptation difference may decline after a longer duration of wear. We did not consider longer study durations considering the age of study participants and their shorter attention span. However, it seems unlikely that the adaptation response becomes complete after longer durations, since the phoria response appears to saturate after 9 minutes of binocular fixation through +2D lenses. The reduced vergence adaptive ability observed in myopic children might be a function of their refractive error or due to the nature of their ocular motor parameters (like accommodative response, AV/A ratio). Previous investigations reported no significant difference in prism adaptation in individuals with early onset myopia, late onset myopia and emmetropia [37]. Comparison of prism adaptation was based on results from adult participants (even for the early onset group) whose refractive condition might have become stabilized and furthermore they did not measure accommodative response or response AV/A ratio to investigate the influence of these parameters on vergence adaptation.

The results of this investigation suggest that reduced vergence adaptation is an important factor in prescribing near adds to young myopes in addition to increased accommodative lags and high AV/A ratios. There are two clinical caveats that result. Based on our study we predict that myopic individuals with near esophoria would respond well to the add since the near add would both reduce the lag of accommodation and act to lessen the esophoria towards orthophoria thereby placing less demand upon reflex convergence. The reduced vergence adaptation would be beneficial in avoiding a return to esophoria. However, such adds may not be well tolerated in myopes with a high exophoria, where the reduced vergence adaptation leads to increased exophoria and hence a greater stress on the vergence system.

4.6 Conclusions

The results of this investigation demonstrate that myopic children exhibit reduced vergence adaptive ability such that higher amounts of exophoria will remain for myopes compared to emmetropes following adaptation to the lenses. The reduced magnitude of vergence adaptation in myopic children seems to be a product of both the AV/A ratio and the refractive error; however, the degree of completeness appears to be primarily associated with the type of refractive error. In the accommodation system, near adds seem to reduce the excessive accommodative lag observed in myopic children and the presence of vergence adaptation helps minimize errors of both accommodation and vergence systems during sustained near fixation.

5 Effect of heterophoria and refractive state on accommodative and vergence responses during sustained near activity in children

The previous chapter (# 4) showed reduced vergence adaptation to plus addition lenses in myopic children with normal near phoria compared to their emmetropic peers. The present chapter deals with the first experiment in the series of studies performed (on the same participants) to understand the role of vergence-bias category and refractive type on binocular adaptation in children. In addition to a different pool of study participants, this series (Chapters 5-7) also had a minor modification in the time course of measurement of phoria and accommodation. Accommodation and phoria were taken at 2 minute intervals (instead of 3 minute intervals in Chapter 4) for the first ten minutes and then after 15 and 20 minutes of sustained viewing.

Here (Chapter 5), accommodative (binocular and monocular) and phoria responses were determined when children with different habitual vergence-bias (eso/exo/normal) and refractive categories (myopia/emmetropia) sustained binocular fixation at a near task through corrective lenses (if any).

5.1 Summary

Purpose: Horizontal heterophoria requires the activation of fusional vergence to maintain binocular vision. This may alter the accommodation and vergence response during sustained near task depending on the type of vergence-bias (phoria). Here, we examined the influence of vergence-bias and myopia on changes to accommodation and vergence during prolonged near-task in children.

Methods: 27 myopic (SE:-1.9±0.1D) and 25 emmetropic children (SE: 0.5±01) between 7-15 years participated in the study. The children were divided into *phoria-normals*;

exophores or esophores based on their near phoria. Measures of phoria, binocular (BA) and monocular accommodation (MA) were obtained before and during a 20 min near-task when participants binocularly fixated a high-contrast target at 33 cm. Tonic accommodation was also measured before and after the near-task.

Results: Binocular but not monocular accommodation was significantly different between vergence-bias categories (P<0.001) in both refractive groups. While BA was significantly greater than MA in exophores (P<0.001) and phoria normals (P=0.030), in esophores, MA exceeded the binocular response (P=0.003). Both refractive groups showed similar pattern of BA vs. MA in the phoria groups; but, myopic children showed larger lags compared to emmetropes (P=0.010). This pattern was not altered by prolonged binocular fixation in both refractive groups. Tonic accommodative adaptation was higher in myopes (P=0.010) but did not demonstrate a significant effect of phoria (P=0.4). In the vergence system, the type of vergence-bias category (eso/exo) altered the direction and magnitude of phoria adaptation (P<0.001) with exophores and esophores displaying convergent and divergent shifts respectively in phoria upon prolonged fixation. Myopic children showed increased divergent (less convergent) shift (P<0.001) in vergence adaptation compared to emmetropes in all phoria groups.

Conclusion: Myopia is associated with increased accommodative lags (monocular and binocular) and increased accommodative adaptation. The direction of near phoria influences the pattern of vergence adaptation and the difference between binocular and monocular levels of accommodation. The differences primarily appear to relate to the varying fusional vergence demands created by the direction of phoria and also due to the interaction between the accommodation and vergence system.

5.2 Introduction

5.2.1 Adaptation effects to sustained near task

Sustained near fixation induces adaptation of the accommodation and vergence systems ([1-7] see [8, 9] for review). This adaptation was attributed to the prolonged rate of decay of the slow controller of vergence/accommodation, which replaces the fast controller and exhibits a shift in the tonic levels of accommodation/vergence. In the accommodation system, factors such as magnitude of adapting stimulus [1], dioptric distance between TA and the steady state accommodative response [10] , and refractive state [11-13] influence the degree of accommodative adaptation. In the vergence system, past studies show convergent (eso) shifts in phoria or tonic vergence after a period of sustained near work [4-6].

Heterophoria (phoria) is a misalignment of the visual axes that occurs in the absence of fusion, and compensated during binocular viewing by the fusional vergence mechanism [14]. The degree and type of fusional vergence required for binocular viewing (convergence/divergence) varies in proportion to the size and the direction of phoria (exo/eso). The presence of exophoria relative to the dioptric demand necessitates an increase in fusional convergence while an esophoric deviation requires an increase in fusional divergence in order to attain binocular single vision. These differing vergence postures (esophoria/exophoria) may produce asymmetries in phoria adaptation since the adaptive magnitude appears to depend upon the degree of fusional stress [5] and the length of time it must be sustained [6]. Ehrlich [5] measured changes to near phoria before and after a two hour near task at 20 cm in adult participants with mixed refractive errors. A mean convergent shift of 1.62Δ and a significant relationship between pre-task near phoria and vergence adaptation was reported. However, it must be noted that the sample consisted of only one esophore (others ranged from ortho to 16 exo) and a closer inspection of the report (Fig 3 of the paper) shows that only individuals with exophoria greater than 5Δ demonstrated a convergent shift similar to the mean. Individuals with low exo/ortho showed a divergent shift in phoria, which may not be readily explained by their fusional demand. The author did not measure accommodative adaptation (changes to dark focus) but reported 0.29D change in distant refraction (transient myopia in closed loop accommodation) after the near task. Differences in accommodative adaptation, combined with varying strength of accommodative-vergence cross-link may explain the divergent shift in vergence adaptation seen in low exo/orthophores.

Most of the above-cited works on accommodative and vergence adaptation were performed in adults; relatively limited studies have measured adaptation in children [12, 13, 15, 16]. Wong et al [16] compared vergence adaptation in children (mean age=9.8 years) and young adults (mean age=25.8 years) by measuring tonic vergence before and after a prolonged near task (reading at a distance of 15 cm for 5 minutes- closed loop accommodation and vergence). Children showed significantly greater vergence adaptation (0.45MA) compared to adults (0.11 MA). However, this study also did not report critical parameters like accommodative adaptation, AV/A ratio which may alter the vergence response and hence, its adaptation. Given that the accommodation and vergence are tightly coupled systems, it becomes crucial to measure changes to both systems, especially when the adapting stimulus involves dual closed-loop conditions. To date, no study has measured adaptation of both accommodation and vergence in response to a sustained near task in children and there is a paucity of information on the role of childhood phoria levels on adaptation to a near task.

5.2.2 Effect of vergence-bias category on the accommodative response

The compensation of phoria, in addition to altering the vergence response, also produces a simultaneous change in accommodation due to the presence of the vergence-accommodation cross-linkage [17, 18]. Consequently, under binocular viewing conditions, the accommodative response receives contributions from disparity vergence in addition to blur, proximal cues and tonic accommodation [19]. The vergence contribution is removed from the aggregate accommodative response under monocular conditions. Thus, it would be expected that binocular and monocular levels of accommodation differ in the presence of a large phoria. Clinical observations using binocular dynamic retinoscopy suggest that esophores have greater lags of accommodation compared to exophores [20, 21]. Scientific reports have confirmed this observation in retrospective clinic-based studies [22] and in a prospective study that included only myopic children [23]. These studies did not measure monocular accommodation, which would be necessary to confirm that the differences seen in binocular viewing conditions were related to the fusional vergence demand and thus, vergence accommodation. Based on an interaction model of accommodation and vergence, Schor [24] showed that uncorrected hyperopia and esophoria increased the accommodative lag while uncorrected myopia and exophoria decreased the lag or produced a lead in accommodation in response to a near target. Hasebe et al [25] tested this interaction model of accommodation and vergence [24] in individuals with intermittent exotropia/decompensated phorias (range of phoria =23 eso to 50 exo; some of whom underwent surgery for correction of strabismus) and measured both binocular and monocular accommodation in the phoria groups. The authors reported a significant correlation between distance phoria and the difference between binocular and monocular accommodative response [25]. However, the study did not identify the relation between phoria and accommodation at the target distance where accommodation was measured (2.5D). Given that near phoria is largely influenced by the strength of the accommodative vergence cross-link under conditions of closed-loop accommodation, large variations in AV/A ratios would be expected to produce different distance and near phorias. The study by Hasebe et al [25] reported a wide range of AV/A ratios (0-14PD/D). Thus, it is unclear whether phoria at the target distance (where accommodation was measured) correlated with the difference between binocular and monocular levels of accommodative response. In addition, the study included participants with habitual refractive errors ranging from +6.8 to -7 D (some had under correction as high as 3.5D) and did not differentiate accommodative responses based on refractive error.

5.2.3 Myopia and adaptation to sustained near task in children

Near work requires the activation of accommodation and vergence systems. The question of refractive error is important because of the association between near work attributes and myopia [26-29]. Myopic individuals exhibit greater accommodative lags when accommodation is stimulated through negative lenses [30-32], with monocular real targets, or under binocular viewing condition through full refractive correction [33] but not always under naturalistic binocular viewing conditions [34, 35]. Several studies that measured binocular accommodation as a function of refractive error did not differentiate their sample based on phoria, which may alter the response through vergence accommodation. Although few studies measured the effect of phoria on binocular accommodation in myopes, they did not measure monocular accommodative response to understand the role of vergence accommodation.

Gwiazda et al [13] showed that myopic children show greater accommodative after effects to a near task compared to emmetropes. Thus, even small refractive differences in the accommodative system may produce larger changes in the vergence system if myopes show higher response AV/A ratio, as demonstrated by past studies [36, 37]. Esophoria (convergent shift) is associated with the onset/progression [38, 39] and higher amounts of myopia. Goss and Rosenfield [40] speculate that vergence adaptation to a prolonged near task may be a source for this convergent shift and possibly a risk factor for myopic development/progression. However, to date, no study has measured vergence adaptation to near task in myopic children.

Accordingly, this chapter evaluated the influence of vergence-bias (i.e. type of habitual phoria) and refractive error on both accommodative and vergence adaptation by measuring changes to binocular and monocular accommodation and near phoria when children binocularly sustained near task at 33 cm. It was hypothesized that esophores would exhibit larger binocular accommodative lags and a divergent (less convergent) shift in vergence adaptation compared to exophores. Myopic children would demonstrate differences in binocular adaptation to near task due to the variations in ocular motor parameters compared to emmetropes.

5.3 Methods

5.3.1 Study participants

Fifty three children (28 myopic and 25 emmetropic; 58% female) between the ages of 7 and 15 years were recruited from the clinic database at the School of Optometry, University of Waterloo. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the nature of the study. The protocol followed the tenets of Declaration of Helsinki and received approval from the University of Waterloo ethics review board.

Participants with normal general and ocular health (determined from their clinical records and confirmed during a screening visit) underwent preliminary examination to ensure the following: myopic refractive error between -0.75 and -6 D or emmetropic refractive error between +0.25 and +1.5 D determined using cycloplegic refraction (two drops of 1% tropicamide added to both eyes, similar to a previous study [41]); astigmatism < 1D; anisometropia < 1D; best corrected visual acuity of at least 6/6 in each eye; non-strabismic; normal amplitudes of accommodation. Further, participants were not taking any medications that might influence the accommodation and vergence systems.

5.3.2 Instrumentation

Heterophoria was measured using the modified Thorington technique (MTT) (described in Chapter 3). This technique showed good validity and repeatability in adults, which has also been confirmed in children [42-45]. The same technique was repeated thrice and near heterophoria was defined as the average of the three responses.

All children were classified into one of three phoria categories (*normo-phores*, exophores or esophores) based on their near phoria (33 cm). Participants were divided into *"normophores"* if their mean near phoria was between 0-4 exo, exophores (>6 exo) or esophores (>2 eso). Table 5-1 lists the number of children in each vergence-bias category and other critical visual parameters of the study groups.

Table 5-1: Critical visual parameters of myopic and emmetropic children

PARAMETER (Mean ± SEM; and range where applicable)	**EMMETROPES**			**MYOPES**		
	Normophores	Exophores	Esophores	Normophores	Exophores	Esophores
No of participants	11	7	7	10	7	11
Age (7-14) in yrs	10.8 ± 0.43	12.2 ± 0.63	11.9 ± 0.43	10.43 ± 0.53	11.2 ± 0.8	11.8 ± 0.63
Refractive error (D)	0.59 ± 0.09D	0.4± 0.09D	0.3± 0.09D	-2.0 ± 0.3D	-2.5 ± 0.2D	-1.7 ±0.3D
Near phoria (Δ)	-2.15 ± 0.49 (0 to 4 exo Δ)	-6.72 ± 0.36 (6 to 10 exo Δ)	2.83± 0.58 (2 eso to 5 eso Δ)	-1.24 ± 0.94 (0 to 4 exo Δ)	-9.7 ± 1.5 Δ (6 to 14 exo Δ)	4.09 ± 0.5 (2 eso to 8 exo Δ)

Accommodative responses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor, the PowerRefractor (Multichannel Co, Reutlingen, Germany).[46] This setting of the instrument determined refraction along the vertical meridian of the participants' eye, sampling at a rate of 25 Hz, coupled with measures of gaze deviations and pupillary diameter. The responses obtained from the PowerRefractor were calibrated using a two-step protocol to ensure relative and absolute accuracy of accommodation similar to previous studies [45, 47, 48]. While the slope of calibration function matched with the instruments default for some participants, others needed separate calibrations functions, possibly due to differences in fundal reflectance [49, 50] In all cases, accommodative responses were calibrated based on individual calibration equations.

A high contrast colour cartoon (contrast =85%; target luminance =15 cd/m^2) was used to measure accommodation in children. This target was chosen as it was expected to be more successful than conventional reading material in holding the participants' attention and has been verified to be an effective stimulus for accommodation [45]. The image of the cartoon was displayed on a 1.77″ wide liquid crystal display monitor (Model No: LT-V18 U; Victor company of Japan) and projected at a distance of 33cms through a semi-silvered mirror. The mirror set 10 cm from the right eye, and angled at 45 degrees allowed the photorefractor to simultaneously record accommodation from the right eye during target viewing. The method has been described elsewhere in detail [45] (Chapter 3).

Binocular accommodation (BA) and monocular accommodation (MA) were recorded continuously for a period of 5sec after confirming steady fixation using the gaze control function displayed on the PowerRefractor interface. For the binocular response, accommodation was recorded from the right eye alone, although both eyes fixated at the target. For measurement of MA, the left eye was occluded. During the 5 sec measurement period, the accuracy of fixation was assessed using the gaze control function displayed on the PowerRefractor interface. Additionally, care was taken to ensure that the child was fixating the near target at the correct fixation distance (33 cm) while measurements were recorded. A volunteer constantly monitored the head position of the child and ensured they did not move away from the chin rest during measurement. If any unsteady fixation was noticed during measurement, or when the examiner (VS) observed off axis gaze errors exceeding 10 degrees, the measures were flagged using keyboard inputs and discarded given the possibility of under or over estimation of accommodation [51, 52]. In these cases, recordings were obtained for an additional 5 sec period to ensure equal data sets across subjects.

5.3.3 Experimental procedure

Prior to the start of the study session, participants sat in total darkness for 3 minutes to dissipate any effects of previous near work and allow the accommodation and vergence system to return to their resting states [6]. Following this, pre-task measures of tonic accommodation were taken when participants' monocularly fixated a 0.2 cpd difference of Gaussian target at 4m in an otherwise dark room. Baseline measures of phoria, binocular and monocular accommodation was then taken at 33 cm prior to sustaining fixation at the near-task. The time taken for one complete measurement block (measurement of phoria, binocular and monocular accommodation) ranged between 60 and 80 sec.

Near task: The "sustaining target" was a cartoon movie, also played at a distance of 33 cm. This target has been used in previous studies [45, 48] and was chosen after considering the age of the participants' to avoid boredom and ensure prolonged near fixation for the scheduled duration of the study (20 min). Measures of phoria, binocular and monocular were repeated after 2, 4, 6, 8, 10, 15 and 20 min to determine the time course of changes in accommodation and vergence. Immediately after the near task (within 30-40 sec) tonic accommodation was recorded to calculate accommodative adaptation.

5.3.4 Data Analysis

Measurement of accommodative response at 25 Hz for 5 sec provided a total of 125 data points. Each data point was screened and accepted if the following criteria were met: the pupil size was above 4mm; the ocular alignment was less than 10 degrees and 5 degrees from the optical axis of the photorefractor in the horizontal and vertical axes respectively (as recommended by the manufacturer [46]) and the responses were free of blinks. Blink artefacts, if any were removed using a method similar to previous studies [45, 53]. Each participant needed to have at least 100 rows of acceptable data after satisfying all of the above criteria in order to be considered for averaging and further analysis. If the participants had more than 100 eligible data points, only the first 100 points were taken for further analysis. The data retained were averaged to obtain the mean accommodative response. Data from one myopic participant was excluded from the averaging process since she failed to provide the minimum levels of acceptable data as a result of pupil diameters less than 4mm.

Repeated measures analysis of variance (ANOVA) was used to compare the mean changes in accommodation and phoria with sustained fixation. In all cases, statistically significant main effects were further examined using Tukey Honestly significant differences (HSD) post-hoc tests to determine the group that showed the significant difference. Differences were considered statistically significant when the likelihood of type-I error was <0.05. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Exponential curve fitting analysis was performed using Graphpad software (Graphpad Inc, USA) to compare the absolute magnitude and time course of adaptation in different groups. Pearson correlations were conducted to look for relationships between phoria and accommodation.

5.4 Results

5.4.1 Pattern of binocular vs. monocular accommodative response in the different vergence-bias categories

Fig 5-1 shows the mean binocular and monocular accommodative responses for each vergence-bias category averaged from the first time point (0 min) in all children (irrespective of their refractive classification). Binocular accommodation significantly (P=0.003) differed across vergence-bias categories but, the monocular measures remained similar between the groups (P=0.90). While BA is significantly greater than MA in exophores (P<0.001) and phoria normals (P=0.030), MA is significantly greater (P=0.003) than BA in esophores. Furthermore, the accuracy of the accommodative response varied as a function of vergence-bias category in the binocular condition such that exophores displayed significantly (P=0.020) larger and more accurate accommodative response compared to esophoric children with larger lags and less accurate accommodative response.

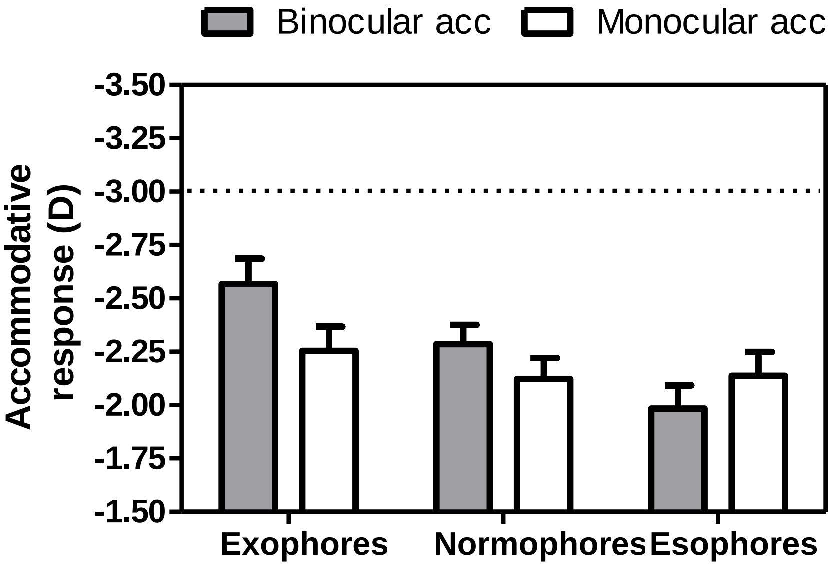


Figure 5-1: Effect of vergence category on the pattern of binocular and monocular accommodation, irrespective of refractive error

The effect of phoria on the difference between binocular and monocular accommodative response (attributed to the output of VA) was quantified using Pearson correlation coefficient. Both refractive groups showed significant correlation between the two variables (Fig 5-2: Emm; r^2=0.54; r= -0.74; P<0.001; Myo; r^2=0.49; r= -0.69; P<0.001) such that exophores showed higher convergence accommodation compared to esophores. Linear regression analysis of the two variables showed similar slope (Emm= -0.04; Myo= -0.03; P=0.32) and intercept (Emm=0.007; Myo=0.01; P=0.87) for both refractive groups, suggesting similar VA/V ratios in the two refractive groups.

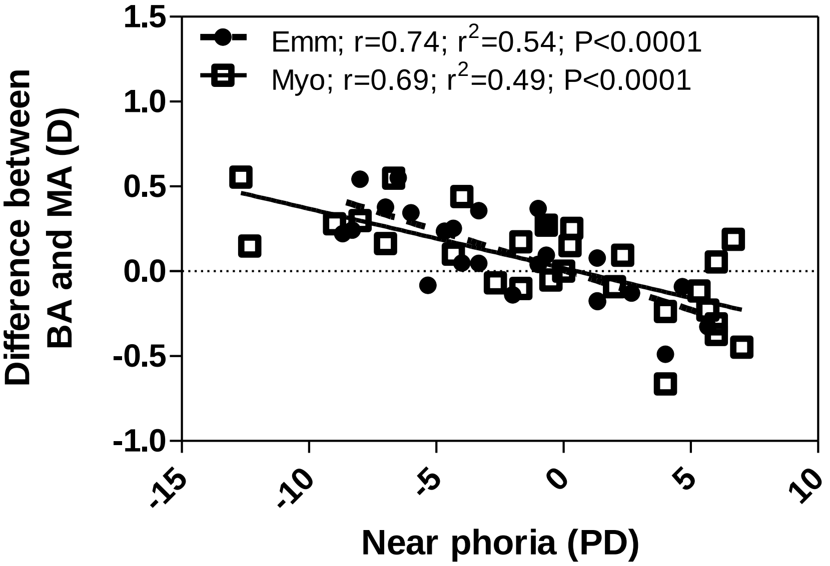


Figure 5-2: Relation between phoria and differences between binocular and monocular accommodation (VA)

Refractive type showed a significant main effect (P=0.010) such that myopes displayed greater accommodative lags compared to emmetropes. However, the presence of a myopic refractive error did not significantly alter the pattern of accommodative response (BA<MA for exophores & phoria normals, and MA<BA for esophores; interaction between phoria and refractive error: P=0.60) in each vergence-bias category but only shifted the overall response towards increased accommodative lag (Fig 5-3).

