Focussing on Near Work: the Impact of Uncorrected Hyperopic Refractive Errors.

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I confirm that the word count in this thesis is less than 100, 000 words.

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Summary

Background:

Uncorrected hyperopia is the most common refractive error in childhood. Uncorrected hyperopia places an extra demand on the accommodative system for near tasks and evidence suggests associations between uncorrected hyperopia and abnormal visual development, and poorer academic scores. However, it is still unclear when, and at what magnitude of hyperopia, optical intervention is necessary.

Methods:

Assessment of sustained accommodative and vergence performance was carried out using photorefraction (PowerRefractor 3™, PlusOptix, Germany) in participants aged 5-10 years with (n=80) and without (n=37) hyperopia. Hyperopia was determined by cycloplegic retinoscopy (1% cyclopentolate) and defined as > +1.00D. Emmetropia was defined as -0.25D to less than +1.00D of cycloplegic refraction. Initially, binocular accommodation measures were obtained without spectacle correction while participants engaged in two sustained near tasks at 25cm: an ‘active’ task (reading small print on an Amazon Kindle), and a ‘passive’ task (watching a stop-clay animated movie on an LCD screen). Both tasks were undertaken for 15-minutes. Measures were repeated after a week with spectacle correction for participants who were hyperopes. Other baseline clinical measures including presenting visual acuity (crowded logMAR letters), stereoacuity (Frisby stereotest) and reading speed (Wilkin’s Rate of Reading test) were assessed. Individual lens calibration slopes were used within the photorefraction data.

Results & Conclusion:

Results of this PhD work demonstrate that:

- Accommodative response during sustained near tasks does not differ significantly between uncorrected hyperopes and emmetropes.
- Instability of the accommodative and vergence responses increases with increasing hyperopia.
- The instability of accommodative and vergence responses is a factor which is often over-looked and could contribute to asthenopia
- Hyperopic spectacle correction is beneficial to optimise the accommodative response.

Abbreviations

AA	Amplitude of Accommodation
AC/A	Accommodative convergence/accommodation
ACD	Anterior Chamber Depth
AR	Accommodative Response
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
BI	Base-in
BO	Base-out
CA/C	Convergence-accommodation/convergence
COA	Coefficient of accuracy
D	Dioptres
DC	Dioptre Cylinder
DoF	Depth of Focus
DoG	Difference of Gaussian
Hz	Hertz
HFC	High Frequency Component
HR	Hirschberg Ratio
ICC	Intra Class Correlation
IOL	Intraocular Lens
IPD	Interpupillary Distance
IQ	Intelligence Quotient
IQR	Interquartile Range
IR	Infrared
LCD	Liquid Crystal Display
LED	Light Emitting Diode
LFC	Low Frequency Component
LOA	Limits of Agreement
MA	Metre Angle
MM	Millimetres
NPC	Near Point of Convergence
PC	Pupil Centre (centre of entrance pupil)
PCT	Prism Cover Test
PI	Purkinje Image
RMS	Root Mean Square
SE	Spherical Equivalent
SLT	Sonksen LogMAR Test
TA	Tonic Accommodation
VA	Visual Acuity
ΔD	Prism Dioptre

Declarations

"I hereby declare that with effect from the date on which the thesis is deposited in the Research Office of the University of Ulster, I permit

1. the Librarian of the University to allow the thesis to be copied in whole or part without reference to me on the understanding that such authority applies to the provision of single copies made for study purposes or for inclusion within the stock of another library.
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Chapter 1: Literature Review of Hyperopia

1.1 Introduction

Good vision is important in the early years of life, as it significantly has an influence on visual development, education and learning (Troilo 1992; Bharadwaj and Candy 2008). To achieve optimum visual function, a combination of factors such as good distance and near vision, accurate accommodation for near work, good binocular coordination, and correction of significant refractive errors are needed (Mutti 2007; Cotter 2007; Leat 2011). However, some children do not achieve optimum visual function and refractive errors are common, particularly hyperopia in younger children. Refractive errors are only measured if a child attends for an eye examination, but in the UK the majority of children do not attend for examination (a BBC news report of a survey by the Association of Optometrists, available at: https://www.bbc.co.uk/news/uk-politics-45258771). This means that hyperopia can go undetected unless the child complains of visual symptoms or performs poorly in school that may prompt action. Myopia, however, tends to come on later in childhood, and the child would likely complain of worsening distance vision, so it does tend to be picked up easily. The accommodative ability of the visual system means that an individual with sufficient accommodation should overcome small amounts of hyperopia. If hyperopia is uncorrected, however, it requires continual accommodative effort to make the distance vision perpetually clear (Wu *et al.* 2016). Consequently, additional accommodative effort is required to focus on any visual object that is close; thus uncorrected hyperopia places additional burden on the clarity of near vision (Horwood and Riddell 2011; Candy *et al.* 2012).

Most school tasks are performed at close/near working distances, and the advent of portable electronic devices, such as smartphones, tablets, and e-readers has led to increased recreational and educational use of screens at close working distances over prolonged periods (Benedetto *et al.* 2013; Narayanasamy *et al.* 2016). Consequently, the efficiency of near vision is increasingly more important for the social and educational learning of children in general, and particularly for the uncorrected hyperope.

Compared to myopia, the subject of uncorrected hyperopia has for a long time received little attention from clinicians and researchers (Grosvenor 1971; Rosner 2004). However, in recent years, there has been renewed interest in the subject, with some large-scale studies undertaken to understand this refractive population. The purpose of this review is to set this PhD research, which sought to investigate the impact of uncorrected hyperopia in children during two sustained near tasks on accommodative and vergence functions, within the context of an up-to-date review of the literature.

1.2 Background to Hyperopia

Hyperopia also referred to as hypermetropia (Charman *et al.* 2015), is the most common refractive error in young children, with various prevalence estimates reported in different study populations (Castagno *et al.* 2014).

1.2.1 Epidemiology of hyperopia

1.2.1.1 Definition:

When the eye views an object at a far distance, it is expected that parallel rays of light will be focused on the retina while accommodation is relaxed. This ideal refractive state, known as *emmetropia,* is less common compared to *ametropia,* which is any other deviation from this ideal refractive condition. Hyperopia exists when, with accommodation relaxed, parallel rays from an object fail to focus on the retina of the eye (Figure 1.1). It usually results from failure of correlation between the axial length and the refractive components (primarily of the cornea and lens) of the eye, and most cases of hyperopia are attributable to reduced axial length of the eye (Ip *et al.* 2008b).