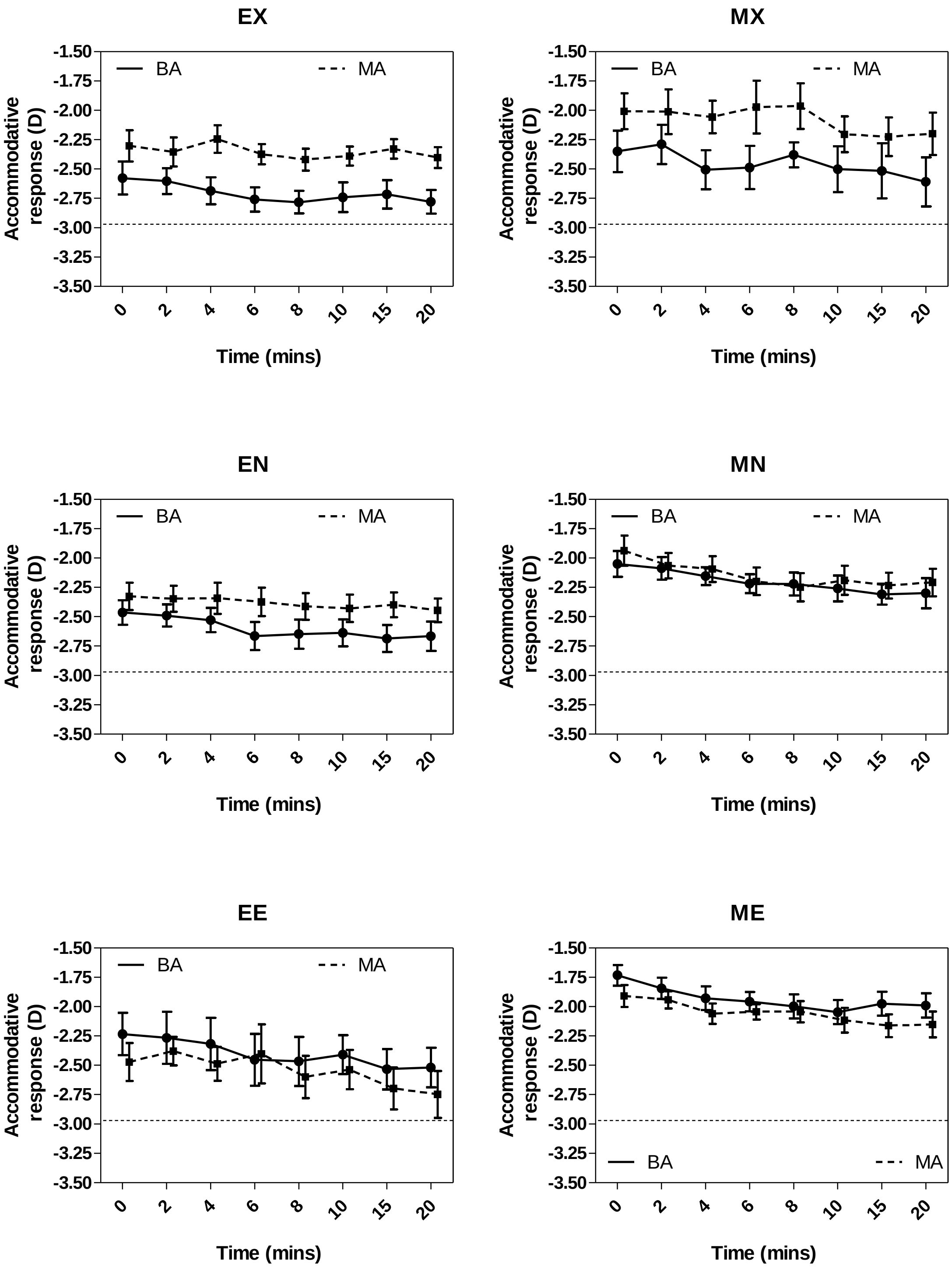


Figure 5-3: Mean changes to the binocular and monocular accommodation over 20 min fixation at 33cm

5.4.2 Time course of changes to accommodation during sustained binocular fixation

The type of phoria (Exo/Eso) continued to have a significant effect ($P<0.0001$) on the pattern of binocular vs. monocular accommodative response over time (Fig 5-3) such that exophores showed larger binocular accommodative response while esophores showed higher monocular response, similar to pre-near task. During the prolonged near task, all myopic phoria groups showed a small but significant increase (0.2-0.3D) in accommodative response (all $P<0.05$) after 4 min of near fixation. Emmetropic children also showed similar small (0.15-0.3) but significant changes after 6 min of viewing. The changes in accommodative response over time for each phoria and refractive category were fit with an exponential function to compare the magnitude of change in closed-loop accommodation and its time constant between groups. The total magnitude of change in accommodation did not show any significant effect of refractive type (Myo $=0.28\pm0.05$D; Emm$= 0.22\pm0.04$D; $P=0.50$), type of vergence-bias (Exo$=0.16\pm0.06$D; Eso$=0.27\pm0.05$D; PN$=0.21 \pm 0.05$D; $P=0.60$) or viewing condition (Bino$=0.24\pm0.05$D; Mono$=0.21\pm0.03$D; $P=0.80$). Similarly, the time constant (ranged between 4-6 min) also did not show any significant difference (all $P<0.50$) between the type of vergence-bias and refractive group in this study sample. It is important to note that accommodation was not adapted monocularly since the prolonged viewing was performed under binocular viewing conditions.

5.4.3 Changes to open-loop accommodative response

Accommodative adaptation was defined as the difference between pre and post TA measures. All phoria categories in each refractive type showed significant myopic shift in TA (all P<0.05) after the near task (Fig 5-4). While myopes showed higher accommodative adaptation compared to emmetropes (P=0.010), the magnitude of accommodative adaptation did not differ between the phoria categories in each refractive group (P=0.40) and interaction between vergence-bias category and refractive error was also not significant (P=0.99).

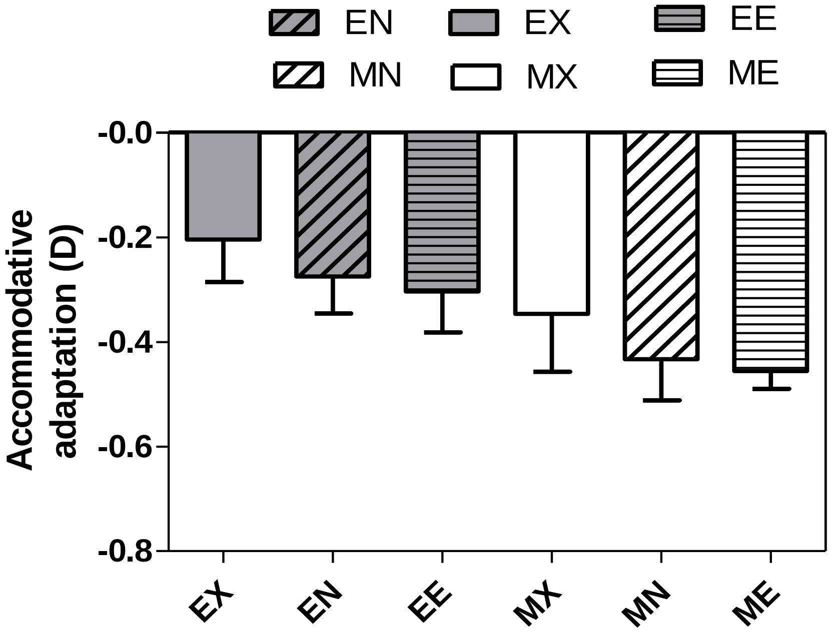


Figure 5-4: Effect of vergence category and refractive type on accommodative adaptation

5.4.4 Time course of changes to near phoria during sustained binocular fixation

The mean baseline phoria for each vergence posture and refractive category is given in table 5-1. One-way ANOVA comparing the baseline phorias between various groups showed that each category of vergence-bias significantly differed (P<0.001) from the others in both refractive groups. However, the baseline near phoria for a given vergence category was not significantly different between myopes and emmetropes (all P>0.050). Figs 5-5 (a, b and c) show the time course of changes to near phoria during 20 minutes of sustained fixation with respect to the vergence-bias categories in the two refractive groups. In the phoria normal category, emmetropes (EN) showed a small and significant convergent shift (P=0.010) that saturated following 2 min of fixation. This convergent shift was non-significant (P=0.10) in myopic phoria-normals (MN), and their phoria responses showed a small but significant divergent shift after 20 min of sustained fixation (time point 0 vs.20 min: P=0.010). In the exophoria category, both emmetropes (EX) and myopes (MX) showed significant convergent shifts (P=0.030) after 4 min of near fixation; however EX displayed larger (P<0.001) shifts compared to MX. Both esophoric groups (EE&ME) showed a different direction of shift in phoria compared to exophores and phoria normals. Sustained fixation in EE and ME resulted in a significant divergent shift (P=0.050) with greater adaptation in ME compared to EE.

In order to analyze the global effect of vergence-bias category and refractive type on the magnitude of vergence adaptation to near task, total adaptation (change in phoria after 20 min) was computed from each participant using an exponential function. Statistical analysis showed a main effect of vergence-bias ($P<0.001$) and refractive type ($P<0.001$) but no interaction between vergence-bias and refractive group ($P=0.80$; Fig 5-6). In all vergence categories, myopes showed more divergent (or less convergent) shift in vergence adaptation.

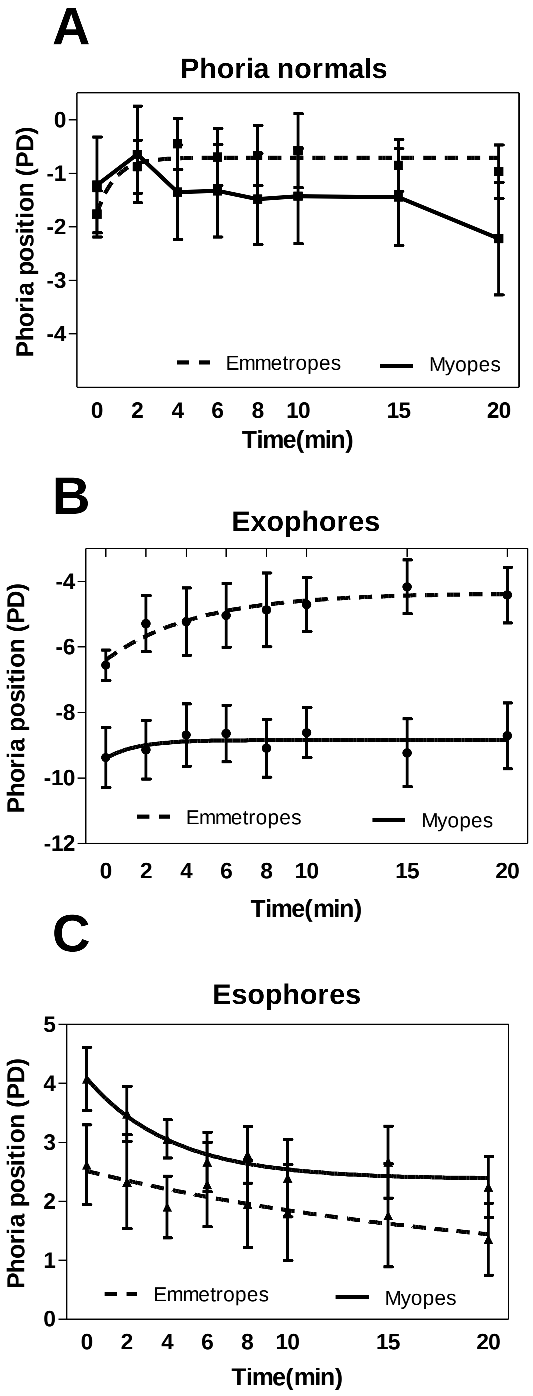


Figure 5-5: Comparison of mean phoria responses between emmetropes and myopes in each vergence bias category during sustained fixation

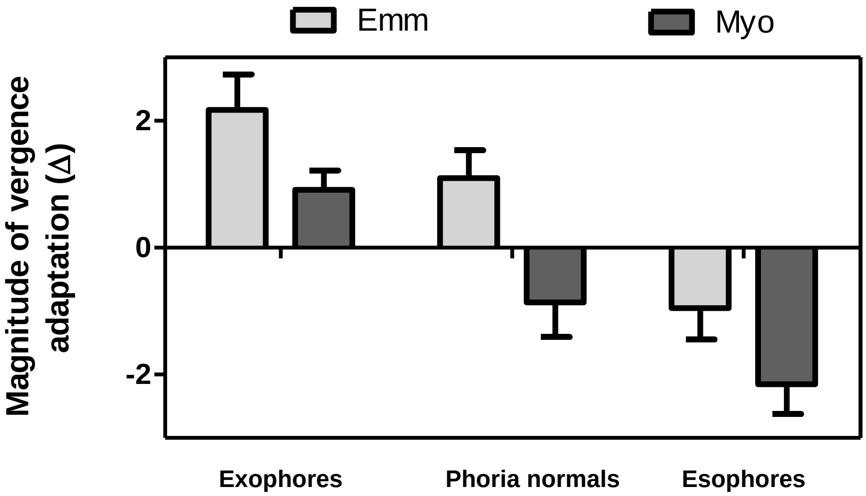


Figure 5-6: Comparison of the total magnitude of adaptation between the various vergence-bias and refractive groups

5.5 Discussion

5.5.1 Vergence-bias category and refractive type on phoria adaptation to near task

Our results indicate that phoria adaptation to a sustained near task does not shift in a convergent direction in all children. The type of vergence-bias and refractive error influence the magnitude and direction of phoria adaptation to a near task. In both refractive groups, exophores showed a convergent shift while esophores showed a divergent shift in near phoria. These differences may be explained based on to the contrasting fusional vergence demands produced by the two phoria groups. The presence of exophoria relative to the dioptric demand of the target necessitates an increase in fusional convergence while an esophoric deviation requires an increase in fusional divergence in order to attain binocular single vision. Since phoria adaptation is related to the demand on the fusional vergence [54], the opposite directions of adaptation seen in esophores and exophores can be attributed to the differing fusional vergence demands. These results are similar to previous studies [4, 5] that also showed significant relationships between pre-task resting state or phoria and the magnitude of adaptation. However, it must be noted that previous studies did not differentiate subjects based on refractive error or measure accommodative adaptation.

This is the first study to show an influence of refractive type on phoria adaptation to near task. For all phoria categories, myopic children show a greater divergent (or less convergent) shift in phoria adaptation compared to emmetropes. One possible explanation could be related to the increased tonic accommodative after effects observed in myopic children [13]. Accommodative adaptation may reduce the output of accommodative vergence cross-link, resulting in an exophoric or divergent shift [55, 56]. This suggestion is consistent with studies that show an exo (divergent) shift in the phoria system due to accommodative adaptation [57] and a reduction in the VA cross-link activity with vergence adaptation [55, 56, 58]. Furthermore, the higher AV/A ratio seen in myopic children [36, 37] may exaggerate the divergent shift due to accommodative adaptation compared to emmetropes.

Near esophoria is believed to be associated with the development [59] and increased rates of progression of myopia [60]. While the phoria categories other than esophores showed a convergent shift in vergence adaptation, esophores, especially myopes showed greater divergent shifts in near phoria with sustained fixation. Goss and Rosenfield [40] speculated that the esophoria induced by vergence adaptation may cause increased accommodative lags under binocular condition, which may produce hyperopic defocus on the retina and induce axial elongation [61, 62]. Based on this hypothesis, we may suspect the convergent shift in phoria normals/exophores to be a risk factor that could induce myopia development. However, the divergent shift in vergence adaptation seen in esophores does not appear to be crucial in the progression or development of myopia.

5.5.2 Type of vergence category and the pattern of binocular vs. monocular accommodative response

Another key finding of this study is the reversal of the binocular vs. monocular accommodative response in children with exophoria and esophoria in both refractive groups. Heterophoria is overcome by fusional vergence, which in addition to maintaining single vision, also alters the binocular accommodative response through the VA/V cross-link. Accordingly, the differences between binocular and monocular viewing conditions observed in the vergence categories were attributed to the activation of vergence accommodation. Exophores employ increased convergence to maintain bifoveal fixation, which enhances convergence accommodation such that binocular measures are greater than monocular levels. On the other hand, esophores exert fusional divergence to maintain single vision, which may result in a reduced output of vergence accommodation and greater monocular compared to binocular accommodation. The findings of this study are consistent with the model predictions [24] that propose changes to binocular accommodation (BA) alone with changes in phoria. The monocular accommodative response (MA) remained unaffected, presumably due to the absence of disparity vergence input. The relationship between binocular accommodative response and phoria seen in this study is consistent with clinical observations [20, 21] and previous reports from retrospective [22] and prospective studies [23].

Clinical tests [20, 21] suggest that greater or smaller binocular lags of accommodation observed in eso or exophoria respectively, may occur because the patient is trying to alter accommodation (and AV) to reduce the phoria and subsequently the demand on the fusional vergence system. In this study, we observed that exophores continued to show smaller binocular lags and esophores showed larger lags during the entire 20 minutes near fixation period. Although all groups showed a small increase in the accuracy of accommodation response, similar to previous studies [63, 64], this increase was not different between the viewing conditions and thus, did not alter the pattern of BA vs. MA observed in the phoria groups. If exophores continually exerted more blur-driven accommodation under binocular viewing condition to compensate their phoria, we may expect them to show larger tonic after effects (accommodative adaptation), since the magnitude of adaptation is proportional to demand on the phasic controller [56]. Similarly, esophores may be expected to show a reduced amount of accommodative adaptation after the near task. Our results show no difference in accommodative adaptation between phoria groups in either refractive type. Consequently, we attribute the relationship between phoria and binocular measures to the activity of VA cross-link modulated by the fusional vergence system.

The presence of myopia did not alter the pattern of binocular vs. monocular accommodative response but resulted in larger lags in all phoria groups under both binocular and monocular conditions. While previous studies showed larger accommodative lags in myopic children under monocular viewing conditions [31, 65], this was not seen when both eyes observed the target [34, 35]. It is important to note that latter studies that showed no refractive group differences under binocular viewing conditions did not differentiate their participant based on vergence-bias category. In addition, past studies indicate that progressive myopic children show larger lags compared to stable myopes [30, 32]. Though this study did not measure progression prospectively, review of past clinical records indicate that 18 out of 27 myopes progressed by at least 0.25-0.50D/yr. Six participants did not have more than one exam at the School of Optometry to determine the amount of progression and 3 had stable refraction. The larger accommodative lags may be due to the relatively progressive nature of the refractive error in this study population.

Our results show that vergence-bias does not influence the monocular accommodation response for the range tested. Previously, Gwiazda et al [36] showed a moderate correlation (their Fig 3b; r= -0.35; P=0.040) between near phoria and monocular accommodation in myopes but not emmetropes. Visual inspection of their data shows similar accommodative responses across most phoria magnitudes except for a few myopic children with extremely high eso and exophoria (±15Δ). Several studies record monocular accommodation in an attempt to study the contribution of phoria. For instance, few [66, 67] studies that measured the effect of progressive addition lenses in reducing myopic progression measured monocular accommodation and quantified the effect of monocular lags in different phoria groups. Based on the results of this study, it appears that studies including individuals with a wide range of phoria should also include the measurement of binocular accommodation as it incorporates the fusional vergence response to overcome phoria.

5.5.3 Vergence category and refractive type on accommodative adaptation to a near task

Sustained fixation of the near task increased the tonic accommodative levels in both myopic and emmetropic children, but myopes showed greater accommodative adaptation to the near task compared to emmetropes. This is consistent with studies that tested the shifts in tonic accommodation in myopic children [13] and late onset myopes, but not with adults who had been early onset myopes [11]. The difference could be related to the duration of myopia since children and adults with recent onset show greater shifts than individuals with long-term myopia [13]. The larger shifts in myopic children are also consistent with reports that show greater NITM (near work induced transient myopia) in myopic children [68], where again the myopic (tonic) shift represents the output of the slow blur-driven accommodative response.

The category of vergence-bias did not influence accommodative adaptation in either refractive group. Accommodative adaptation is the result of prolonged rate of decay of the slow accommodative controller, which receives input from the phasic controller [56]. In this study, a 3D stimulus produced similar monocular blur-driven accommodation response (phasic) in all phoria groups, which may explain the similarity in accommodative adaptation between the phoria groups. Past reports have shown that convergence accommodation is capable of inducing accommodative adaptation under open loop conditions, which would suggest greater adaptation in exophores [55, 63].

However, vergence adaptation in exophores (Fig 5-6) may have reduced the VA cross-link activity and eliminated these differences.

5.5.4 Conclusion

The primary findings of this study are that the type of vergence-bias category and myopia altered the behavior of accommodative and vergence parameters during near fixation in children. In the accommodative system, the type of vergence-bias modified the binocular but not monocular steady-state accommodative response to a near target such that exophores and phoria normals displayed larger binocular measures while esophores demonstrated larger monocular measures. In the vergence system, the category of vergence-bias (eso/exo) altered the direction and magnitude of phoria adaptation with exophores and esophores displaying convergent and divergent shifts respectively upon prolonged fixation. The presence of myopia did not alter the pattern of changes produced by the type of phoria, but only resulted in an overall shift in the responses. In all phoria groups, myopic children showed greater lag of accommodation and a divergent (or less convergent) shift in vergence adaptation compared to emmetropes.

6 The role of vergence-bias category and myopia on binocular adaptation to near addition lenses in children

6.1 Summary

Purpose: Near adds are prescribed for various reasons including the treatment of binocular anomalies and myopia control. Little empirical information is available on how the binocular motor system adapts to near adds in children. This study examined the effect of habitual vergence-bias category and refractive error on vergence adaptation to +2D and -2D adds.

Methods: 25 myopic and 25emmetropic children between 7-14 years of age participated in the study. The children were divided into emmetropic and myopic *phoria-normals* (EN & MN; 0-4Δexo); emmetropic and myopic exophores (EX & MX; > 6 exo) or emmetropic and myopic esophores (EE & ME; >2 eso) based on their near phoria. Measures of accommodation and near phoria were taken at frequent intervals when children sustained near task through +2D and -2D adds over corrective lenses at 33 cm. Vergence adaptation was quantified using an exponential decay function. In addition, tonic accommodation was measured pre and post near task.

Results: AV/A ratios (and the lens induced phorias) significantly differed as a function of vergence-bias category (P=0.02) and refractive error (P=0.01) such that esophores and myopic children showed higher response AV/A ratios compared to other groups. Vergence adaptation to lens-induced exo and esophorias significantly differed as a function of add condition (P<0.0001), type of vergence-bias category in each add condition (P<0.001), and type of refractive error in +2D (P<0.0001) but not -2D add

condition (P=0.14). In the emmetropic group, the pattern of vergence adaptation was opposite in the phoria categories for the +2D (EX>EN>EE) and -2D add (EE>EN>EX). In the myopic groups, only esophores showed significantly less and greater adaptation compared to other phoria categories to the opposite add conditions (+2D: MX=MN>ME; -2D: ME>MN=MX). Nevertheless, vergence adaptation significantly correlated with the demand of fusional vergence in both refractive groups (Emm r^2=0.83; Myo; r^2=0.72; P<0.0001). All myopic vergence-bias categories showed significantly reduced adaptation (P<0.001) through plus adds compared to their respective emmetropic groups. The reduced adaptation appears beneficial for the ME as it resulted in a mean phoria closer to orthophoria than that found for the other phoria groups (MN & MX). Vergence adaptation did not significantly differ between the refractive groups when children sustained fixation through minus adds. Further, adaptation of tonic accommodation was significantly greater in the -2D add condition compared to +2D add condition. Myopic children showed significantly (P=0.01) greater accommodative magnitude compared to emmetropes in the minus add condition only.

Conclusion: The differing demand on fusional vergence appears to explain the asymmetrical pattern of vergence adaptation between +2D and -2D adds observed in the emmetropic phoria groups. However, the demand on fusional vergence only partly describes the pattern of adaptation seen in the myopic phoria groups. The asymmetry in the effect of refractive error on vergence adaptation to +2D and -2D adds may be related to higher accommodative adaptation seen in myopic children. Vergence adaptation to plus adds appears most compromised in MN & MX, which could lead to a greater vergence stress in this group wearing high plus adds for myopia control.

6.2 Introduction

A previous study (chapter 4) showed that myopic children with normal near phoria exhibit reduced vergence adaptation to +2D adds compared to emmetropes. The decreased adaptation was also seen in myopes with low AV/A ratios, suggesting that the higher AV/A ratios seen in young myopes [1, 2] (at least), does not necessarily correlate with high levels of vergence adaptation as found in adult populations[3, 4]. It is unclear whether myopic children with habitual near exophoria or esophoria also show decreased adaptive behavior compared to emmetropes. Several clinical studies on myopic children have shown that esophores display greater myopia reduction through plus adds compared to exophores [5-7]. Due to the interaction between accommodation and vergence [8, 9] , it is common clinical practice to expect that plus adds will reduce the binocular vergence stress in an esophoric child [10]. However, in the case of esophores, where plus adds reduce the stress of over convergence, vergence adaptation would reduce the efficacy of the correction.

Previous studies have not identified the role of habitual vergence-bias category on the degree of vergence adaptation to near addition lenses. Models of accommodation and vergence [11-13] suggest that the adaptive (tonic) element receives input from phasic controller, indicating a directly proportional relationship between the magnitude of vergence adaptation and the demand on the phasic controller. Several empirical studies have also confirmed this prediction by showing larger amounts of adaptation to higher prismatic disparities [14-16]. Following these suggestions to lens-induced conditions, we would expect a child with habitual divergent phoria to experience increased fusional convergence demand (increased phasic activity) and therefore increased adaptation to plus adds. Similarly, esophores may experience less fusional vergence stress and reduced adaptation to plus adds compared to exophores. If vergence adaptation depends on the demand on fusional vergence, opposite pattern of adaptation would be expected for exophoric and esophoric children when they sustain fixation through minus adds, which increase the stimulus for accommodation and induce esophoria.

The broader objective of this study was to use near addition lenses as a means to understand the mechanism of binocular adaptation in children. The specific goals were two-fold. First, to assess the role of baseline vergence-bias category on adaptation to near addition lenses in children. Here, we hypothesize that the degree of adaptation will be proportional to the demand on the fusional vergence and would thus expect opposite patterns of adaptation to plus and minus adds. The second objective was to evaluate the influence of myopia on vergence adaptation to plus and minus adds in children. Since myopic children exhibit differing ocular motor characteristics such as higher accommodative lags, [17, 18], greater accommodative adaptation [19] and larger response AV/A ratios [1, 2], they may exhibit dissimilar adaptive behavior compared to emmetropes.

6.3 Methods

The study protocol was approved by the University of Waterloo ethics review board and adhered to the tenets of the Declaration of Helsinki. Participants were recruited from the clinic database at the School of Optometry, University of Waterloo. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the procedures involved in the study.

6.3.1 Participants

A total of 53 children (28 myopic and 25 emmetropic; 57.5% female) between the ages of 7 and 15 years were examined. Participants underwent preliminary examination to ensure the following: myopic refractive error between -0.75 and -6 D or emmetropic; refractive error between +0.5 and +1.5 D determined using cycloplegic refraction (performed using 1% Tropicamide[20]); astigmatism < 1D; anisometropia < 1D; best corrected visual acuity of at least 6/6 in each eye; non-strabismic; normal amplitudes of accommodation and had no history of bifocal/PAL use in the past. Participants had no systemic or ocular disease (determined from their clinical records) and were not taking any medications (parental report) that may influence the accommodation or vergence system.

6.3.2 Instrumentation and targets

The overall study design involved prolonged binocular viewing through the near addition lenses for 20 min with periodic measurements of accommodation and phoria, to quantify the time course of changes in either system. The instrumentation used for obtaining phoria and accommodative responses have been described in Chapter 3. Briefly, horizontal near phoria (33cm) was measured using the modified Thorington technique (MTT) [21]. A red Maddox rod was placed before the right eye and the resulting phoria was measured using a “flashing technique” similar to previous studies. [22, 23] Near phoria was defined as the average of the three responses. Children were divided into *“normophores”* (mean near phoria between 0-4 exo), exophores (>6 exo) or esophores (>2 eso) based on their phoria measures through distance-corrective lenses at 33cm. Table 6-1 lists the number of children in each vergence-bias category and other critical visual parameters of the study groups.

Table 6-1Critical visual parameters of myopic and emmetropic children

PARAMETER	***Emmetropes***			**Myopes**		
	Normophores	Exophores	Esophores	Normophores	Exophores	Esophores
No of participants	11	8	7	10	7	11
Age (7-14) in yrs	10.8 ± 0.43	12.2 ± 0.63	11.9 ± 0.43	10.43 ± 0.53	11.2 ± 0.8	11.8 ± 0.63
Refractive error (D)	0.59 ± 0.09D	0.4± 0.09D	0.3± 0.09D	-2.0 ± 0.3D	-2.5 ± 0.2D	-1.7 ±0.3D
Near phoria (Δ)	-2.15 ± 0.49 (0 to 4 exo Δ)	-6.72 ± 0.36 (6 to 10 exo Δ)	2.83± 0.58 (2 eso to 5 eso Δ)	-1.24 ± 0.94 (0 to 4 exo Δ)	-9.7 ± 1.5 Δ(6 to 14 exo Δ)	4.09 ± 0.5 (2 eso to 8 exo Δ)

Accommodative responses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor, the PowerRefractor (Multichannel Co, Reutlingen, Germany). [24, 25] This setting determined refraction along the vertical meridian, coupled with measures of gaze deviations and pupillary diameter at a sampling rate of 25 Hz. Two high contrast accommodative targets were used to measure and sustain closed-loop accommodation. The accommodative (measuring) stimulus was a fixed high contrast (85%) color cartoon frame (target luminance = 15 cd/m^2), which allowed a constant level of retinal illumination during the photorefractive measures of accommodation. Children viewed a looping cartoon movie at a plane 33 cm from the eye to sustain prolonged fixation for 20 min. This format has been used previously where the cartoon frame has been confirmed to be an effective stimulus for accommodation. [23] The targets were displayed on a 1.77″ wide liquid crystal display monitor (Model No: LT-V18 U; Victor company of Japan) and projected at a distance of 33cms through a semi-silvered mirror. The mirror, set 10 cm from the right eye, and angled at 45 degrees allowed the photorefractor to simultaneously record accommodation from the right eye during target viewing. The method has been described elsewhere in detail. [23]

Binocular accommodation (BA) and monocular accommodation (MA) were recorded continuously for a period of 5sec after confirming steady fixation using the gaze control function displayed on the PowerRefractor interface. For the binocular response, accommodation was recorded from the right eye alone, although both eyes fixated at the target. For measurement of MA, the left eye was occluded. During the 5 sec measurement period for each of BA and MA, the accuracy of fixation was assessed using the gaze control function displayed on the PowerRefractor interface. Additionally, care was taken to ensure that the child was fixating the near target at the correct fixation distance (33 cm) while measurements were recorded. A volunteer constantly monitored the head position of the child and ensured they did not move away from the chin rest during measurement. If any unsteady fixation was noticed during measurement, or when the examiner (VS) observed off axis gaze errors exceeding about 10 degrees, the measures were flagged using keyboard inputs and discarded given the possibility of under or over estimation of accommodation. [26, 27] In these cases, recordings were obtained for an additional 5 sec period to ensure equal data sets across subjects.

In addition to closed-loop accommodation, tonic accommodation was measured by instructing participants to monocularly (left eye occluded) fixate a low spatial frequency (0.2 cpd) difference of Gaussian target' at 4m. This target has been considered to be effective stimulus to open the accommodative feedback loop.

6.3.3 Experimental procedure

The experimental procedure consisted of two study sessions performed on different days (separated by at least by 24hrs) with the order of testing randomized to avoid bias. One session was performed with the children wearing +2D lenses mathematically added over their corrective lenses (if any) in a trial frame (referred to as *"plus add condition"*) and the other involved measurements through -2D lenses (referred to as *"minus add condition"*) added over their correction. The addition lenses were inserted at a distance of 12 mm from the participants' eyes and the trial frame was adjusted for the participants near pupillary distance so as to reduce any prismatic effect.

Prior to the start of the study session, participants sat in total darkness for 3 minutes to dissipate any effects of previous near work and allow the accommodation and vergence system to return to their resting states [28]. Pre-task measures of tonic accommodation were taken in an otherwise dark room. The lighting in the examination room was then reduced to approximately 10 lux to obtain sufficiently large pupil sizes for the measurement of accommodation. Following this, measures of phoria, binocular and monocular accommodation were taken at 33 cm through best corrective lenses to establish the baseline response without adds. Subsequently, participants were instructed to close their eyes and +2D or -2D lenses were binocularly added over the corrective lenses. The examiner confirmed clear vision through the adds when fixation was monocular (right eye occluded) and performed a measure of phoria before permitting any binocular viewing through the addition lenses. This response was defined as the lens-induced phoria for which adaptation was to be quantified. Phoria measures were followed by binocular and monocular accommodation. The time taken for one complete measurement block (measurement of phoria, binocular and monocular accommodation) ranged between 60 and 80 sec.

Participants were then instructed to watch a cartoon movie that was played at a distance of 33 cm and subsequent measures of phoria, binocular and monocular accommodation were repeated after 2, 4, 6, 8, 10, 15 and 20 minutes of near fixation. Participants were instructed to report any blurriness of vision anytime during the session. Immediately after the near task (within 40-50 sec) tonic accommodation was recorded to calculate accommodative adaptation.

6.3.4 Data Analysis

Each measurement of the accommodative response lasted for 5 sec, which at the Power Refractor sampling rate of 25 Hz provided a total of 125 data points. Each data point was screened and accepted according to criteria outlined in earlier reports. [23, 25, 29]All measures obtained from the PowerRefractor were calibrated based on individual calibration equations using a two-step protocol similar to previous studies. [23, 30]. The calibrated PowerRefractor responses represented the plane of focus of the eye[23]. The actual accommodative responses were then adjusted for the effective power of the near adds because lens manipulations were conducted at the spectacle plane in all cases. All data were analyzed such that the stimulus to accommodation and the accommodative responses were adjusted for lens effectivity using equations described in previous reports[2, 31].

Data from three participants were excluded from analysis. Of these, two were myopic esophores who complained of blurred vision through adds [1 (see footnote)] and one (myopic exophore) showed pupil diameters less than 3 mm which prevented reliable Power Refractor measures. Thus the data of 25 myopic and 25 emmetropic children were considered for further analysis.

Repeated measures analyses of variance (RM-ANOVA) was used to determine the effect of lens add condition and time on accommodation and phoria response. In all cases, statistically significant main effects were further examined using Tukey Honestly significant differences (HSD) post-hoc tests to determine the precise time point that showed the significant difference. Differences were considered statistically significant when the likelihood of type-I error was <0.05. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Phoria adaptation was quantified using two parameters derived using an exponential decay function similar to a previous study (Chapter 4). The ”magnitude” of adaptation was defined as the overall change in phoria after 20 min fixation through the near adds while the ”completeness” of adaptation, was defined as the return of adapted phoria to the habitual level. Curve fitting and analysis were performed using Graphpad software (Graphpad Inc, USA).

1: Testing was conducted with a low powered add (1D) in the two children and the pattern of adaptation was similar to 2D add. The results were not included for analysis due to a different magnitude of near add

6.4 Results

6.4.1 Changes to near phoria through plus and minus addition lenses

The mean habitual near phorias (Table 6-1) in each vergence-bias category and refractive category were similar between the plus add and the minus add sessions (P>0.9). However, in both add sessions each type of vergence-bias category significantly differed (P<0.001) from the others in myopes and emmetropes. Furthermore, the habitual near phoria for any given vergence-bias category was not significantly different between the two refractive groups (P>0.1). Plus and minus addition lenses induced exophoria and esophoria respectively in all children, based on their AV/A ratios (Table 6-2). The AV/A ratios and lens-induced phorias were similar between the two add conditions (AV/A: P=0.22; Lens-induced phoria: P=0.75) but differed between the phoria categories (AV/A: P=0.02; Lens-induced phoria: P<0.001) and refractive groups (AV/A: P=0.01; Lens-induced phoria: P=0.005) such that myopes and esophores showed higher AV/A ratios and lens-induced phorias compared to emmetropes and exophores.

Table 6-2: Parameters of adaptation for the plus add (dark grey) and minus add (light grey) conditions in all study groups.

Refractive error → ***Parameters ↓***	***Emmetropes***			***Myopes***			***Emmetropes***			***Myopes***		
	EX	EN	EE	MX	MN	ME	EX	EN	EE	MX	MN	ME
Induced exophoria	-4.0±0.4	-5.2±0.4	-6.8±0.3	-5.5±1.5	-6.9±0.6	-7.9±0.6	4.7±0.3	5.0±0.5	7.2±1.0	4.6±0.7	6.0±0.8	9.2±0.8
RAV/A	4.3±0.6	4.5±0.3	5.9±0.4	4.8±1.5	6.8±0.8	8.4±1.2	4.2±0.6	4.1±0.8	5.6±0.4	4.5±0.9	6.4±1.2	8.1±0.8
Magnitude of adaptation	4.7±0.3	4.6±0.5	3.8±0.4	2.6±0.5	3.9±0.5	2.8±0.5	-0.6±0.5	-2.0±0.5	-5.0±1.1	1.1±0.2	2.8±0.6	7.4±0.7
Time constant	1.7±0.5	0.8±0.1	1.2±0.5	2.0±1.5	1.2±0.3	1.2±0.2	2.5±1.2	1.3±1.0	3.0±1.0	3.3±0.6	1.8±0.5	3.5±0.6
Completeness	121.7±10.7	86.1±4	55±5.3	54.3±7.5	56.0±6.7	36.5±7.1	13.5±11	41±8.6	66.1±8.5	24.1±11.9	42.6±6.3	78.2±7.6

Negative sign denotes exophoria and positive sign denotes esophoria

6.4.1.1 Time course of changes to phoria through plus adds

Sustained binocular fixation through +2D adds resulted in a significant reduction of lens-induced exophoria ($P<0.0001$) in all vergence-bias and refractive categories. In EN and EE groups, the entire reduction of exophoria occurred within 2 minutes (Fig 6-1, $P<0.001$) of binocular fixation while EX continued to decrease beyond 2 minutes (time point: 2 min vs. other time points: $P<0.05$, Fig 6-1) but reached saturation (no significant change) at the 4 minute time-point. In the myopic groups, although majority of the change in phoria occurred within the first two minutes, all myopic groups showed further small and significant reductions with sustained fixation (2min vs. 20 min: reduction =0.75-1Δ: $P<0.05$, Fig 6-1).

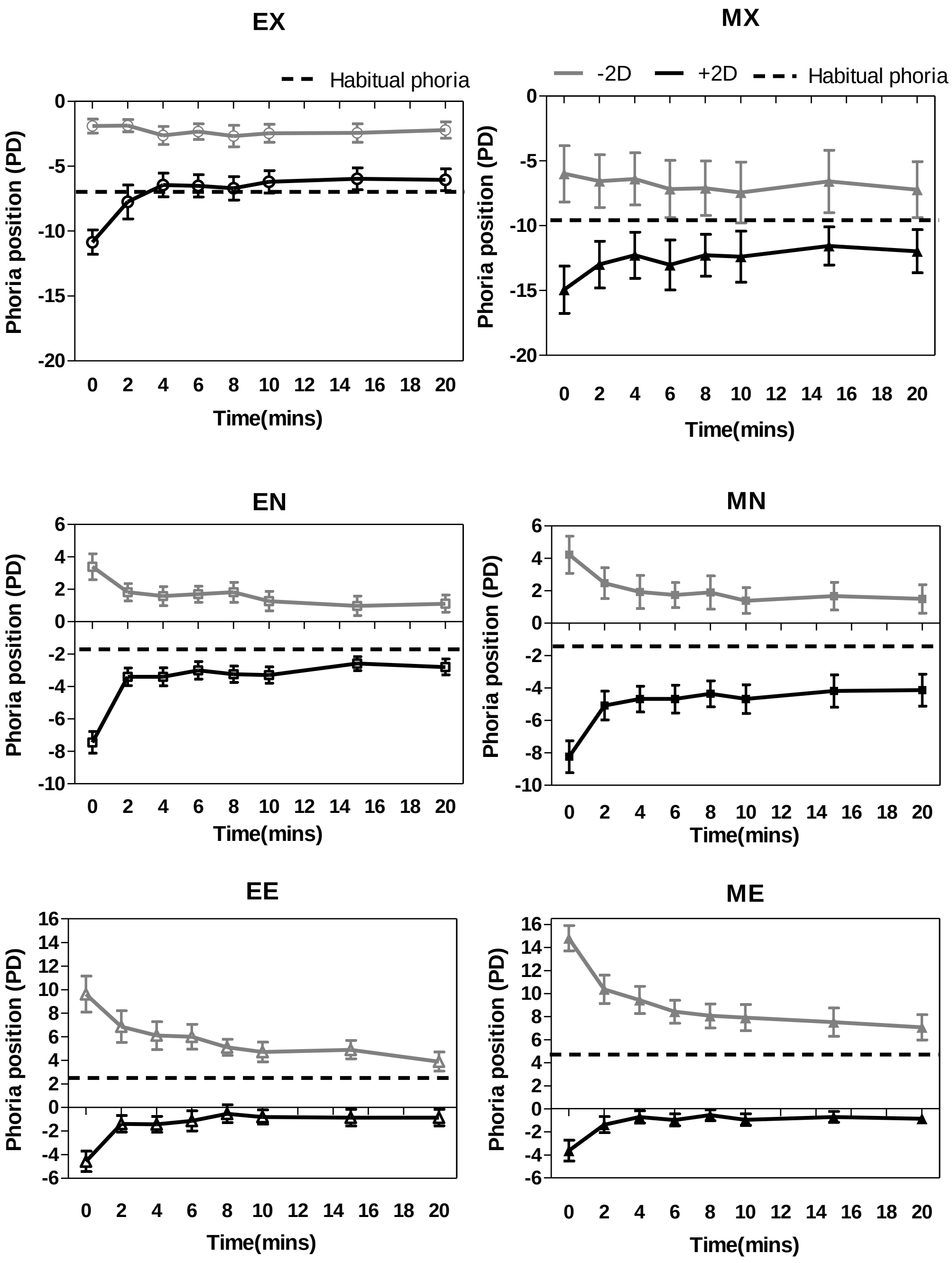
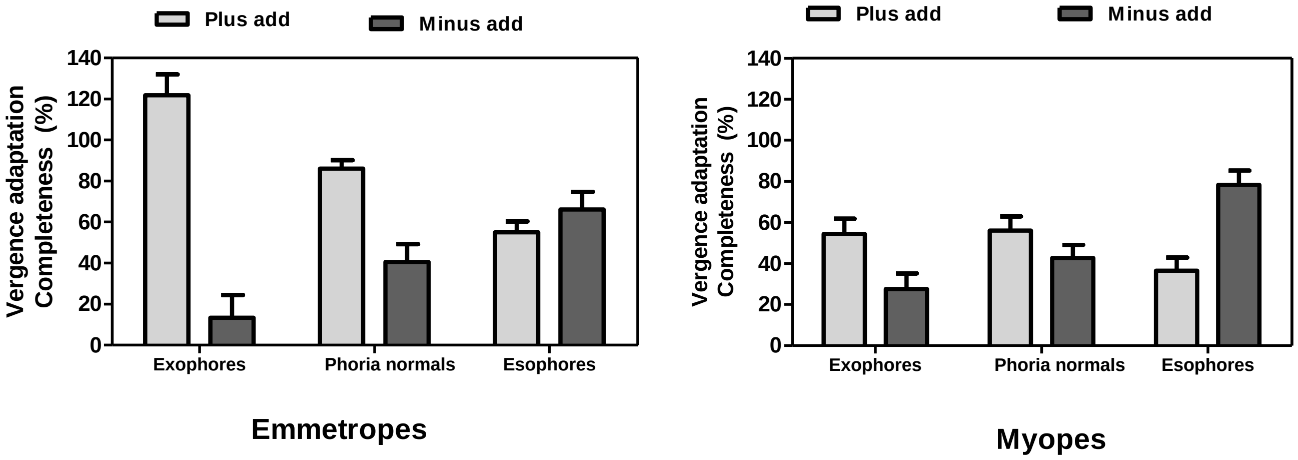


Figure 6-1: Comparison of mean phoria adaptation responses through +2D and -2D add .

Grey solid line represents responses in emmetropes (E) and myopes (M) in each vergence bias category(X, N, E) during sustained fixation. Dashed line represents the position of habitual phoria prior to lens addition. Error bars indicate mean ± SEM

In order to analyze the global effect of vergence-bias category and refractive type on phoria adaptation to plus adds, each participant's phoria response was fit using an exponential decay function in order to derive the magnitude and completeness of adaptation. Both these parameters of phoria adaptation were then subjected to ANOVA with phoria categories (3 types) and refractive error (2 types) as factors. The main effect of vergence-bias category was significant (Fig 6-2 A; Main effect P<0.0001), where exophores displayed significantly higher completeness compared to phoria normals (P=0.01) and esophores (P<0.001). However, post-hoc analysis only showed significant differences in completeness between emmetropic vergence-bias category groups (EX vs. EN:P=0.001; EX vs. EE:P<0.0001; Table 6-2). Myopic exophores do not show significantly greater completeness compared to MN (P=0.86) and ME (P=0.06). Myopic esophores showed significantly less adaptation compared to myopic phoria normals (P=0.02). Furthermore, the interaction between vergence-bias category and refractive type was also significant (Fig 6-2, P=0.006), demonstrating that the type of vergence-bias category had a greater effect on emmetropes compared to myopes. Completeness of adaptation significantly differed as a function of refractive type (Fig 6-2B , P<0.0001), indicating that the mean completeness of adaptation to plus adds was less in myopes compared to emmetropes. Post-hoc analysis indicated that for each vergence-bias category, myopic children showed significantly lower completeness of adaptation (EX vs.MX: P<0.0001; EN vs.MN: P=0.001; EE vs.ME: P=0.006; Table 6-2) compared to emmetropic children.

A: Comparison between add condition in each refractive group



B: Comparison between refractive groups in each add condition

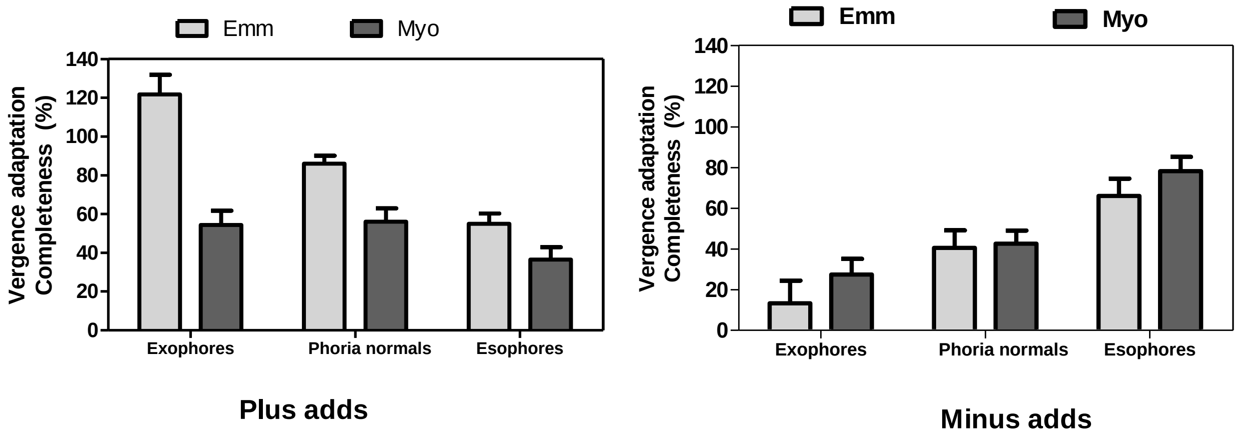


Figure 6-2: (A) Comparison of the total completeness of adaptation between the phoria categories for emmetropes and myopes. (B) Total completeness of adaptation compared between myopes and emmetropes in each add condition. Error bars indicate mean ± SEM

Statistical analysis comparing the magnitude of adaptation indicated significant main effect of refractive error (Table 6-2; P=0.002) such that myopic groups showed less magnitude of adaptation compared to emmetropes (MX vs EX; P<0.005; MN vs EN: P=0.09; ME vs EE: P<0.005). The main effect of vergence-bias category (P=0.37) and interaction effect were not significant (P=0.36).

6.4.1.2 Time course of changes to near phoria through minus adds

Minus add induced esophoria showed a significant decrease with sustained binocular fixation in all groups (Main effect of time: P<0.05) except emmetropic exophores (Fig 6-1; P=0.33). In the phoria normal category, emmetropes and myopes showed the majority of the reduction in esophoria within 2 minutes of fixation (EN & MN: P<0.0001), although further small but significant changes occurred with sustained fixation (Fig 6-1: time point 2 min compared to 20 min: EN: P= 0.03; MN: P=0.02). EE and ME reached saturation at 8 minutes (0, 2, 4, 6 min compared to 20 min: P<0.05) and 10 minutes (0, 2, 4, 6, min vs. 20: P<0.05; 8 min vs 20 min: P=0.05) respectively. MX showed very small change (0 vs 20 min=1.1Δ; P=0.04; Fig 6-2) with sustained fixation.

The overall effect of the vergence-bias category and refractive type were determined by comparing the magnitude and completeness of adaptation derived using exponential decay function similar to plus adds. Factorial ANOVA showed a significant main effect of vergence-bias category on phoria adaptation to minus adds as a function of magnitude (Table 6-2, P<0.0001) and completeness (P<0.001; Fig 6-2A and Table 6-2). Esophores showed significantly higher magnitudes and completeness of adaptation compared to phoria normals (P<0.001) and exophores (P<0.0001) in both refractive groups (Fig 6-2A). The main effect of refractive type was non-significant for both parameters of adaptation (P=0.08 for magnitude and P=0.14 for completeness- Fig 6-2B). Additionally, the interaction between vergence bias category and refractive error was also non-significant (Fig 6-2, P<0.7).

Since myopic children showed larger AV/A ratios, we determined the relationship between the AV/A ratio and adaptation to plus and minus adds in myopes and emmetropes (Fig 6-3) in each add condition. Myopes showed significantly (P<0.0001) less completeness in their adaptation to adds both plus and minus compared to emmetropes (Plus add: Emm= -11.07±3.2; Myo= -1.34±1.54; Minus add: Emm=15.01±3.4; Myo=2.72±2.0). Further, it is interesting to note significant reversal of slopes between plus and minus adds in emmetropes (P<0.001) but not myopes (P=0.11) such that in emmetropes the completeness of adaptation is inversely related to AV/A for plus adds but directly proportional to the AV/A through the minus adds.

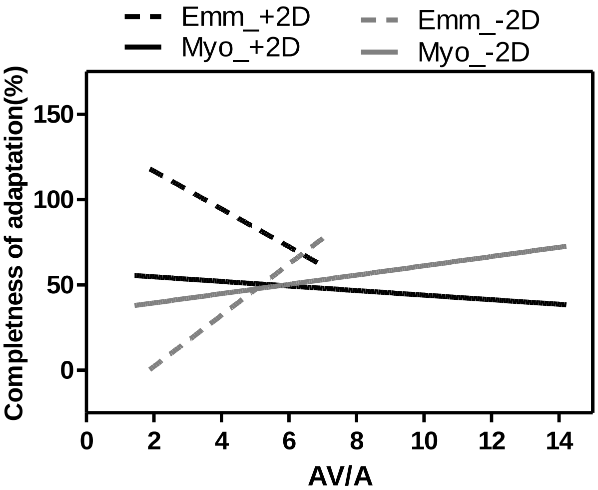


Figure 6-3: Plot showing the degree of completeness of adaptation in both refractive groups in each add condition as a function of the Response AV/A ratio.

Individual symbols have been excluded for the sake of clarity

6.4.1.3 Comparison of vergence adaptation between plus and minus add conditions

Repeated measures ANOVA was performed to compare the completeness of phoria adaptation between the plus and minus add conditions in all groups. Statistical analysis showed a highly significant main effect of add condition ($P<0.0001$), interaction between add condition and type of vergence-bias category ($P<0.0001$), and a significant interaction between add condition and refractive type ($P<0.0001$). These results indicate that the asymmetry in phoria adaptation between the plus and the minus add conditions is dependent on the type of vergence-bias category and refractive group (Fig 6-2). Emmetropic exophores ($P<0.0001$; Difference in completeness=108%; Fig 6-2A) and myopic esophores ($P<0.0001$; Difference in completeness=42%; Fig 2A) showed the greatest asymmetry in adaptation between the add conditions. However, the other groups MX ($P=0.06$) and EE ($P=0.40$) did not show statistically significant differences in the completeness of adaptation between the +2D/-2D add conditions (Fig 6-2A).

In an effort to understand the asymmetric adaptation pattern to near adds, we determined the fusional vergence demand (This value was calculated by determining the amount of divergence or convergence required to overcome the resulting eso or exo phoria respectively) required for each subject upon the onset of viewing through either the + or –ve near add. For both parameters of adaptation (magnitude and completeness; Figs 6-4A&B) we found a significant correlation ($P<0.05$) between the demand on fusional vergence and adaptation (Magnitude of adaptation: Emm: +2D and -2D combined: $P<0.0001$; overall $r=-0.91$; $r^2=0.83$; Myo: $P<0.0001$; $r=-0.85$; $r^2=0.72$). This relationship was also evident when groups were classified based on vergence bias category (r^2 ranging from 0.5-0.8).

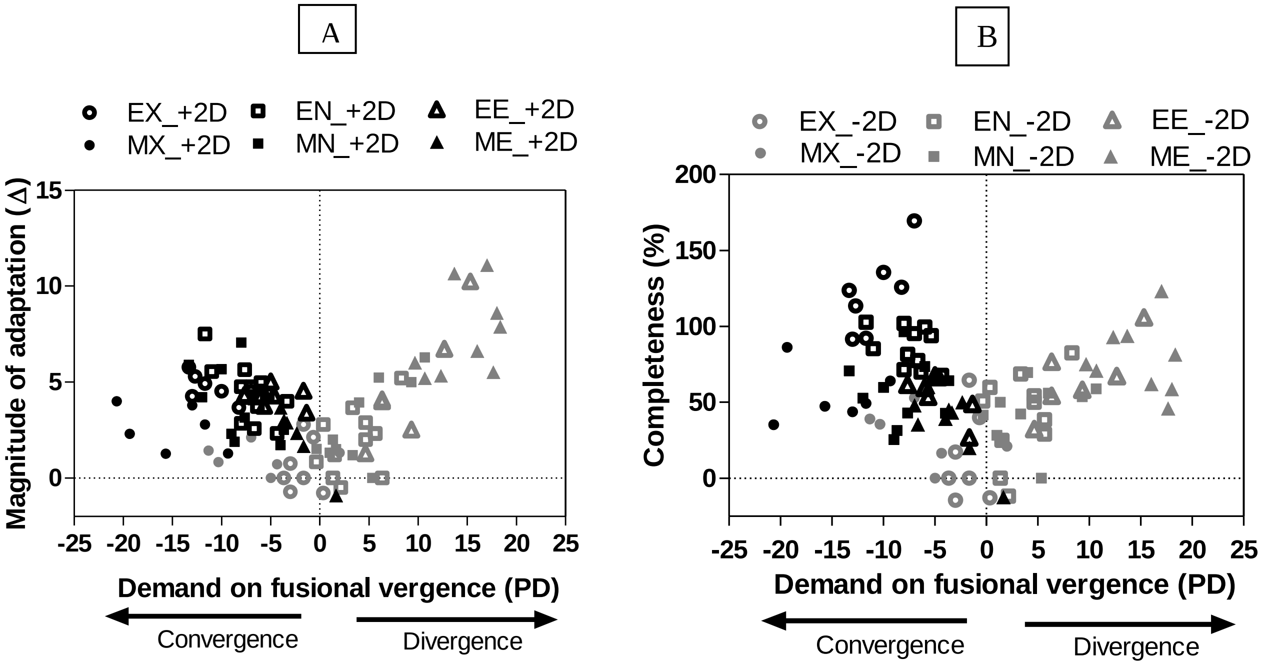


Figure 6-4: Plot showing the relationship between the magnitude of adaptation and demand of fusional vergence (A) and the completeness of adaptation and the demand on fusional vergence (B) in all study groups.

6.4.2 Changes to accommodative responses through plus and minus addition lenses

The mean accommodative responses through corrective lenses i.e. no add (Fig 6-5) were statistically similar between the two add sessions under both binocular (P=0.9) and monocular viewing conditions (P=0.3) across all groups. Viewing condition (BA vs. MA), type of vergence-bias category and refractive state, significantly influenced the magnitude of accommodative response, similar to the results reported in Chapter 5. Myopic children displayed significantly lower accommodative response compared to emmetropes (P=0.01). In both refractive groups, exophores showed significantly higher BA compared to MA (P<0.01), whereas esophores displayed higher MA compared to BA (P<0.05).

Introduction of plus and minus adds significantly (P<0.0001) reduced and increased the accommodative response respectively in all groups (Fig 6-5). Fixation through plus adds (Fig 6-5 black lines) altered the pattern of BA vs. MA (main effect of viewing condition: P<0.05 except MX: P=0.13) such that, BA was significantly higher than MA (P<0.05) in all groups, especially at the onset of near work (time point 0). In both refractive groups, sustained fixation reduced the BA alone (main effect of time: BA: P<0.05; MA: P>0.3) in exophoric (EX: P=0.005; MX:P=0.05) and phoria normals (EN: P<0.0001; MN: P=0.01). Both esophoric groups (ME and EE) displayed a non-significant effect of time on BA (P>0.2); however, ME showed a small and statistically significant (P<0.005) increase in monocular accommodation with sustained fixation. Only the exophores and phoria normals showed significant interaction between viewing condition and time (P<0.005) suggesting greater effect of time on BA compared to MA when viewing through plus adds.

Compared to the plus add condition, fixation through minus adds reversed the pattern of BA vs. MA in some groups (In EE, ME and MN: MA>BA) and reduced the difference between BA and MA in others. Immediately after the addition of -2D lenses, BA vs. MA was significantly different in esophores (Fig 6-5; EE & ME: P<0.0001) and exophores (P=0.01) but not phoria normals (P>0.5). Sustained fixation significantly increased the accommodative response in both binocular and monocular viewing conditions in all groups (P<0.05) except MX (P=0.18). Interaction between viewing condition and time was significant only in the esophoric groups (EE &ME; P<0.05) such that BA changed more than MA in both groups within the first 4 minutes of fixation. Changes to BA and phoria during sustained fixation through minus adds was significantly correlated (P<0.05) in EE & ME but not the other groups (P>0.4).

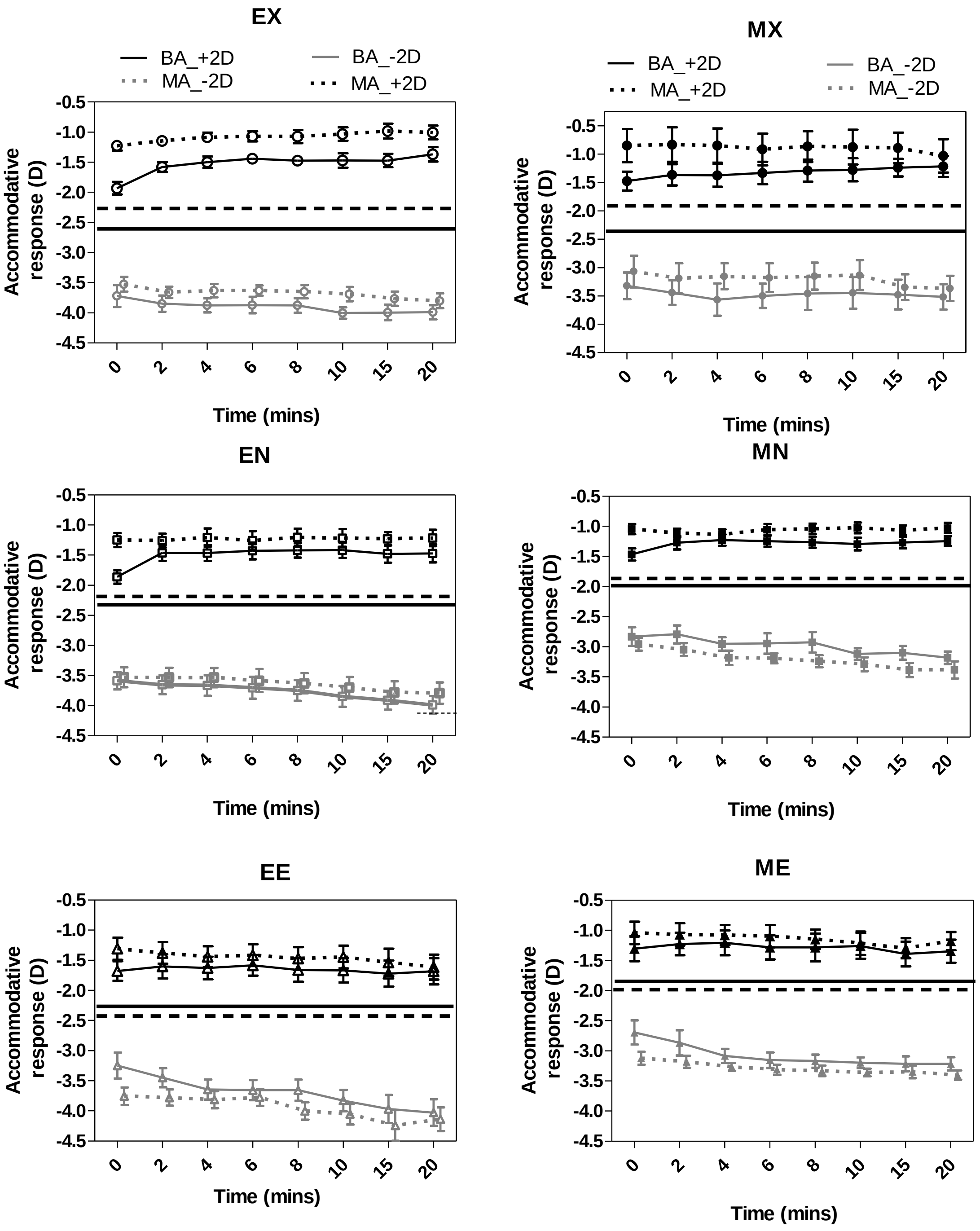


Figure 6-5: Mean changes to the binocular and monocular accommodative responses through +2Dand -2D add adds at 33cm.

Grey lines indicate responses for the minus add condition, while black lines indicate responses from + add condition. The thick solid black line (binocular) and thick dashed black line (monocular) represent the mean accommodative responses through distance corrective lenses (no add) in all the refractive and vergence bias groups. Error bars indicate mean ± SEM

6.4.2.1 Accommodative adaptation through plus and minus adds in the groups

Accommodative adaptation was defined as the difference between pre and post-task tonic accommodation. Fig 6-6 shows the pattern of accommodative adaptation through plus and minus adds in the refractive and phoria categories. All groups except myopic esophores show non-significant accommodative adaptation (i.e post task TA similar to pre-task TA; $P>0.2$; ME: $P=0.01$) through plus adds. On the other hand, all groups but exophores (MX: $P=0.5$; EX:$P=0.06$;) show significant accommodative adaptation to minus adds ($P<0.001$). The magnitudes of accommodative adaptation between the add condition, refractive type and phoria categories were compared using RM-ANOVA. The overall effect of refractive type was approaching significance ($P=0.08$), however, post hoc tests indicated that myopic children showed significantly greater accommodative adaptation to minus adds compared to emmetropic children ($P=0.01$).

The type of add condition significantly influenced the amount of accommodative adaptation ($P<0.0001$) such that greater adaptation was seen through minus adds compared to plus adds. Post-hoc tests revealed that all groups except EX showed this pattern of greater accommodative adaptation to minus adds compared to plus adds ($P<0.05$). Although the main effect of vergence-bias category was significant ($P<0.005$) statistically significant differences were not observed between all vergence-bias category categories in the two add conditions. In the plus add condition, only ME showed significantly higher accommodative adaptation compared to other groups ($P<0.01$). In the minus add condition, exophores showed significantly lower accommodative adaptation compared to esophores in both refractive groups (EX vs. EE: $P=0.01$; MX vs. ME:

P=0.002) but only compared to phoria normals in myopic category (MX vs. MN: P=0.01; EX vs. EN=0.09).

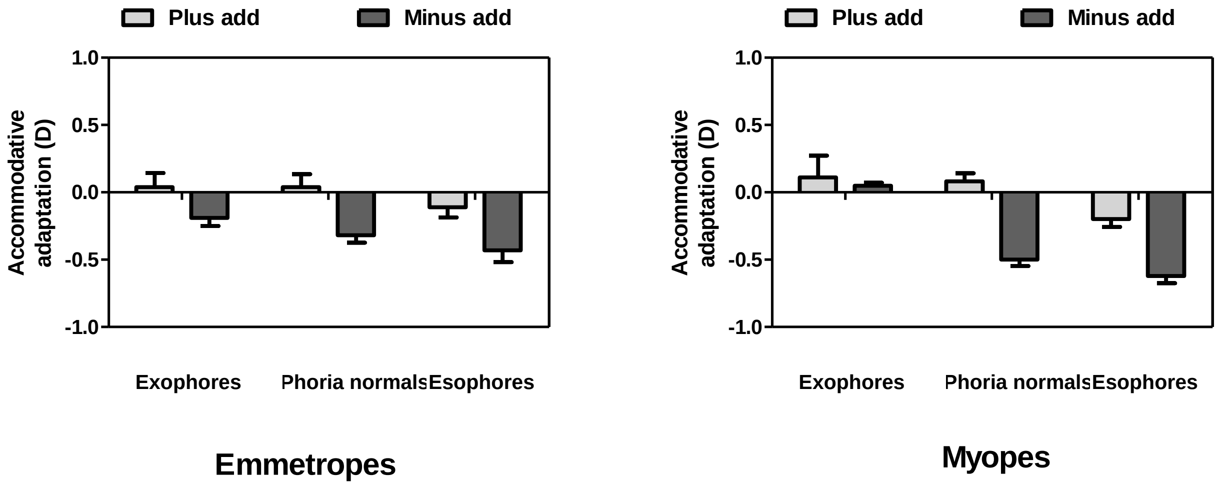


Figure 6-6: Mean tonic accommodative change (Pre task – post task) in myopic and emmetropic children with +2D and -2D adds after 20 minutes of near activity. Error bars indicate mean ± SEM

6.5 Discussion

This study employed near addition lenses as a means to investigate vergence adaptation in children. The primary findings of this study were that both the category of phoria and refractive error influence the pattern of vergence adaptation to near adds in children.

6.5.1 Role of habitual vergence-bias category on vergence adaptation to near adds

Introduction of positive and negative addition lenses reduced and increased the accommodative response relative to the near target (3D), inducing exophoria and esophoria respectively in all study groups, in accordance with their AV/A ratios. The lens-induced shifts in phoria are consistent with previous reports [23, 32-34] and models of accommodation and vergence. [12, 13] All groups showed an ability to adapt to adds with prolonged fixation, similar to previous studies. [23, 33, 35] However, the pattern of vergence adaptation differed between groups depending on the type of add, direction of baseline vergence-bias category, and refractive type.

In emmetropic children, prolonged fixation through plus and minus adds produced opposite patterns of vergence adaptation (Fig 6-2A), consistent with our hypothesis. Exophores showed more than 100% vergence adaptation to plus adds but displayed no vergence adaptation to minus adds. On the other hand, esophores showed the least adaptation of the three vergence categories through plus adds (EX>EN>EE) but showed the highest adaptation through minus adds (EE>EN>EX). The contrasting vergence adaptation to plus/minus adds could be explained to a large extent by the significant correlation between differing fusional vergence demands produced by the addition lenses. For an EX, the presence of exophoria relative to the dioptric demand necessitates an increase in fusional convergence to compensate for the deviation and achieve binocular single vision. The addition of positive lenses further increases the exophoria, which in-turn increases the demand on fusional convergence. On the other hand, binocular viewing through negative lenses reduces the exophoria and hence fusional vergence demand relative to no addition lenses (i.e. habitual exophoria). Since phoria adaptation is related to the demand on the fusional vergence, [14, 15, 36] we postulate that the reversal of vergence adaptation to plus and minus adds seen in EX is related to the differing fusional vergence demands. Similarly, the pattern of adaptation to +2D vs. -2D lenses observed in emmetropic esophores may also be explained based on the fusional demand theory. The high correlation between the demand on fusional vergence and the degree of adaptation (r^2=0.83) further confirmed our hypothesis indicating that 83% of variability in the adaptation can be explained by the demand on fusional vergence in emmetropic children.

Though this is the first study to show the effect of vergence-bias category on adaptation to near adds, previous studies have shown a similar dependence of vergence-bias category on the magnitude of adaptation. [37-39] Nevertheless, it should also be noted that few other studies have reported no significant relationship between baseline phoria and adaptation [40, 41]. Of these, one study measured prism adaptation in esophoric and exophoric participants with abnormal binocular vision or asthenopia [40] and in the other study, the majority of the participants were exophoric (only one esophore). [41] Thus differences in these studies can likely be attributed to attenuated adaptive processes found in individuals with binocular anomalies [40] in the former case and a lack of full spectrum of vergence bias in the latter [41].

In the present study, it is fascinating to observe that vergence adaptation was consistently less when the lens-induced phorias reduced rather than increased the baseline vergence-bias category. Of particular interest is the adapted phoria position in emmetropic and myopic esophores fixating through +2D adds. In both groups, the mean adapted phoria position was close to orthophoria through plus adds and the small error bars indicate that this pattern was seen in majority of the children. The current study findings seem to support the view that vergence adaptation is a mechanism that operates to reduce the demand on the fusional vergence system [11, 15, 36]. It can be seen that these adaptive processes underlie orthophorization of heterophoria [42-44].

6.5.2 Role of refractive state on vergence adaptation to near adds

Myopic children regardless of vergence-bias category showed reduced vergence adaptation to lens-induced exophoria when accommodation was relaxed beyond the target through positive adds but not when accommodation was increased through minus addition lenses. A previous chapter (#4) showed reduced adaptation to +2D adds in a different sample of myopic children with normal near phoria [33]. The current study, in addition to confirming previous results, shows that other myopic groups (MX and ME) also exhibit reduced vergence adaptation to plus adds compared to their respective emmetropic groups. On the other hand, myopic children showed either similar (MN and MX) or higher (ME) vergence adaptation to minus adds compared to their respective emmetropic groups.

Past studies show a reciprocal relationship between the degree of vergence adaptation and AV/A ratio (or induced phoria) to plus adds such that larger AV/A ratios are associated with reduced completeness of adaptation. [23, 33, 35] The larger response AV/A ratios observed in myopic vs. emmetropes groups [1, 2] may be considered to be a cause for the reduced adaptation (to plus adds) in myopic groups. However, our results indicate that AV/A ratio has little relation to the adaptive behavior seen in myopic children (Fig 3) since even children with low AV/A ratios show-reduced adaptation to plus adds. These findings are consistent with the hypothesis proposed by Rosenfield [45] that the vergence adaptive property itself might be reduced in myopes. North and colleagues [46] compared adaptation to 6 $^{\Delta}$ base-in and base-out in adult groups of emmetropes, early onset and late onset myopes and reported no significant difference in the magnitude of prism adaptation between the three groups. However, they reported that the time course of adaptation response was significantly different between late-onset myopes compared to early-onset myopes. The authors do not mention the progression of the refractive groups. Since the study was performed on adults, it may be possible that the early-onset myopes achieved stability in their refractive state while the late-onset myopes were still progressing. The current study was performed on early-onset myopic children where most children showed progression based on retrospective clinical records.

The reversal of vergence adaptation observed in the emmetropic vergence-bias category categories (+2D: EX>EN>EE; -2D = EE>EN>EX) was only seen in myopic esophores but not myopic exophores (+2D: MX=MN>ME; -2D = ME>MN=MX), who show non-significant adaptation compared to children with normal near phoria. This may have occurred if the two groups (MN & MX) had similar habitual and lens-induced phorias. Table 6-1 & 6-2 clearly indicate that this was not the case. The non-significant difference could be due to the lower number of participants (MX; N=6) and more variable data (wide error bars in Fig 1) in myopic exo group compared to myopic esophores (nine) However, the demand on fusional vergence significantly correlated with the magnitude of adaptation even in myopic children ($r^2 = 0.72$).

The asymmetry in the effect of myopia on vergence adaptation to plus vs. minus adds could be due to differences within the vergence system or may be related to the influence of accommodation on the vergence system. In the vergence system, it may be possible that myopic children deal better with stimuli that require divergence (produced by minus adds) than stimuli that require convergence (produced by plus adds). Previous studies have suggested that the rate of adaptation may be related to the frequency with which the ocular motor system deals with the type of disparity.[16, 22] Myopic children show less exo or more convergent distribution of near phoria (requiring divergence) compared to emmetropic children, which could explain the better adaptive response through minus adds compared to plus adds. Furthermore, children with myopia are habitually accustomed to wearing negative lenses for distance and near fixation. Since their corrective lenses are centered for distance pupillary distance, this may induce a small amount of base-in prism when viewing is shifted from distance to near (approximately 2Δ based on the mean refractive error), resulting in exposure to additional disparities that require divergence.

The other possible explanation for the asymmetric refractive group differences between plus and minus adds may be related to the influence of accommodative parameters on the vergence system.

6.5.3 Influence of accommodation on vergence adaptation to plus/minus adds

Under binocular viewing conditions, near addition lenses alter both blur driven and disparity driven accommodation (Fig 6-5). Plus and minus addition lenses reduced and increased both the binocular and monocular accommodative responses respectively in all groups, with respect to the 3D near target. It is this change in accommodative response that resulted in the lens-induced phorias, for which adaptation was quantified. However, it is important to note that any subsequent changes to the blur-driven (monocular) accommodative response may also alter the vergence response through the AV cross-link and thus impact vergence adaptation. Likewise, any changes to vergence system may modify the binocular accommodative response through VA cross-link.

When plus adds are added to all groups the stimulus and hence the response to blur driven accommodation is reduced. Due to the reduced activity of the accommodative phasic controller, which provides input for adaptation and the cross-links[12, 47], there is less chance for accommodative vergence or accommodative adaptation to play on vergence adaptation during binocular fixation through plus adds. The unchanged monocular accommodative responses and absence of accommodative after-effects trough plus adds confirm this suggestion (Fig 6-5 and Fig 6-6).

However, when negative adds are set before the eyes, the stimulus to blur driven accommodation becomes significant as does the accommodative convergence. Thus when groups (myopes in this study) show differences in AV/A ratios and adaptation of accommodation these differences will affect accommodation and vergence responses [4, 48] through AV/A cross-link. Thus, during dual closed loop conditions, patterns of vergence adaptation may be influenced by accommodative as well as vergence adaptation. The steep phoria adaptation curve for the myopic esophores who had high accommodative adaptation could be a product of both vergence and accommodative adaptation.

Vergence adaptation to near adds have important clinical implications, particularly because plus adds are a widely researched treatment option to reduce the progression of myopia [5, 7, 49-56]. The results of this study indicate that all myopic children show reduced vergence adaptation to plus addition lenses. For myopic children with esophoria, the plus addition lens decreased the lag of accommodation and placed the baseline convergent position towards orthophoria thereby placing less demand upon reflex vergence and accommodation system. The reduced vergence adaptation in ME would be beneficial in avoiding a return to esophoria. However, such adds may not be well tolerated in myopes with a high exophoria, where the reduced vergence adaptation leads to increased exophoria and hence a greater stress on the vergence system.

7 Vergence adaptation in myopic and emmetropic children under open-loop accommodation

7.1 Summary

Purpose: In previous studies we have shown that myopic children exhibit reduced vergence adaptation to +2D addition lenses under closed-loop accommodation. Here, we have extended the work by comparing vergence adaptation to 10Δ base-out under conditions of open-loop accommodation in myopic (M) and emmetropic (E) children.

Methods: 20 emmetropic and 24 myopic children between 7 and 15 years were examined. Habitual tonic vergence (TV, distance phoria through 0.5mm pupils) and open-loop accommodative response (0.2 cpd difference of Gaussian target) were first measured through best corrective lenses. Following this, 10 Δ base-out (BO) was added in front of the left eye and measures were repeated at frequent intervals (after ensuring fusion) when children sustained binocular fixation (4M) through 0.5mm infra-red pupils. Vergence adaptation was quantified by the overall TV change (magnitude) as well as the percentage return to the habitual level (completeness) derived using an exponential decay function. Tonic accommodation was also measured before and after the sustained task.

Results: Habitual TV and binocular open-loop accommodative responses were similar between the two refractive groups. 10BOΔ induced significant exo shift and increased convergence accommodation, which were non-significant between the refractive groups. With sustained fixation, both refractive groups showed significant ($P<0.001$) reduction in induced TV but the magnitude ($E=6.3\pm0.3$; $M=5.0\pm0.4$; $P=0.030$) and completeness of prism adaptation were reduced in myopes compared to emmetropes ($E=70.7\pm3.2$; $M=58.0\pm4.4$; $P=0.040$). When children with varied baseline tonic vergence were pooled

together, the degree of adaptation significantly correlated with the demand on fusional vergence in both refractive groups (Emm: P=0.010; Myo: P=0.030). Thus, a second analysis was performed including children with normal TV alone in either refractive group. Nevertheless, myopic children continued to show significantly (P=0.010) reduced prism adaptation compared to emmetropes. In the accommodative system, prolonged fixation reduced the binocular open-loop accommodative response, which significantly correlated with the reduction in prism-induced exo-shift in emmetropic TV normals (R^2=0.8; P=0.003) but not in myopes (R^2=0.01; P=0.80). Myopic children with normal TV showed significant increase in open-loop accommodation with sustained fixation, which was also evident in the increased post-task tonic accommodative shift (E=0.07± 0.1D; M= -0.41± 0.1D; P=0.030).

Conclusion: Myopic children show reduced vergence adaptation to BO prism under open-loop accommodation. This behavior suggests that myopic children show reduced vergence adaptive ability irrespective of the nature of accommodative influence when fusional convergence is stimulated either through BO prisms or binocular viewing through plus adds.

7.2 Introduction

In our previous studies [1] (Chapters 4 & 6) we have shown that myopic children exhibit reduced vergence adaptation compared to emmetropes when reflex convergence is stimulated through plus addition lenses but not when reflex divergence is stimulated through minus addition lenses . The magnitude of disparity induced by an ophthalmic lens depends on the strength of the AV/A ratio. On the other hand, the disparity created by a prism is constant. Several researchers have investigated vergence adaptation to prismatic disparities [2-10]. A consistent pattern is found where the phoria induced by a prism returns to the original baseline value after sustained binocular fixation. [2-6] Factors such as the magnitude and duration of the adapting stimulus [7, 8], presence of asthenopic symptoms and abnormal binocular vision [9], influenced the degree of vergence adaptation to prism. Limited evidence exists concerning the effect of myopia on vergence adaptation to prisms.

North and colleagues [10] compared adaptation to 6 $^{\Delta}$ base-in and base-out in adult groups of emmetropes, early onset and late onset myopes at 4M and 0.4M. The authors reported no significant difference in the magnitude of prism adaptation at either testing distances between the three groups. It should be noted however, that these adults had reached an age where their myopia has possibly stabilized (no details on progression provided in the paper). Further, this investigation was performed under closed-loop accommodation, which is controlled by an interactive negative feedback mechanism. Thus, any changes to accommodation (such as accommodative adaptation) may alter the fast controller, thereby influencing the vergence system through the accommodative-vergence cross-link. [11, 12] Evidence suggests that myopes are susceptible to greater accommodative after-effects [13, 14] and also show higher response AV/A ratios [1, 15, 16], which may produce larger changes in the vergence system compared to emmetropes.

In our previous reports that measured vergence adaptation to lens-induced disparities, accommodation was measured under closed-loop conditions to a near target at 0.33M (Chapter 6). We found that accommodative adaptation differed between refractive groups when the stimulus to accommodation was increased relative to the near target through minus addition lenses but not when the stimulus was reduced through +2D addition lenses. But there would be very little accommodation in play for any group through plus adds because they reduce the stimulus for (reflex) accommodation, leaving little opportunity for adaptation [12, 17]. Vergence adaptation, on the other hand, was significantly reduced in myopic children through plus adds but not minus adds. Two possibilities exist. First, vergence adaptation in myopes may only be attenuated in the case of stimuli that require convergent activity compared to divergent activity. Second the results may show the influence of the greater accommodative adaptation. Adaptation of accommodation reduces the activity of the accommodative vergence cross-link, resulting in a divergent shift in the vergence system [12, 18, 19]. Thus, it may be possible that myopic children have poor vergence adaptive ability but the influence from accommodation system concealed it in the case of fixation through minus addition lenses. Due to the interaction between accommodation and vergence [20, 21], accurate estimation of vergence adaptive ability requires the elimination of cues for accommodation so that adaptation may primarily be determined by the vergence controller. Accordingly, this study measured vergence adaptation to a prismatic stimulus (10 Δ base-out) under open-loop accommodation at a testing distance of 4M (to reduce the effect of knowledge of nearness or proximity) in myopic and emmetropic children.

7.3 Methods

7.3.1 Study participants

The children enrolled in this study were a part of a larger study that measured ocular alignment and closed-loop accommodation through plus and minus addition lenses (Chapter 6). For the add studies, children were recruited based on their near phorias (*normo-phores*: 0-4 exo, exophores: >6 exo or esophores: >2 eso). It is important to note that the current (prism) protocol was only performed in children who were eligible and completed the add studies based on their near phoria.

The study sample consisted of 53 children (Table 7-1; 25 emmetropic and 28 myopic; 30 females) between the ages of 7 and 15 years, recruited from the clinic database at the School of Optometry, University of Waterloo. The protocol followed the tenets of the Declaration of Helsinki and received approval from institutional review board. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the nature and possible consequences of the study.

Participants had normal general and ocular health (determined from their clinical records and confirmed during a screening visit), myopic refractive error between -0.75

and -6 D or emmetropic refractive error between +0.25 and +1.5 D determined using cycloplegic refraction (two drops of 1% tropicamide added to both eyes, similar to a previous study[23]); astigmatism < 1D; anisometropia < 1D; best corrected visual acuity of at least 6/6 in each eye; non-strabismic; and were not taking any medications that might influence the accommodation and vergence systems.

Table 7-1: Critical visual parameters of myopic and emmetropic children

Parameter (Mean ± SEM; and range where applicable)	Emmetropes	**Myopes**
No of participants	25	28
Age	10.8 ± 0.43 yrs (7-15)	11 ± 0.31 yrs (7 -15)
Refractive error	0.5 ± 0.12D (0.5 to 1D)	-2.06 ± 0.3D (-0.75 to -3.75D)
AV/A ratio (Δ/D)	4.3±0.3	6.7±0.6
VA/Vratio (D/ Δ)	0.05D±0.01	0.04D±0.01

7.3.2 Instrumentation

Tonic vergence (TV) was determined by measuring horizontal heterophoria (modified Thorington technique) at 4M through 0.5 mm pinhole pupils. Measurements were performed using a flashing technique similar to previous studies [4, 22]. TV was defined as the average of the three responses.

Accommodative responses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor, the PowerRefractor (Multichannel Co, Reutlingen, Germany) [23, 24]. This setting of the instrument determined refraction along the vertical meridian of the participants' eyes, sampling at a rate of 25 Hz, coupled with measures of gaze deviations and pupil diameter. The Power Refractor was positioned 1M away from the participant and the infra-red light source has been established to be safe for use in children. All accommodative measures obtained from the PowerRefractor were calibrated using a protocol similar to previous studies (Appendix A) [1, 22, 25].

7.3.3 Experimental procedure

This experiment was conducted under conditions of open-loop accommodation, achieved by adding 0.5mm infra-red pinhole pupils over corrective lenses (if applicable) in a trial frame. Sufficient care was taken to ensure that the pinholes were centered within the participant's pupil. Prior to the start of the study session, participants sat in total darkness for 3 minutes to dissipate any effects of previous near work and allow the accommodation and vergence system to return to their resting states. [26] Following this, a baseline measure of tonic vergence was taken when children wore their corrective lenses. Participants then fixated a 0.2 cpd difference of Gaussian (doG) target in an otherwise dark room and baseline open-loop binocular and monocular (pre-task tonic accommodation) accommodation were recorded for 5 sec. The doG target was generated on a laptop and projected on a 20-inch television monitor (Panasonic PV-C2080) at 4M.

Subsequently, a 10 BO prism was added in front of the occluded left eye. Tonic vergence was measured prior to any binocular viewing through the prism and this represented the induced TV for which adaptation was to be quantified. Binocular fusion/suppression through the prism was then evaluated by presenting monocular nonius lines using polarizing glasses. Participants with suppression/diplopia through the prisms were excluded from the study. Measures of binocular open-loop accommodation were then taken through the prism and the induced change in accommodation was considered as convergence-accommodation (because other components of accommodation were either eliminated {blur} or kept constant {proximity}).

Sustaining task: The "sustaining target" was a cartoon movie, also displayed at a distance of 4M on the CRT monitor. This target has been used in previous studies [1, 22] and was chosen after considering the age of the participants to avoid boredom and to ensure prolonged near fixation for the scheduled duration of the study (20 min). Measures of TV and binocular open-loop accommodation were repeated after 2, 4, 6, 8, 10, 15 and 20 min of binocular fixation through the prism. Participants were instructed to report if they experienced diplopia anytime during the session. Additionally, the examiner ensured that the infra-red pinholes were within participant's pupils for the entire duration of the near task through the PowerRefractor (infra-red) interface. Immediately after the sustained task (within 20-30 sec) tonic accommodation was recorded to calculate accommodative adaptation.

7.3.4 Data Analysis

Measurement of the sustained accommodative response for 5 sec at 25 Hz provided a total of 125 data points. Each data point was screened and accepted according to criteria outlined in earlier reports (Chapters 4-6 and published reports [1, 22, 27]). The data retained were averaged to obtain the mean accommodative response.

Repeated measures analyses of variance (RM-ANOVA) was used to determine the effect of binocular fixation on tonic vergence and binocular open-loop accommodative responses. In all cases, statistically significant main effects were further examined using post-hoc tests to determine the group that showed the significant difference. Differences were considered statistically significant when the likelihood of type-I error was <0.05. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Vergence adaptation was quantified using two parameters derived using an exponential decay function similar to a previous studies. [1, 22] Magnitude was defined as the overall change in phoria after 20 min fixation through the prism. Completeness as the name suggests, was defined as the return of adapted phoria to the habitual level. Curve fitting and analysis were performed using Graphpad software (Graphpad Inc, USA).

7.4 Results

Of the 53 children enrolled into the study, data from 44 children were included for the analysis. Nine children did not complete the study for the following reasons: diplopia reported when viewing through the prism (E=1; M=2); suppression of either eye (E=2; M=1); difficulty in viewing through pinholes (E=1); or the prism induced disparity was out of the measuring range of the tangent scale i.e. beyond ± 15 Δ (E=1; M=1). Thus, data from 20 emmetropic and 24 myopic children were included for analysis.

Figs 7-1A&B show the mean changes to tonic vergence and binocular open-loop accommodative response, respectively through 10 Δ BO in the emmetropic and myopic groups. Differences in the baseline tonic vergence through corrective lenses (Fig 1A) was non-significant between the refractive groups (P=0.15). The addition of 10 Δ BO significantly increased exophoria (P<0.001) whose magnitude was also similar between the two refractive groups (E=8.9±0.2; M=8.7±0.3; P=0.50). Prolonged binocular fixation significantly reduced the prism-induced exophoria (P<0.001) in myopic and emmetropic children. This is taken to be indicative of a change in tonic vergence to a more convergent position reflecting vergence adaptation. The exponential decay curves in the myopic children showed a significantly reduced magnitude (E=6.3±0.3; M=5.0±0.4; P=0.030) and completeness of vergence adaptation (E=70.7±3.2; M=58.0±4.4; P=0.040) in myopic children compared to emmetropes.

Differences in the binocular open loop accommodative responses prior to the addition of prisms (Fig 7-1B) was non-significant between the refractive groups

(P=0.48). Introduction of 10 Δ BO significantly increased the binocular open loop accommodative response in both refractive groups ($P<0.005$). Statistical analysis showed a significant effect of time ($P<0.0001$) such that the binocular accommodative response reduced concurrent with the reduction in prism-induced exophoria (Pearson r=0.9, $r^2=0.83$; P=0.001) in emmetropic children alone. Myopes showed a non-significant effect of time (P=0.36) on the binocular-open-loop accommodative response, despite significant changes to prism-induced exophoria (correlation: Pearson r=0.2, $r^2=0.08$; P=0.49).

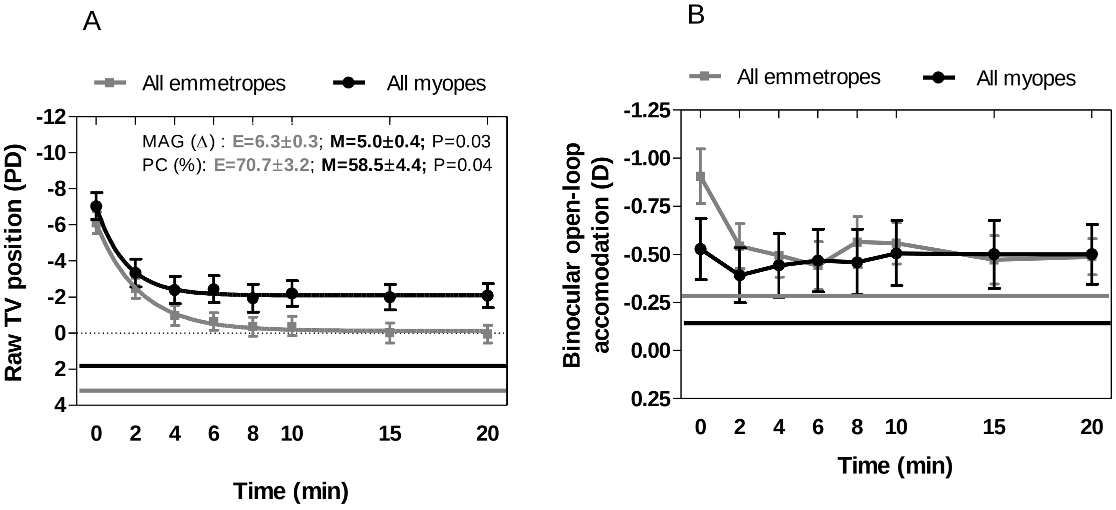


Figure **7-1** A&B: Comparison of mean changes to tonic vergence (Fig 1A) and binocular open-loop accommodation (Fig 1B) during sustained binocular fixation through 10 Δ base-out in all myopic (black) vs. emmetropic children (grey).

Solid straight lines represents the position of baseline tonic vergence/binocular accommodative response in each refractive category. Error bars indicate mean ± SE.

In both refractive groups, the magnitude of vergence adaptation significantly correlated with the fusional vergence demand created by the prism and their habitual tonic vergence position (Fig 7-2: Emmetropes: Pearson r= -0.58, $r^2=0.34$; P=0.010; Myopes: r=-0.43, $r^2=0.19$; P=0.030). This suggests that the starting position (i.e. baseline tonic vergence) influences the degree of vergence adaptation such that a lower demand created by a convergent vergence posture resulted in a smaller degree of adaptation compared to a divergent vergence posture. Linear regression analysis showed statistically similar slopes (P=0.54) for the refractive groups but significantly lower intercept for the myopic group, indicating reduced adaptation compared to emmetropes (P=0.010).

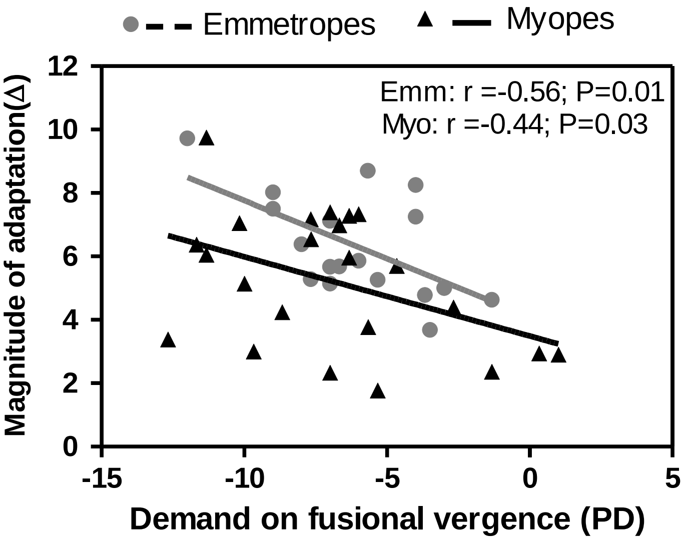


Figure 7-2: Plot showing the relationship between the magnitude of adaptation and the demand of fusional vergence .

Myopic children are represented by black line and triangle symbol and emmetropic are indicated as grey line and circle symbol.

Given this relationship between fusional vergence demand (attributed to habitual tonic vergence posture) and the degree of adaptation (Fig 7-2), the reduced magnitude and completeness of adaptation observed in myopic group (Fig 7-1A) could be seen if this group consisted of more children with baseline convergent vergence posture compared to emmetropes. To test this, we divided children into different vergence-bias categories based on their distance tonic vergence position: eso (TV=>4Δ eso), exo (TV=<1Δ Exo) or normal (TV=1Δ eso to 3Δ eso). This classification was based on normative values for distance heterophoria in children, [28] which were converted to tonic vergence using the formulae proposed by Rosenfield and Cuiffreda. [29] Based on this grouping schema, we had 28 children with normal tonic vergence (E=14; M=14), 11 children with convergent TV (Emm=5; Myo=6) and 4 with divergent TV (E=1; M=3). This classification indicates that the pooled myopic group (Fig 7-1A) had almost equal number of children with convergent vergence position compared to emmetropes.

Nevertheless, Fig 7-3A confirms that_myopic children show significantly reduced amount (EN=6.8±0.4; MN=5.2±0.4; P=0.010) and completeness of vergence adaptation (EN=74.3±2.6; MN=58.9±4.8; P=0.010) even with normal baseline TV position. This pattern was seen despite showing the same levels of induced tonic vergence through the prism compared to emmetropes (EN=8.9±0.4; MN=8.98±0.3; P=0.90).

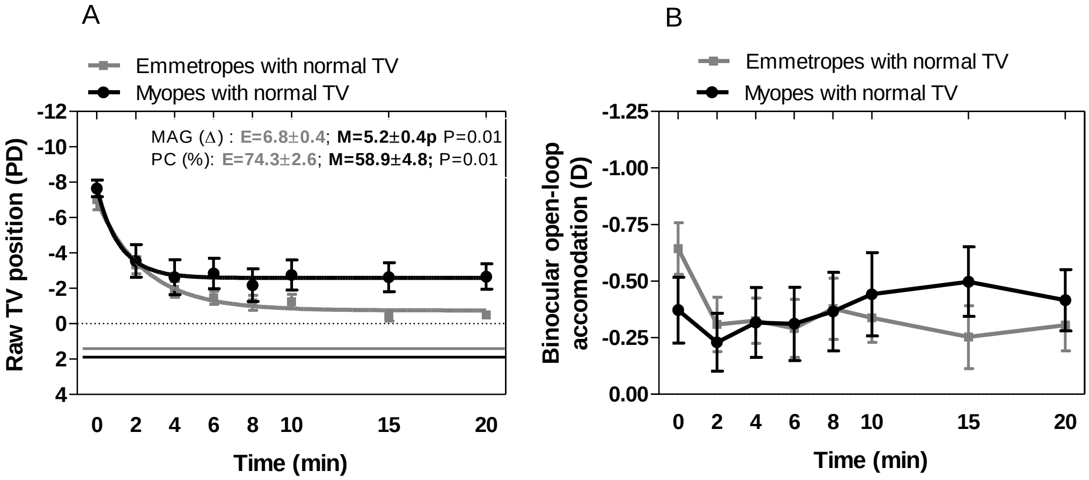


Figure 7-3 A&B: show comparison of mean changes to tonic vergence and binocular open-loop accommodation in children with habitually normal tonic vergence position (1 eso to 3 eso).

Solid straight lines represent the position of baseline tonic vergence/binocular accommodative response in each refractive category. Error bars indicate mean ± SE.

The binocular open-loop accommodative response revealed a different pattern in myopic children with normal tonic vergence. The open-loop accommodative response varied significantly over time in these groups (Fig 7-3B; P=0.004) unlike the pooled data (Fig 7-1B). Post-hoc analysis show a significant reduction in open-loop accommodative response after 2 min (P=0.03) but an increase thereafter, which reaches statistical significance at time points 10, 15 and 20 (all P<0.05). Accommodative adaptation (difference between monocular pre and post task tonic accommodation) was significantly greater in myopic children compared to emmetropes for both the pooled data (Emm=0.1±0.1; Myo= -0.35±0.05; Fig 7-4A; P=0.007) and for children with normal tonic vergence alone (Emm= 0.07± 0.1; Myo= -0.4±0.03; P=0.030; Fig 7-4B).

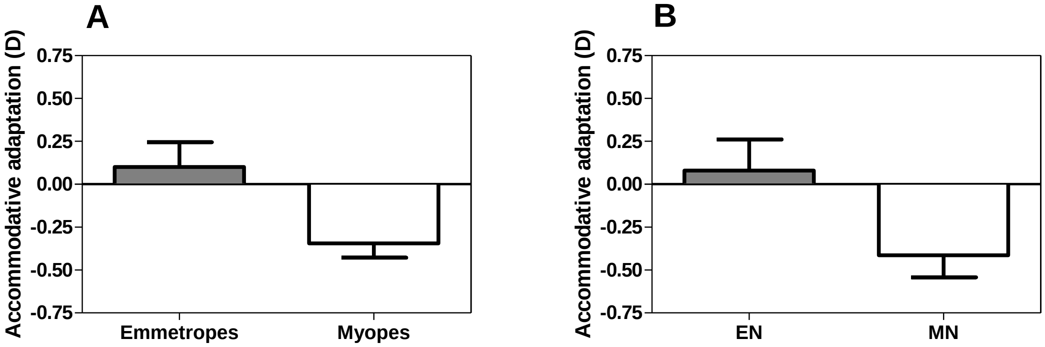


Figure 7-4 A &B: Mean tonic accommodative change (Pre task – post task) in all myopic and emmetropic children (Fig 4A) and only in children with normal tonic vergence (Fig 4B) after 20 minutes of sustained activity. Error bars indicate mean ± SEM

Fig 7-5A&B shows the exponential decay of the prism-induced TV in the various categories of vergence bias in emmetropic and myopic children, respectively. Despite unequal sample sizes, the pattern of vergence adaptation suggests similarity to the pattern seen through plus addition lenses (Chapter 6) such that children with convergent vergence position adapt less to a 10 Δ BO compared to children with a divergent vergence posture. Further, the exponential decay curves of myopic groups showed significantly less adaptation compared to their respective emmetropic group (all phoria groups P<0.05).

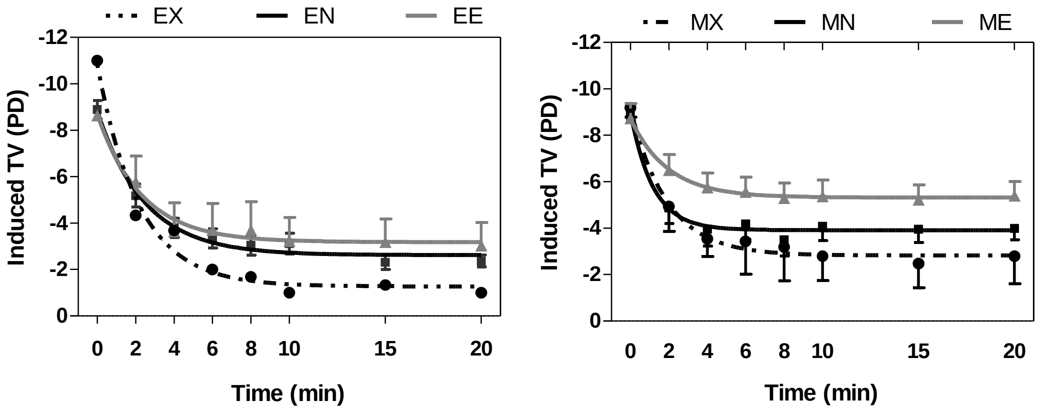


Figure 7-5: Comparison of the prism-induced exponential TV decay functions in emmetropic (Fig 7-5A) and myopic (Fig 7-5B) children divided into three categories (Normal/eso/exo) based on the direction and magnitude of their baseline TV position.

7.5 Discussion

The primary finding of this study is that myopic children show reduced magnitude and completeness of vergence adaptation to base-out prism despite the absence of an active feedback from the accommodation system. Given the significant relationship between fusional vergence demand and the magnitude of adaptation, the reduced adaptation observed in the pooled myopic group (Fig 7-1A) (i.e. including varied baseline tonic vergence positions) may be seen if the myopic sample (N=24) consisted of a greater number of children with baseline convergent TV positions compared to emmetropes. However, this was not the case, because both refractive groups had almost equal number of children with convergent baseline vergence position (E= 5; M=6). Further, the decreased prism adaptation was evident in myopic children despite including children with normal TV alone in either refractive group (Fig 7-3A).

It appears that, only one previous investigation studied the effect of refractive error on vergence adaptation to prisms. North and colleagues [10] compared adaptation to 6 $^{\Delta}$ base-in and base-out at 4m and 0.4m in adult groups of emmetropes, early onset and late onset myopes and reported no significant difference in the magnitude of prism adaptation between the three groups. Several differences, such as the size of the adapting stimulus, age of the participants, and nature of accommodative influence (closed vs. open-loop) may explain the dissimilarity between the two studies. The current investigation used a larger adapting stimulus (10 Δ base-out) compared to 6Δ base-out used by North and Colleagues [10], which may have facilitated a better distinction between the refractive groups. The age of participants could influence the ocular motor parameters depending on the progressive nature of myopia. Evidence in both early onset [16, 30-32] and late-onset myopes [33, 34] suggest greater accommodative lags, convergent vergence posture and larger AV/A ratios when the myopia is actively progressing compared to a stable refractive condition. Since the present study enrolled school aged myopic children, it may be possible that they show more progression [32, 35] compared to adult participants. Furthermore, the investigation by North et al [10] was performed under closed-loop accommodation in contrast to the current study, which used pinholes to open the loop of accommodation. The characteristic feature of a closed-loop system is the feedback mechanism that allows the response to be compared with the stimulus to improve the accuracy of the system. [36] Moreover, sustained fixation under closed loop condition initiates adaptation of the motor system, which reduces the demand on the fast controller and decreases the cross-link activity. [12] Thus, any changes to accommodative response (such as accommodative adaptation) may initiate a change in the fast controller, thereby influencing the vergence system depending on the strength of the AV cross-link. In North et al's study [10] prism adaptation was induced under closed-loop accommodation, thus, there is a possibility that myopes exhibited larger accommodative adaptation [13, 14] which produced greater changes in vergence in myopes compared to emmetropes due to their higher AV/A ratios. [15, 16, 33]

Our results show accommodative adaptation to the base-out prisms in myopic but not emmetropic children despite eliminating any stimulus for accommodation (Fig 7-5). This difference in accommodative adaptation is also manifest in the binocular open loop accommodation response (Fig 7-3B), which includes contribution from convergence accommodation and tonic accommodation. Both refractive groups exhibited an increased accommodative response immediately after the addition of 10 base-out prisms, which can be attributed to convergence accommodation. In the emmetropic group, sustained binocular fixation reduced the binocular open-loop accommodative response that significantly correlated with the reduction in exo TV, similar to previous reports. [1, 12, 22, 37] The absence of accommodative adaptation in emmetropes confirms that the reduction in binocular open-loop response is due to the reduction in VA cross-link activity associated with vergence adaptation. On the other hand, myopic children with normal TV showed a small but significant increase in accommodative adaptation following 10 minutes of sustained viewing through the prism (Fig 7-3B), This suggests that accommodative adaptation is more easily activated by convergence adaptation. Previous studies [17]and models of accommodation and vergence [12] suggest that cross-links are capable of inducing adaptation of the opposite system (i.e. VA inducing accommodative adaptation). While the present study supports these findings in myopic children, emmetropic children do not show any significant shift in post-task tonic accommodative measures after sustained binocular fixation through the base-out prism. Several possibilities may explain this difference. First, since adaptation is related to the magnitude of the stimulus [17], the larger accommodative adaptation observed in myopes may be due to a greater output from convergence accommodation as a result of reduced vergence adaptation. Second, this discrepancy may also be possible if myopic children showed larger VA/V ratios, as a result of reduced vergence adaptation, which may initiate greater accommodative adaptation compared to emmetropes. However, the present study (table 7-1) and previous studies [33, 38] show similar VA/V ratios between the two refractive groups. Lastly, the greater accommodative adaptation may be a function of a higher gain /lower threshold of accommodative adaptation in myopes similar to the results of past reports that show greater accommodative after-effects in myopes compared to emmetropes. [13, 14]. Importantly, this lower threshold is present for both reflex accommodation (Chapter 6) and VA (Fig 7-4).

The pattern of vergence adaptation to base-out prisms in myopic children is similar to the plus add condition (Chapter 6) This behaviour suggests that myopic children show reduced vergence adaptive ability when fusional convergence is stimulated either through BO prisms or binocular viewing through plus adds. It is important to note that refractive error did not show significant effect on accommodative adaptation through +2D adds (Chapter 6 and published reports [1, 22]), suggesting little/no influence on the reduced pattern of vergence adaptation seen in myopic children. On the other hand, sustained binocular fixation through -2D adds showed greater accommodative adaptation in myopes, which may have resulted in the non-significant differences in vergence adaptation between myopes and emmetropes (Chapter 6). Binocular fixation through 10 BO prisms under open-loop accommodation resulted in greater accommodative adaptation in myopes compared to emmetropes, but due to the absence of negative feedback and no input to the phasic accommodative controller (which provides input to the AV cross-link) it is unlikely that accommodative adaptation influenced the reduced vergence adaptation seen in myopic children. Thus, these results appear to suggest that the decreased vergence adaptive ability in myopic children is associated with the different parameter settings of accommodation and vergence in the myopic eye. A lower threshold to stimulate accommodative adaptation seems to accompany a higher threshold to stimulate vergence adaptation. However, their AV/A and VA/V findings are not readily explained from these models. It appears that the high AV/A ratio in myopes cannot be explained by the interactions of phasic and adaptive accommodative responses. These interactions in fact would argue for a smaller not greater AV/A ratio. It is evident that the etiology of the increased AV/A in myopes requires other variables perhaps not unlike those which define an independent gain regulation of the AV (and VA) ratio [39].

8 Effect of near adds on the variability of accommodative response in myopic children

This chapter is published as follows:

Vidhyapriya Sreenivasan, Elizabeth L Irving, William R Bobier. Effect of near adds on the variability of accommodative response in myopic children Ophthalmic Physiol Opt. 2011 Mar;31(2):145-54. doi: 10.1111/j.1475-1313.2010.00818.x.

The analysis of closed-loop accommodative behaviour through habitual lenses and near addition lenses at 33 cm (Chapters 5 and 6) revealed interesting differences with regards to the variability of accommodative response in myopic and emmetropic children. The following chapter discusses the effect of near adds on the variability of accommodative response as a function of vergence-bias category and refractive type.

8.1 Summary

Purpose: Higher variability of accommodative response (VAR) has been reported in myopes and speculated to be a possible risk factor for the progression of myopia. We investigated whether near (+2D and -2D) adds are capable of altering accommodative variability and also determine the influence of near phoria and viewing condition (binocular vs. monocular) on the VAR in myopic and emmetropic children.

Methods: 27 myopic and 25 emmetropic children between 7 and 14 years were examined. All children were classified into "*normophores*" (0 to 4 exo), exophores (>6 exo) or esophores (>2 eso) based on their near phoria. Binocular and monocular steady-state measures of accommodation were obtained for 5 sec using a PowerRefractor (Multichannel Co) while children fixated a high contrast target (33 cm) with distance correction, and then with +2D add and -2D add over the corrective lenses. The variation in accommodative responses (VAR) was defined as the standard deviation of the accommodative response during the 5 sec period.

Results: Myopic children showed higher VAR through their distance spectacle corrections compared to emmetropes (Emm=0.23± 0.03D; Myo=0.37± 0.07D; P<0.001). Plus adds significantly reduced the VAR in myopic children to the level of emmetropes (Emm=0.2± 0.03D; Myo=0.19± 0.02D; P=0.98). Introduction of a -2D add significantly increased the VAR in both refractive groups; however, myopes showed greater VAR compared to emmetropes (Emm=0.39± 0.03D; Myo=0.53± 0.07D; P<0.001). Near phoria or binocular viewing did not alter the magnitude of fluctuations in either refractive group. VAR significantly correlated with the monocular accommodative error in both refractive groups (Emm r^2=0.34; p<0.0001; Myo: r^2=0.35; p<0.001). Pupil size while varying with add type, did not confound the VAR.

Conclusion: The near steady state accommodative response of young myopes shows greater variability than non-myopes. This difference is maintained when accommodative responses are increased beyond the vergence plane using - 2D adds. However, accommodative fluctuations were reduced to emmetropic levels when the stimulus to accommodation is reduced using a +2D add. The resulting VAR through adds appear to follow that expected from variations in accommodative demands and hence properties of the accommodative controller. Vergence-bias categories (eso and exo) do not appear to influence the VAR with and without near adds.

8.2 Introduction

When focusing a stationary target the accommodative response exhibits small variations in refractive power (around 0.1D-0.5D) termed microfluctuations [1-5] (see [6] for review). This variation has been expressed as the root mean square value (RMS) [7-10] or the standard deviation (SD) of the accommodative response [11,12] in the time domain and as the amplitude of low, middle and high frequency components in the frequency domain [2,3,7,10,11,13,14]. Power spectrum analysis of the fluctuation waveform reveals two dominant frequency bands: a wider low frequency component (LFC at <0.5 Hz) and a narrower high frequency component (HFC between 1.3-2.2 Hz) [3,6] The HFC is believed to result from noise in the accommodative plant and correlates with the systemic arterial pulse [6,13,15]. The LFC, on the other hand, appears to be an integral part of the accommodative controller system and varies with factors that modulate the depth of focus of the eye [6]. Small pupil size, [7] low target luminance [8] and low spatial frequency content of the target [16-18] increase the ocular depth of focus, resulting in an increased magnitude of microfluctuations. Several studies also report a significant association between the microfluctuations and stimulus to accommodation such that the magnitude of fluctuations increases with an increase in accommodation. [4,5,19] The majority of these studies were performed under monocular viewing conditions (i.e. absence of disparity cues to accommodation). However, earlier reports do not report any substantial improvement in the stability of accommodative response under binocular viewing conditions [20,21].

Recently, numerous studies have reported refractive group differences in the magnitude and power of accommodative fluctuations. Most of these studies show increased microfluctuations in myopes [9,11,12,22] ; however, a few other studies found no relationship between myopia and the variability of accommodative response [14,23]. This discrepancy may reflect differences in the experimental protocols used to measure accommodation, the age of participants and the pattern of their myopic progression. Increased fluctuations have been reported in late-onset myopes, [9,22] adult early-onset myopes tested during progression, [22] in stable myopic adults [11] and in myopic children (progression not defined) [12]. This larger variability has been reported when accommodation was tested under monocular [9,22] or binocular viewing conditions. [11,12] Studies show that myopic individuals demonstrate the greatest variability and largest refractive group differences at the closest testing distance [11,12.] Since myopic children perform near work at closer reading distances, [24-26] they might constantly experience larger accommodative demands and greater variability of accommodation compared to emmetropes. This may result in hyperopic retinal defocus, which might trigger axial elongation and myopia [27-29].

Plus adds have been considered as a possible optical treatment in an effort to reduce the progression of myopia. These lenses have been prescribed to reduce accommodation, with the recent rationale of eliminating the large accommodative lags that might trigger axial elongation [30,31]. Studies that measured accommodative lag through the plus adds show that these lenses are capable of reducing the accommodative lags in myopic adults [32] and children [33-35]. Yet, clinical trials indicate that plus adds have been more successful in slowing myopic progression only in some groups such as children with esophoria, [36-38] combined with larger lags of accommodation [30, 31, 37].

Phoria, particularly esophoria has been found to be associated with larger accommodative lags, [39] greater myopia progression, [40] higher amounts of myopia[41] and better prognosis of reduction of myopia with near adds [26,31,37]. It is not clear if increased VAR is found in myopic esophores compared to other phoria groups. Further, it is not known whether near adds have a differential effect on phoria groups. While it would be expected that plus adds would reduce the stimulus to accommodation, it is not clear if like accommodative lag, the plus adds would reduce the variability observed in myopic children. On the contrary, since minus lenses increase the demand for accommodation and result in greater lags of accommodation, (more so in myopes compared to emmetropes) [42-44] they may exaggerate the variability of accommodative response to a greater extent in myopic children. Though several studies have investigated the effect of plus adds on the accommodative response of myopes, [33-35] to date, no study has measured the influence of plus and minus adds on the variability of accommodative response (VAR) in myopic children. Thus, the aim of this paper is to determine the effect of near adds on the VAR under both binocular and monocular viewing conditions in myopic and emmetropic children with varying degrees and directions of near phorias. Accommodative responses were analysed in the time domain and VAR was expressed as the standard deviation of accommodative response.

8.3 Methods

This study is a part of a larger study that measured ocular alignment and accommodation in children. Measures of accommodation only are presented in this study.

8.3.1 Study participants

Fifty three children (28 myopic and 25 emmetropic; 58% female) between the ages of 7 and 14 years were recruited from the clinic database at the School of Optometry, University of Waterloo. Informed consent (parents) and assent (children) were obtained after verbal and written explanation of the nature of the study. The protocol followed the tenets of Declaration of Helsinki and received approval from the University of Waterloo ethics review board.

Participants with normal general and ocular health (determined from their clinical records and confirmed during a screening visit) underwent preliminary examination to ensure the following: myopic refractive error between -0.75 and -6 D or emmetropic refractive error between +0.25 and +1.5 D determined using cycloplegic refraction (two drops of 1% tropicamide added to both eyes, similar to a previous study[45]); astigmatism < 1D; anisometropia < 1D; best corrected visual acuity of at least 6/6 in each eye; non-strabismic; normal amplitudes of accommodation; and that participants were not taking any medications that might influence the accommodation and vergence systems. All participants were further divided into *"normophores"* (0-4 exo), exophores (>6 exo) or esophores (>2 eso) based on their near phoria measured using the modified Thorington technique (MTT) [46] at 33cm. Table 8-1 lists the age and critical visual parameters of the study groups.

Table 8-1: Critical visual parameters of myopic and emmetropic children

PARAMETER (Mean ± SEM; and range where applicable)	**EMMETROPES**			**MYOPES**		
	Normophores	Exophores	Esophores	Normophores	Exophores	Esophores
No of participants	11	7	7	10	7	11
Age (7-14) in yrs	10.8 ± 0.43	12.2 ± 0.63	11.9 ± 0.43	10.43 ± 0.53	11.2 ± 0.8	11.8 ± 0.63
Refractive error in spherical equivalent (D)	0.59 ± 0.09D	0.4± 0.09D	0.3± 0.09D	-2.0 ± 0.3D	-2.5 ± 0.2D	-1.7 ±0.3D
Near phoria (Δ)	-2.15 ± 0.49 (0 to 4 exo Δ)	-6.72 ± 0.36 (6 to 10 exo Δ)	2.83± 0.58 (2 eso to 5 eso Δ)	-1.24 ± 0.94 (0 to 4 exo Δ)	-9.7 ± 1.5 Δ (6 to 14 exo Δ)	4.09 ± 0.5 (2 eso to 8 exo Δ)

8.3.2 Instrumentation and experimental procedure

Accommodative responses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor, the PowerRefractor (Multichannel Co, Reutlingen, Germany) [47]. This setting of the instrument determined refraction along the vertical meridian of the participants' eye, sampling at a rate of 25 Hz, coupled with measures of gaze deviations and pupillary diameter. The responses obtained from the PowerRefractor were calibrated using a two-step protocol to ensure relative and absolute accuracy of accommodation similar to previous studies [48-50]. While the slope of calibration function matched with the instruments default for some participants, others needed separate calibrations functions, possibly due to differences in fundal reflectance

[51,52]. In all cases, accommodative responses were calibrated based on individual calibration equations.

A high contrast colour cartoon (contrast =85%; target luminance =15 cd/m^2) was used to measure accommodation in children. This target was chosen as it was expected to be more successful than conventional reading material in holding the participants' attention and has been verified to be an effective stimulus for accommodation [49]. The image of the cartoon was displayed on a 1.77″ wide liquid crystal display monitor (Model No: LT-V18 U; Victor company of Japan) and projected at a distance of 33cms through a semi-silvered mirror. The mirror set 10 cm from the right eye and angled at 45 degrees allowed the photorefractor to simultaneously record accommodation from the right eye during target viewing. The method has been described elsewhere in detail [49].

The study design consisted of three experimental sessions that were performed on separate days with the order of sessions randomized to avoid bias; one session was performed with the children wearing their corrective lenses (referred to as *"no add condition"*) and the other two involved measurements with +2D/-2D lenses (referred to as *"plus and minus add condition"*) added over their correction (if applicable). A trial frame set 12 mm from the eye housed ophthalmic lenses, which provided the distance correction and near add. The frame was adjusted for the participants' near pupillary distances to reduce any prismatic effect.

Prior to the start of each study session, participants were dark adapted for 3 minutes to avoid effects of previous near work [53]. The lighting in the examination room was then reduced to obtain sufficiently large pupil sizes (greater than 4mm as recommended by the manufacturer of PowerRefractor) for the measurement of accommodation. Binocular and monocular measures of accommodation were recorded continuously for a period of 5sec after confirming steady fixation using the gaze control function displayed on the PowerRefractor interface. For the binocular response, accommodation was recorded from the right eye alone, although both eyes fixated at the target. For measurement of monocular accommodation, the left eye was occluded. During the 5 sec measurement period, the accuracy of fixation was assessed using the gaze control function displayed on the PowerRefractor interface. Additionally, care was taken to ensure that the child was fixating the near target at the correct fixation distance (33 cm) while measurements were recorded. A volunteer constantly monitored the head position of the child and ensured they did not move away from the chin rest during measurement. If any unsteady fixation was noticed during measurement, or when the examiner (VS) observed off axis gaze errors exceeding 10 degrees, the measures were flagged using keyboard inputs and discarded given the possibility of under or over estimation of accommodation [54,55]. In these cases, recordings were obtained for an additional 5 sec period to ensure equal data sets across subjects.

8.3.3 Data Analysis

VAR was defined as the standard deviation of the accommodative response across the 5 sec period. Each data point was screened and accepted if the following criteria were met: the pupil size was above 4mm; the ocular alignment was less than 10 degrees and 5 degrees from the optical axis of the photorefractor in the horizontal and vertical axes respectively (as recommended by the manufacturer [47]) and the responses were free of blinks. Blink artefacts, if any were removed using a method similar to previous studies [49,56]. Each participant needed to have at least 100 rows of acceptable data after satisfying all of the above criteria in order to be considered for averaging and further analysis. If the participants had more than 100 eligible data points, only the first 100 points were taken for further analysis. The data retained were averaged to obtain the VAR. Data from one myopic participant was excluded from the averaging process since she failed to provide the minimum levels of acceptable data as a result of pupil diameters less than 4mm.

Repeated measures analysis of variance (ANOVA) was used to determine the effect of +2D/-2D add condition on VAR. In all cases, statistically significant main effects were further examined using Tukey Honestly significant differences (HSD) post-hoc tests to determine the group that showed the significant difference. Differences were considered statistically significant when the likelihood of type-I error was <0.05. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Pearson correlations were conducted to look for relationships between variables like pupil size, accommodative error and VAR. Analysis of co-variance (ANCOVA) was performed to ensure that pupil size did not confound the main findings.

8.4 Results

8.4.1 VAR through best corrective lenses (no add condition)

Fig. 8-1 B (middle) shows representative raw data from a myopic and emmetropic child when fixating a high contrast near target over 5 sec in the no add condition. Visual inspection shows that the myopic child exhibits greater fluctuations in the accommodative response compared to the emmetrope. This pattern (i.e. larger fluctuations in myopes compared to emmetropes- $p<0.001$) was found when the mean values were compared in binocular (Fig. 8-2 A) and monocular viewing condition (Fig 8-2B) in all three phoria groups. The findings were independent of the direction of near phoria $P=0.94$) or viewing condition ($P=0.49$).

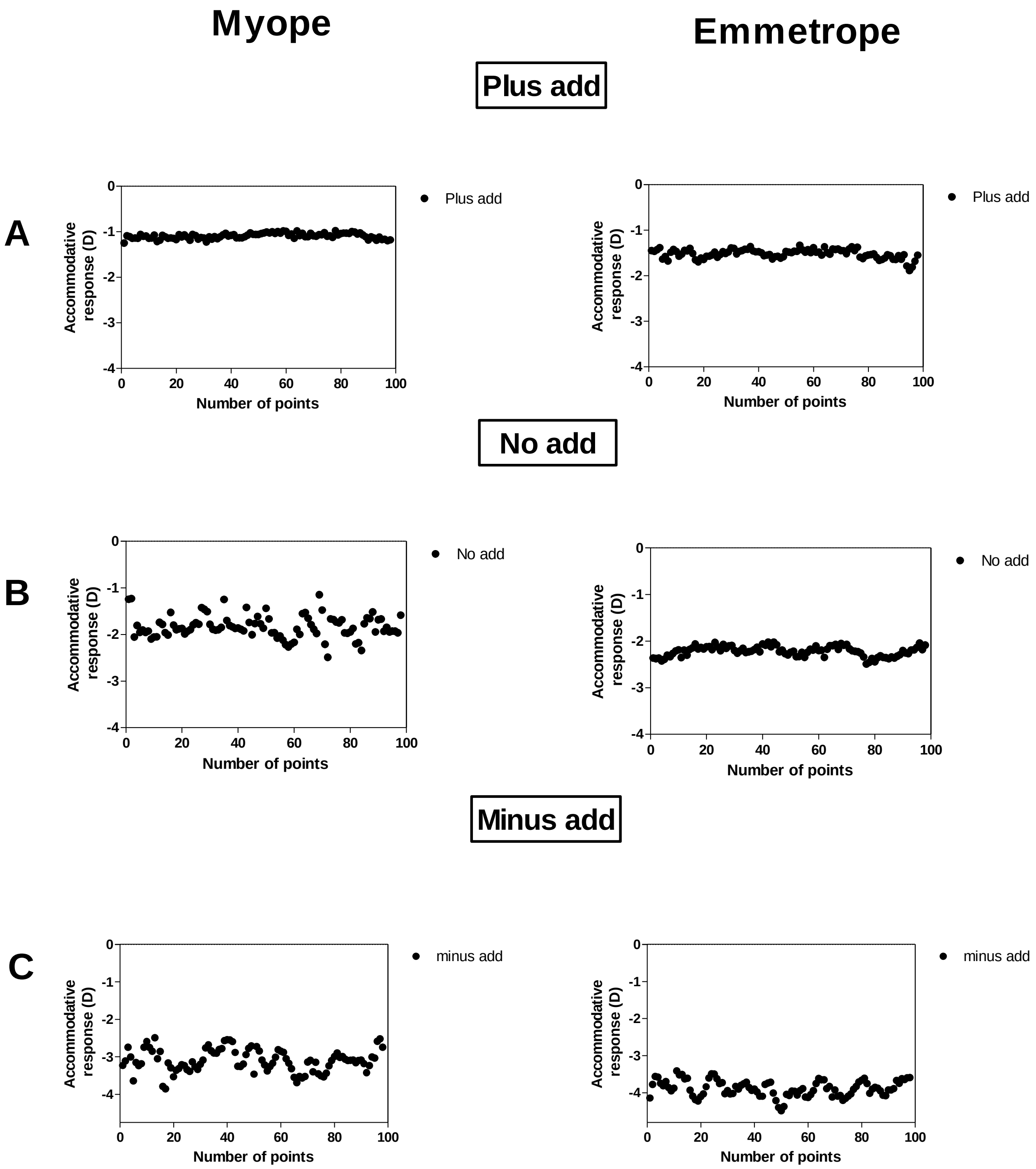


Figure 8-1: Example of VAR in the no add, plus add and minus add conditions from a myopic child (left) and an emmetropic child (right).

Compared to the no add condition (middle), the plus add (top) reduces the VAR in the myopic child while the VAR of the emmetropic child is unchanged. The minus add (bottom) however, increases the VAR for both the myopic and emmetropic child, but the myopic child shows greater variability than the emmetrope.

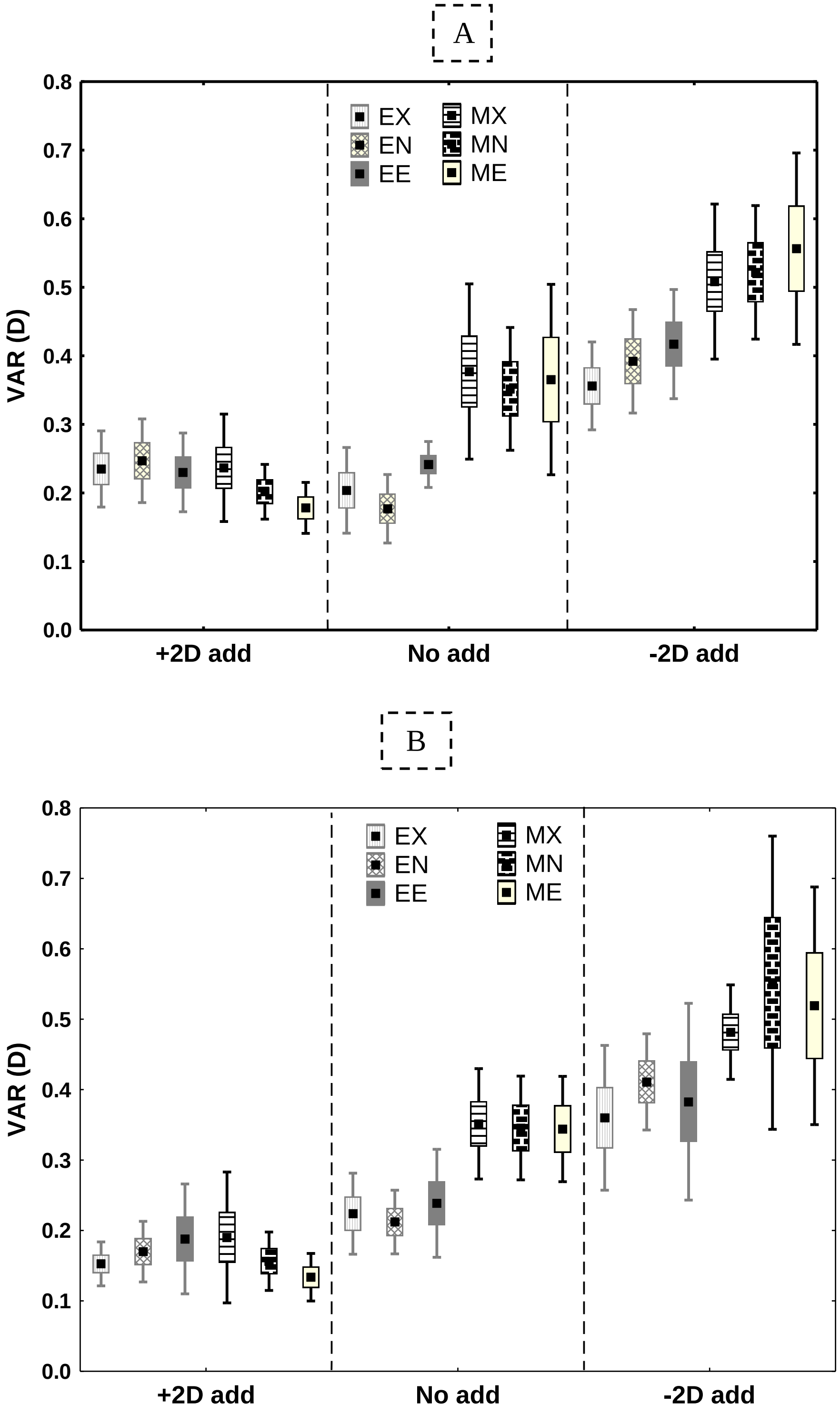


Figure 8-2 A and B: Box plot showing VAR in myopic and emmetropic children with different near phoria and add conditions in the binocular (8-2A) and monocular viewing condition (8-2B).

In both viewing conditions, myopes showed significantly larger variability compared to emmetropes in the no add and minus add condition. The VAR through plus adds were similar in the two refractive groups.

8.4.2 Variability of accommodative response through +2D/-2D near adds

Fig 8-1 A and C (top and bottom graphs) shows that near adds differentially alters the pattern of VAR in the myopic and the emmetropic child. The plus add reduces the VAR in the myopic child while the normal VAR of the emmetropic child is unchanged. The minus add however, increases the VAR for both the myopic and emmetropic child, but the myopic child shows greater variability than the emmetrope. The mean VAR through plus and minus adds follows the same pattern as the representative raw data. Figs 8-2A and B shows the VAR in children with different near phorias under binocular and monocular viewing conditions respectively. Statistical analysis showed a significant main effect of add type ($P<0.0001$), refractive error ($P=0.002$) and a presence of refractive group* add interaction ($P<0.0001$) but no main effect of phoria ($P=0.73$) and no main effect of viewing condition (binocular vs. monocular) ($P=0.18$). Post-hoc results revealed that plus adds significantly reduced the VAR in all phoria groups (all $P<0.05$) of myopic children to a level equal to that of emmetropes (Grouped mean: Emm=0.2± 0.03D; Myo=0.19± 0.02D; $P=0.98$). However, emmetropic controls did not show any significant change in VAR through the plus adds. On the other hand, minus adds significantly increased ($P<0.001$) the VAR in both emmetropes and myopes compared to the +2D and the no add conditions but myopic groups exhibited significantly higher VAR ($P<0.001$) compared to emmetropic children (Grouped mean: Emm=0.4± 0.03D; Myo=0.53± 0.07D; $P=0.001$). For both add types, near phoria or binocular vs. monocular viewing did not alter the pattern of VAR in either refractive groups.

8.4.3 Effect of pupil size on the VAR

Evidence has shown that VAR increases as pupil size decreases. [3,7] Hence it is important to investigate whether changes in pupil size contributed to the differences in VAR observed between the add conditions and the refractive groups. For the purpose of this analysis, data from all phoria groups were combined together as near phoria did not influence the VAR in any of the add conditions. ANOVA showed a significant main effect of add type ($P<0.001$) but not refractive group ($P=0.22$) and no significant interaction between add type and refractive group ($P=0.67$). Post-hoc comparisons show that the mean pupil size was significantly ($P=0.005$) decreased through the minus add (Emm=5.2± 0.2D; Myo=4.9± 0.07D) compared to the plus add (Emm=5.8± 0.2D; Myo=5.6± 0.15D) as expected in both refractive groups. However, the diameter of the pupil did not significantly differ between refractive groups in any of the add conditions. Furthermore, to ensure that decreased pupil size was not the only cause for increased variability observed through the minus add, an analysis of co-variance was performed with pupil diameter as a co-variate. ANCOVA confirmed a significant effect of add type and refractive error on the VAR with a constant pupil size.

8.4.4 Effect of accommodative error on the VAR

Fig 8-3 shows the mean monocular accommodative response in the two refractive groups (with phoria groups collapsed) through the three test conditions. Myopic children show significantly less accommodative response compared to emmetropes in the no add (Myo=2.08±0.12D; Emm=2.34±0.07D; $P=0.020$) and minus add conditions

(Myo=3.27±0.15D; Emm=3.63±0.09D; P=0.01) but not when viewing through plus addition lenses (Myo=0.98±0.11D; Emm=1.12±0.1D; P=0.3). Moreover, accommodative error (calculated as the difference between accommodative stimulus and accommodative response where positive number denotes lag and negative number denotes lead of accommodation) correlated significantly with the VAR such that larger accommodative errors were associated with greater variability of accommodative response in both refractive groups (Fig 8-4, MYO: r^2=0.34; p<0.001; EMM r^2=0.35; p<0.0001). Linear regression analysis of accommodative error and VAR (Fig 8-4) shows similar slopes (Myo=0.09±0.01D; Emm=0.06±0.01D) significantly different intercepts between the refractive groups (Myo=0.30±0.02D; Emm=0.24±0.01D). This suggests that both refractive groups show similar rate of increase/decrease in VAR with increase/decrease in lag respectively but myopes show greater VAR than emmetropes.

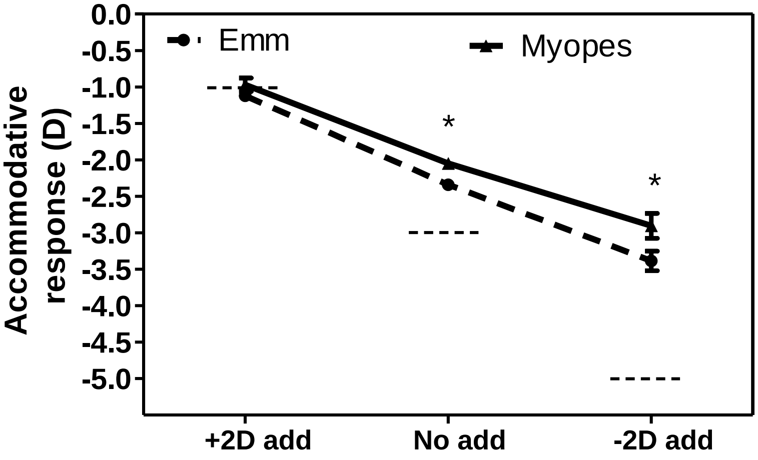


Figure 8-3: Mean monocular accommodative responses in the myopic and emmetropic groups in the different add conditions.

Dashed line represents the accommodative demand through the respective add condition. Myopes show significantly reduced responses compared to emmetropes in the no add and the minus add conditions (*P<0.05). Error bars indicate ± SE.

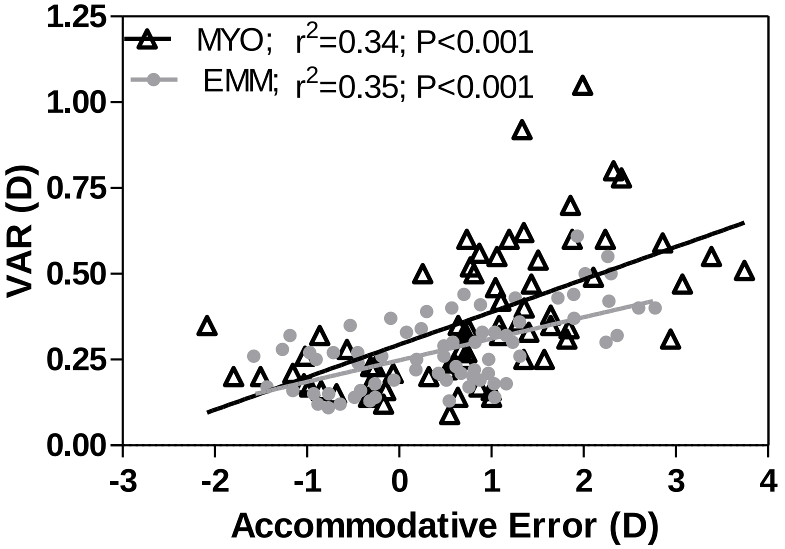


Figure 8-4: Correlation between accommodative error and VAR in the two refractive groups. In both groups, accommodative error significantly correlated with the VAR.

Linear regression analysis showed similar slopes but significantly higher VAR (intercept) in myopes compared to emmetropes.

8.5 Discussion

The primary finding of this study is that plus and minus adds have a differential effect on the VAR in myopic and emmetropic children. Plus adds reduced the VAR for myopic but not for emmetropic children such that myopes exhibit fluctuations that are reduced to a level equal to emmetropes. Minus adds, on the other hand, increased the VAR in both refractive groups; however, the increased variation found in myopic children through best corrective lenses were maintained with the negative add. Vergence posture (eso or exo) did not alter the pattern of VAR to plus/minus adds in either myopic or emmetropic group. Further, the fluctuations through near adds were not significantly modified whether accommodation was driven monocularly or binocularly. The VAR significantly correlated with the accommodative error in both refractive groups, suggesting that the change in accommodative demand induced by the adds would explain their effect on the VAR.

It is well known that near adds alter the accommodative demand depending on the magnitude and direction of the add. In this study, the accommodative target was placed at 33 cm (accommodative demand=3D), thus fixation through +2D and -2D adds changed the accommodative demand to 1D and 5D respectively. Past studies show that the accommodative response becomes more variable with an increase in accommodative demand [4,5,9,11,12,19]. This finding is partly supported in our emmetropic sample since the VAR increased when the accommodative response increased through a minus add (mean increase=0.17±0.03D) but did not show a significant reduction when accommodation was relaxed through a +2D add (mean decrease=0.04±0.03D). This may be because emmetropes exhibited small fluctuations to a 3D stimulus (Mean = 0.23±0.07D) and it is possible that there is a floor effect such that VAR cannot decrease considerably beyond a certain extent due to the mechanical and elastic properties of the accommodative plant. [5,6] Further, these results are similar to a previous study, which also showed no significant change in the stability of accommodation for similar stimuli (1.25 and 3D) in emmetropic adults [10]. Myopic individuals showed the expected [4,5,9,11,12,19] decrease and increase in VAR when accommodative demand was changed to 1D and 5D through the plus and minus adds respectively. Refractive group differences in VAR were only observed for the higher accommodative demands (3D and 5D) consistent with previous studies [11,12].

An important outcome of this study is the presence of a significant association between accommodative error and VAR in both refractive groups (Fig 8-4). It is known that accommodative error varies with the stimulus to accommodation such that greater accommodative lags are seen through minus lenses [42-44] and reduced accommodative lags are observed through plus adds [32,34,35,49,57,58]. While our results agree with these findings in both myopes and emmetropes, it is also interesting to note that the refractive group differences in the accommodative response closely match the pattern of VAR seen in the three add conditions. Myopic children show larger accommodative lags compared to emmetropes in the no add and minus add conditions but not through the plus add. However, past studies do not show refractive differences in the accommodative response (through corrective lenses) or a correlation between accommodative error and VAR under binocular viewing conditions [11,12]. Harb et al [11] showed a linear relationship between the accommodative response and VAR and also reported that lags increased with closer reading distance in stable adult myopes. But, it is not clear whether past studies find any association between accommodative error and variability. The increased VAR in myopes has been attributed to reduced blur sensitivity [9,11,12]. Adult myopes are less sensitive to defocus signals that drive accommodation compared to emmetropes, [59] although a similar study in children suggest myopes may have similar blur detection thresholds compared to age matched emmetropes [60]. If myopes have elevated blur thresholds, then the accommodative response of a myopic eye could also be reduced since these individuals may not perceive the blur that is required to drive any changes in the accommodative system. However, in some of the past studies, increased VAR was found in myopes who did not show greater lags compared to emmetropes even at higher stimulus levels [11,12]. Larger lags have been reported when myopia is progressing but the response improves as the refractive error stabilizes [43,44]. Though this study did not measure progression prospectively, review of past clinical records indicate that 18 out of 27 myopes progressed by at least 0.25-0.50D/yr. Six participants did not have more than one exam at the School of Optometry to determine the amount of progression and 3 had stable refraction. The larger accommodative lags may be due to the progressive nature of the refractive error in this study population. Nevertheless, past evidence indicates that the increase in hyperopic defocus/ more blurred target associated with larger accommodative errors may contribute to the change in accommodative microfluctuation [17].

The differential effect of plus and minus adds on the two refractive groups may be attributed to factors such as small pupil diameter [3,7,19,61] or low target luminance [8,61] that alter the depth of focus thereby increasing the microfluctuations. However, these factors were either controlled or did not change between the refractive groups and therefore are not likely responsible for the observed pattern of VAR through near adds. In this study, pupil diameter did show small and significant reductions when accommodation was increased through -2D add. Yet, this decrease cannot completely explain the higher VAR seen through minus adds since analysis of covariance showed a significant effect of the add despite holding pupil size constant. Moreover, it is unlikely that this reduction can explain the changes in VAR between the add conditions since pupil diameter was always greater than 4mm (as recommended by the manufacturer) for both the add conditions in all children. Previous work suggests that depth of focus is not significantly increased until pupil diameter becomes <2mm or <3 mm. [3,7,61] In addition, there were no refractive group differences in the pupil diameter in any of the add conditions, similar to previous studies [62], suggesting that pupil size did not influence the refractive differences observed in the current study. Other factors such as low target luminance also cannot explain the results because the target luminance was much higher (15 cd/m^2) than the levels that increase the depth of focus (0.004-0.002 cd/m^2)[8] and kept constant between add conditions and refractive groups.

Esophoria is associated with higher amounts [41] or progression of myopia [40]. In the present study, myopic esophores did not show larger VAR compared to exophores or phoria normals. These findings could be attributed to the similarity in refractive error between the phoria groups (Table 8-1). On the other hand, it could be argued that the similarity in refractive error provides a means to conclusively show that the direction of phoria does not influence the stability of accommodative response in a myopic eye.

Clinical trials that measured the efficacy of near adds show that only some groups such as esophores [36-38] or esophores combined with higher accommodative lags show a meaningful reduction in progression of myopia [26,31]. It would appear that VAR is not a critical factor in this effect as the present study shows that myopes in all phoria groups show a reduction in VAR through plus adds. Further longitudinal studies in progressive myopic children may be helpful in determining the role of VAR and plus adds in the development and progression of myopia.

9 General discussion and conclusions

Under natural viewing conditions, accommodation and vergence systems mutually interact through cross-links, AV and VA, such that variations in one system alter the response of the other. Previous investigations have measured vergence adaptation using designs of prism adaptation [1-12]. None of these studies measured adaptation in children. Measurements described changes to the vergence system alone, and did not investigate the role of refractive error or vergence-bias category. Limited reports have measured adaptation to disparities induced by ophthalmic lenses [7, 13, 14]. To date, no study has measured adaptation to lens-induced disparities created by near addition lenses in children with myopia.

This thesis used near addition lenses as a means to investigate binocular adaptation in children. using varying demands for accommodation and vergence, stimulated by binocular fixation at near, through the addition of plus and minus lenses (closed loop accommodation) and using base-out prisms (open-loop accommodation).

Overall, this thesis makes three major contributions to the literature: first, it outlines the mechanism The specific aims of this thesis were three-fold: first, to gain insight into the mechanism of changes to accommodation and vergence through near addition lenses in children; second, to determine the role of vergence-bias category on adaptation and lastly to evaluate the influence of myopia on adaptation. A battery of studies were designed to evaluate adaptation of accommodation and vergence during sustained (over a 20 minute period) binocular adaptation in children; second, it shows that the direction of the phoria and the compensating fusional vergence directly influences vergence adaptation which in turn varies the output of binocular vs. monocular accommodation through the binocularly driven CA cross link and lastly, the work demonstrates that myopic children show reduced vergence adaptation when fusional convergence was initiated through plus adds, or base-out prisms but not when fusional divergence was initiated through minus addition lenses. Overall, it appears that myopic children exhibit a reciprocal relationship in adaptive gains of accommodation and vergence such that vergence adaptation is reduced (to stimuli that require convergence) but accommodative adaptation is greater under conditions of closed and open-loop accommodation.

It should be noted that the model of reflex (phasic) and adaptive mechanisms for accommodation and vergence and their cross links as defined by Schor [15] was found to be consistent in providing the appropriate structure for the interpretation of most of these results. The model is shown in Fig 1-3 in the thesis.

9.1 Mechanism underlying changes to the ocular motor system during sustained binocular fixation

Under closed-loop accommodation, the introduction of plus /minus addition lenses significantly altered the accommodative response (Chapter 4 & 6; Figs 4-1 & 6-5); increased lens-induced phorias (Chapter 4 & 6; Figs 4-4 & 6-1); and resulted in a greater mismatch between the binocular and monocular accommodative responses (Chapter 4 & 6; Figs 4-1& 6-5). These changes to the ocular motor system are consistent with the current models of accommodation and vergence [15, 16] (discussed in Chapter 1) and can be explained as follows: Under binocular viewing conditions, the lens-induced phoria would trigger the fusional vergence system to produce an increase in reflex vergence through the negative feedback mechanism. The increased fusional vergence, in-turn drives an immediate change in binocular accommodation through the vergence accommodation crosslink (Chapter 4 & 6: Figs 4-1 & 6-5). This then leads to a greater discrepancy between the binocular and monocular accommodative responses (Chapter 4 & 6: Figs 4-1 & 6-5).

Sustained binocular fixation through the plus/minus addition lenses decreased the lens-induced phorias (Chapter 4 & 6; Figs 4-4 & 6-1). This reduction was attributed to vergence adaptation based on Schor's model of adaptation [7, 17]. The fast component would mediate the initial increase in fusional vergence required to overcome the lens-induced phorias. With sustained binocular viewing, the fast fusional vergence provides input to the slow fusional component, which is characterized by long decay time constant and termed vergence adaptation [15, 17]. The reduction in lens-induced phorias were accompanied by an adjustment of the binocular accommodation through plus adds (Chapter 4 & 6; Figs 4-1 & 6-5; EX, EN and MN) and minus adds (Chapter 6; Fig 6-5; EE&ME) in all groups that showed substantial vergence adaptation. Reduction of VA cross-link activity was also seen when vergence adaptation was initiated through base-out prism (Chapter 7; Fig 7-3). These results are consistent with the model of accommodation and vergence [15, 17] that places the cross-link (AV and VA) in between phasic and tonic controllers such that adaptation of the motor system reduces the activity of its respective cross-link.

Sreenivasan, Bobier, Irving & Lakshminarayanan [18] compared the simulation results of two adaptation models [15, 19, 20] that differ in identifying the effect of controller adaptation on their respective cross-links between vergence and accommodative systems. Model simulations were compared with empirical data (phoria and accommodation) obtained from emmetropic adults when near fixation was sustained through +2D lens addition [14]. Both models [19, 20] showed good agreement with the empirical measures of vergence adaptation. However, only one model [19] predicted the experimental time-course of reduction in vergence accommodation. The pattern of empirical results seem to be best described by the adaptation model that indicates the total vergence response to be a sum of two controllers, phasic and tonic, with the output of phasic controller providing input to the cross-link interactions [19]. A similar reduction of the vergence-accommodation cross-link with vergence adaptation was observed when using wedge prisms [21]. Analogous results were also seen in the accommodative system where accommodative adaptation reduced the output of accommodative-vergence [22].

9.2 Role of vergence-bias category on accommodation and vergence responses

Heterophoria is overcome by fusional vergence, which in addition to maintaining single vision, also alters the binocular accommodative response through the VA/V cross-link. The direction of the near phoria consistently altered the pattern of binocular vs. monocular accommodative response in experiments that measured accommodation and vergence under dual-closed loop conditions in the various phoria categories (Chapter 5, Fig 5-1 and Chapter 6-5). The differences between binocular and monocular responses (attributed to vergence accommodation) correlated with the direction of near phoria (Chapter 5, Fig 5-2). The influence of vergence-bias category on the pattern of binocular vs. monocular accommodation was evident in exophores viewing through plus adds (BA>MA; chapter 6, Fig 6-5: EX & MX) and esophores viewing through minus adds (MA>BA chapter 6, Fig 6-5: EE & ME). These differences are consistent with model predictions [15, 19] and can be attributed to the variations in the direction and magnitude of the resulting fusional vergence, required to overcome a given phoria. Fusional vergence will then dictate the output of vergence accommodation thereby changing binocular accommodation. Other cues such as proximity were not believed to influence the pattern of adaptation or changes to accommodation over time since the testing distance was constant for both add conditions.

Furthermore, the direction of the phoria influenced the degree of vergence adaptation. This relationship was constantly observed whether adaptation was stimulated by binocular fixation at near through corrective lenses (Chapter 5; Fig 5-6), addition of plus and minus lenses (Chapter 6; Fig 6-2), or prism viewing (Chapter 7; Fig 7-5). The most plausible explanation would again be attributed to be the differing fusional vergence demands produced by the vergence-bias category for each stimulus condition (Chapter 6 & 7; Figs 6-4 & 7-2). These results agree with the model of adaptation [7, 19], where the slow (tonic) element receives input from the phasic controller, such that the strength of adaptation directly proportional the output of the phasic controller.

Further, vergence adaptation was consistently less when near adds acted to reduce phorias and hence fusional vergence (Chapter 6; Fig 6-1). Of particular interest is the adapted phoria position in emmetropic and myopic esophores fixating through +2D adds. In both groups, the mean adapted phoria position was close to orthophoria through plus adds. The findings from this thesis seem to support the view that vergence adaptation is a mechanism that operates to reduce the demand on the fusional vergence system [6, 7]. It can be seen that these adaptive processes underlie orthophorization of heterophoria [8, 23-25].

9.3 Influence of myopia on the accommodation and vergence response

The effect of myopia, on binocular adaptation was evaluated for two reasons. First, several attributes of near-work have been identified to be different in myopic individuals compared to emmetropes. However, limited information is available about the differences in adaptation of accommodation and vergence during a prolonged near task in these groups. Second, although plus addition lenses have been investigated as a treatment option to reduce myopic progression studies have not measured simultaneous changes to accommodation and vergence output, which are key elements of near viewing.

9.3.1 Effect of myopia on ocular motor parameters in children

This thesis confirms previous reports that showed variations in several near-work attributes in myopic children [26-30] such as larger accommodative lags (Chapters 4, 5 & 6-minus add), higher variability of accommodative response (Chapter 8- no add condition), greater accommodative after-effects (Chapters 5 & 6-minus add) and elevated AV/A ratios (Chapters 4 & 6) compared to emmetropes. VA/V ratios were similar between the refractive groups, comparable to past studies [31, 32].

An unique but consistent outcome of this thesis is the reduced vergence adaptive ability observed in myopic children when fusional convergence was stimulated through binocular viewing of plus adds (Chapters 4 & 6; Fig 4-4 & Fig 6-2) or base-out prism (Chapter 7, Fig 7-1). It is interesting to note that this reduced vergence adaptation was observed irrespective of the nature of accommodative influence (plus adds- closed loop vs. prism condition- open loop). However, vergence adaptation was similar in myopes and emmetropes upon binocular viewing through minus adds (Chapter 6; Fig 6-2-b).

Accommodative adaptation was higher in myopes than emmetropes when the accommodative stimulus was higher (chapter 5: 3D for the near task; Chapter 6: 5D with the minus add) but not when the stimulus was reduced through plus adds (1D- Chapter 6, Fig 6-6). Based on the model of accommodation and vergence [15, 19], and supported by these empirical measures, accommodative adaptation will reduce the activity of the phasic controller, and thereby the AV cross-link, inducing a divergent shift in the overall vergence response [17, 22]. The higher accommodative adaptation, combined with the larger AV/A ratios seen in myopes (Chapter 6, Table 6-2), might explain the asymmetric pattern of vergence adaptation to plus and minus adds found in myopes. Further, myopic children also showed increased accommodative adaptation when fusional convergence was stimulated through base-out prism under open-loop accommodation (Chapter 7, Fig 7-4). This suggests that accommodative adaptation in myopes is more easily activated by convergence in accordance with models [15, 17] that suggest the capability of cross-links to induce adaptation of the opposite system. Clearly, the reciprocal difference between vergence and accommodative adaptation in myopes occurs specifically in the case of convergence and positive accommodation. However, their AV/A and VA/V findings are not readily explained from these models and the interactions of phasic and adaptive responses [15, 17]. These interactions in fact would argue for a smaller not greater AV/A ratio. It is evident that the etiology of the increased AV/A in myopes requires other variables perhaps not unlike those which define an independent gain regulation of the AV (and VA) ratio [33].

9.3.2 Implications for the control of myopia through plus addition lenses

The current rationale for prescribing plus adds for myopia is to reduce the large accommodative lags that may create hyperopic retinal defocus and possibly trigger axial elongation of the eye. Several studies that evaluated the ability of the bifocals/progressive addition lenses in reducing myopic progression found that children with specific ocular motor profiles such as large baseline accommodative lags [34, 35] and esophoria [34-36] manifested less myopic progression through near addition lenses compared to children with low accommodative lag or exo/orthophoria. However, these clinical trials did not measure changes to accommodative lag/phoria through the plus adds to identify whether the elimination of accommodation/ vergence error influenced the successful reduction of myopia progression in children.

This thesis indicated that plus addition lenses are capable of reducing the excessive accommodative lag and maintaining the reduction in all groups of myopic children, for the duration of binocular viewing tested in the current study (Chapter 6). Further, the higher accommodative variability observed in this group with corrective lenses were also reduced to the level of emmetropes through plus adds (Chapter 8). If increased accommodative lags and large variability of accommodation were indeed risk factors for the development of myopia, then one would expect that myopic progression would be eliminated / reduced through progressive/bifocal lenses. The modest treatment effect in clinical trials suggests that these parameters may not be critical to the development of myopia, presuming good compliance in children who receive these near addition lenses. Compliance is a challenging aspect of prescribing near adds to children. It is important to recognize that young myopes may not always look through the addition lenses, which may reduce efficacy unlike presbyopes who receive an instant feedback of clear vision when looking through the plus add. Furthermore, it is possible that some groups of myopic children (e.g.myopic exophores) may chose not to look through the add section to avoid stress on their vergence system based on the result of this thesis. All myopic children show reduced vergence adaptation to plus addition lenses. However, for myopic children with esophoria, the plus addition lens decreased the lag of accommodation and placed the baseline convergent position towards orthophoria, thereby placing less demand upon reflex vergence system. The reduced vergence adaptation in myopic esophores would be beneficial in avoiding a return to esophoria. On the contrary, myopic exophores culminated with a larger exophoria compared to their habitual level after prolonged binocular fixation through plus adds and this group would be expected to experience a greater stress on the vergence system. It may be possible that successful reduction of myopic progression occurs only if errors of both accommodation and vergence are minimized during prolonged fixation, highlighting the importance of evaluating binocular adaptation before prescribing plus adds to myopic children.

In a broader perspective, the overall results of this thesis provide further insights into the causative or consequential role of accommodative lag (blur hypothesis) in myopia development. The blur hypothesis postulates that excessive accommodative lags produce hyperopic retinal defocus that may signal axial elongation, based on evidence from animal models [37-40-] The results of this thesis suggests that accommodative lags may not be crucial for myopia development because plus adds reduced/eliminated accommodative lags in all myopic children. These results are in agreement with recent longitudinal studies that showed no association between myopic progression and large accommodative lags [41, 42]. The results appear to suggest that the higher accommodative lags seen in myopic children may likely be a consequence of parameters within the myopic eye or varying innervation patterns to it such as an increased AV/A ratio [29, 32, 43]. It may be possible that myopic individuals display higher accommodative lags to avoid over convergence due to high AV/A ratios in order to preserve single binocular vision. The etiology of the elevated response AV/A ratios in progressing myopes has not been determined. Investigators have attributed its high gain to motor, sensory or mechanical characteristics [29, 32, 43]. However based on their empirical investigations, Schor and Horner [43] showed evidence for high AV/A cross link to be associated with weak accommodative adaptation and strong vergence adaptation. The results of this thesis show the opposite relationship between the accommodative and vergence adaptive components in myopic children. Thus the high AV/A cannot be attributed to the adaptive parameters in myopic children. Few researchers [45, 46] suggest that myopic individuals have reduced sensory perception (increased threshold) for blur. Reduced sensitivity to blur has been modelled in infant studies as an increased depth of focus[47, 48]. Models of accommodation unanimously place depth of focus element prior to the accommodative controller. A high depth of focus would certainly reduce accommodation (and accommodative lags) but it should also reduce not increase accommodative vergence as observed in myopes.

The most parsimonious explanation at this point would be that the accommodative plant of the myopic eye (lens, ciliary body and zonules requires greater levels of accommodation to effect a given dioptric change in comparison to an emmetropic eye. This increased innervation would lead to the high AV/A due to increased accommodative effort, which may then lead to the high accommodative lag. Longitudinal evaluation of these factors may merit consideration as possible explanations for the development of myopia.

10 Future work

This thesis used plus and minus adds to study adaptation under closed-loop accommodation but only employed base-out prisms to study adaptation under conditions of open-loop accommodation. The asymmetric adaptive pattern between add conditions in myopes may be related to the accommodative influence (i.e. higher accommodative adaptation through minus adds) or due to the type of reflex vergence initiated, such that myopic children show reduced vergence adaptation only to fusional convergence but not fusional divergence. It may be worthwhile to measure binocular adaptation to base-in prisms under open-loop accommodation to understand if variations are produced by accommodative influence (closed vs open loop), or type of disparity (convergence vs. divergence) or purely related to the refractive error . For instance, if myopes show less adaptation compared to emmetropes through base-in prism, it may be concluded that the myopic eye is associated with poor vergence adaptive ability whether adaptation is induced by divergence or convergence stimulus. It may follow that the equal vergence adaptive behavior in myopes and emmetropes to minus adds was due to the greater accommodative adaptation in myopes. On the other hand, equal or greater adaptation to base-in prism in myopes compared to emmetropes, may indicate that myopic children are able to deal better with stimuli that require divergence compared to those that require fusional convergence.

The pattern of vergence and accommodative adaptation to near addition lenses were obtained when accommodation (and thereby vergence) demands were altered with respect to a 3D (33 cm) target. It would be logical to look at how accommodation and vergence adaptation act at other test distances. For instance, a near target at 20 cm (5D accommodative demand) through +2D lenses may create a relaxation of accommodation while still providing sufficient levels of reflex accommodation so accommodative adaptation can occur [1, 2]. If myopes show different accommodative adaptation to such stimulus condition, they may exhibit greater shifts in vergence compared to emmetropes, at least in a population similar to the current study.

In this thesis, characteristics of accommodation and vergence were measured at two-minute intervals for the first ten minutes of binocular fixation. This time interval was chosen after considering the subjective nature of the phoria evaluation, time taken for one measurement block of binocular, monocular accommodation and phoria (approximately 60-80 sec) and the age of participants. However, inspection of changes to near phoria through adds (Chapter 6, Fig 6-1) or tonic vergence through prism (Chapter 7, Fig 7-1) indicates that more frequent measures within the first 4-6 minutes of adaptation might provide a better estimate of time constants of vergence and accommodative adaptation.

Several differences in ocular motor parameters were observed in the myopic child compared to emmetropes. Some parameters (like accommodative lag, AV/A ratio, tonic accommodation) were examined in longitudinal designs by previous authors in order to determine their ability to predict the onset of myopia [3-7]. Goss & Rosenfield [8] suggested that vergence adaptation to near task may produce convergent shifts, which may lead to axial elongation due to the increased accommodative lags associated with esophoria. This thesis found a less convergent (or more divergent) shift in vergence adaptation to near task compared to emmetropes (Chapter 5), presumably related to their higher accommodative adaptation. However, these children were already myopic and it is unclear whether vergence adaptive ability plays any role in predicting the onset of myopia. It may be beneficial to longitudinally evaluate the role of other ocular motor parameters including accommodative/ vergence adaptation in pre-school children prior to the development of myopia. Nevertheless, given the uncertain role of accommodative lags in the development of myopia (as discussed in Chapter 9), it is unclear whether other ocular motor factors such as adaptation play a major role in myopia development. Other factors (such as mechanical reasons –involving accommodative apparatus) may merit further consideration as possible explanations for the development of myopia.

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Chapter 1

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Appendices

Appendix A: Results of calibration of PowerRefractor responses

Calibration of the PowerRefractor was done in a two-step process to ensure both relative and absolute accuracy of accommodation response (description in Methods section 3.1.3).

Relative accuracy

This experiment verified that the PowerRefractor provided accurate changes within a certain stimulus range. The following table (Table A1) shows the slopes for the individual calibration function in all study participants.

Table A1: Slopes for the individual calibration function in all study participants

Participant initials	***Slope of the calibration***	***R squared***
CC	1.03	0.99
LC	0.9	0.98
RL	0.81	0.99
NG	1.18	0.99
KG	1.1	0.93
DL	1.01	0.99
LM	1.05	0.99
WA	1.15	0.99
MR	1.05	0.99
SW	1.05	0.98

Participant initials	**Slope of the calibration**	**R squared**
TH	0.89	0.98
MV	0.98	0.98
GK	1.06	0.99
DM	1.11	0.98
SM	0.92	0.87
FA	0.90	0.97
DS	1.10	0.99
HC	1.80	0.99
KS	0.91	0.99
EP	0.93	0.99
AV	0.89	0.98
MK	1.08	0.98
EC	1.17	0.99
AD	1.15	0.99
KD	1.09	0.99
SC	0.83	0.99
RC	0.94	0.99
AA	1.4	0.94
EB	0.96	0.98
MS	1.28	0.99

Participant initials	**Slope of the calibration**	**R squared**
ZS	1.12	0.99
MT	1.06	0.99
TA	1.14	0.99
KH	0.99	0.94
JL	1.03	0.99
TC	1.29	0.99
IR	1.49	0.96
GP	1.02	0.99
RF	0.96	0.98
CG	1.0	0.97
CAB	1.19	0.97
CLB	1.10	0.98
MX	1.23	0.98
AM	1.06	0.99
CN	1.13	0.99
JM	1.04	0.94

FK	1.1	0.98
MG	1.28	0.99
IB	1.2	0.99
EN	1.05	0.99
KT	1.06	0.99
JB	0.90	0.99

Absolute accuracy

The accuracy of the accommodative responses obtained with the PowerRefractor was determined by comparing the photorefractor responses with those obtained with dynamic retinoscopy (vertical meridian) at two stimulus conditions (3D and 2D), created by viewing a near target at 33 cm with and without +1D lenses. This measurement was performed on 20 children (emmetropes=10 and myopes=10). The order of testing method and stimulus condition were randomized to avoid bias. Fig A1 shows the mean accommodative response obtained using the two techniques pooled across refractive groups. It can be seen that the PowerRefractor, on average showed a more hyperopic response at both viewing distances compared to retinoscopy (Fig A1; Bias = 0.39±0.2D at 3D and 0.41±0.3D at 2D through +1D lens; $P<0.05$ between two distances; range = +0 to 1.1D). This difference was non-significant between refractive groups tested in this study (P>0.05). Based on these findings, a correction factor of 0.4D was added to all accommodative measures obtained using the PowerRefractor.

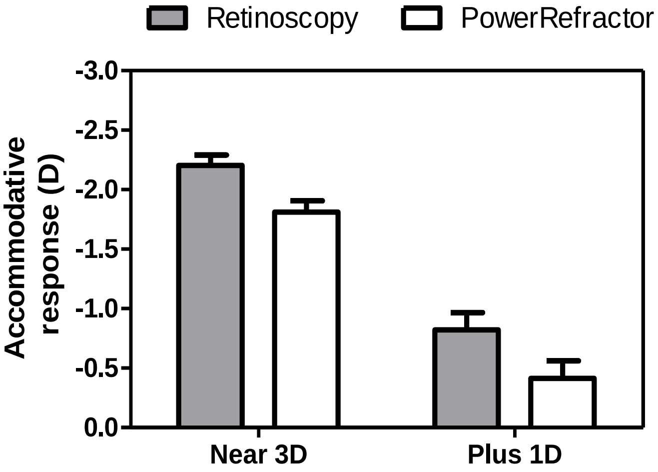

Fig A1: Comparison of accommodative response measured using PowerRefractor and retinoscopy.

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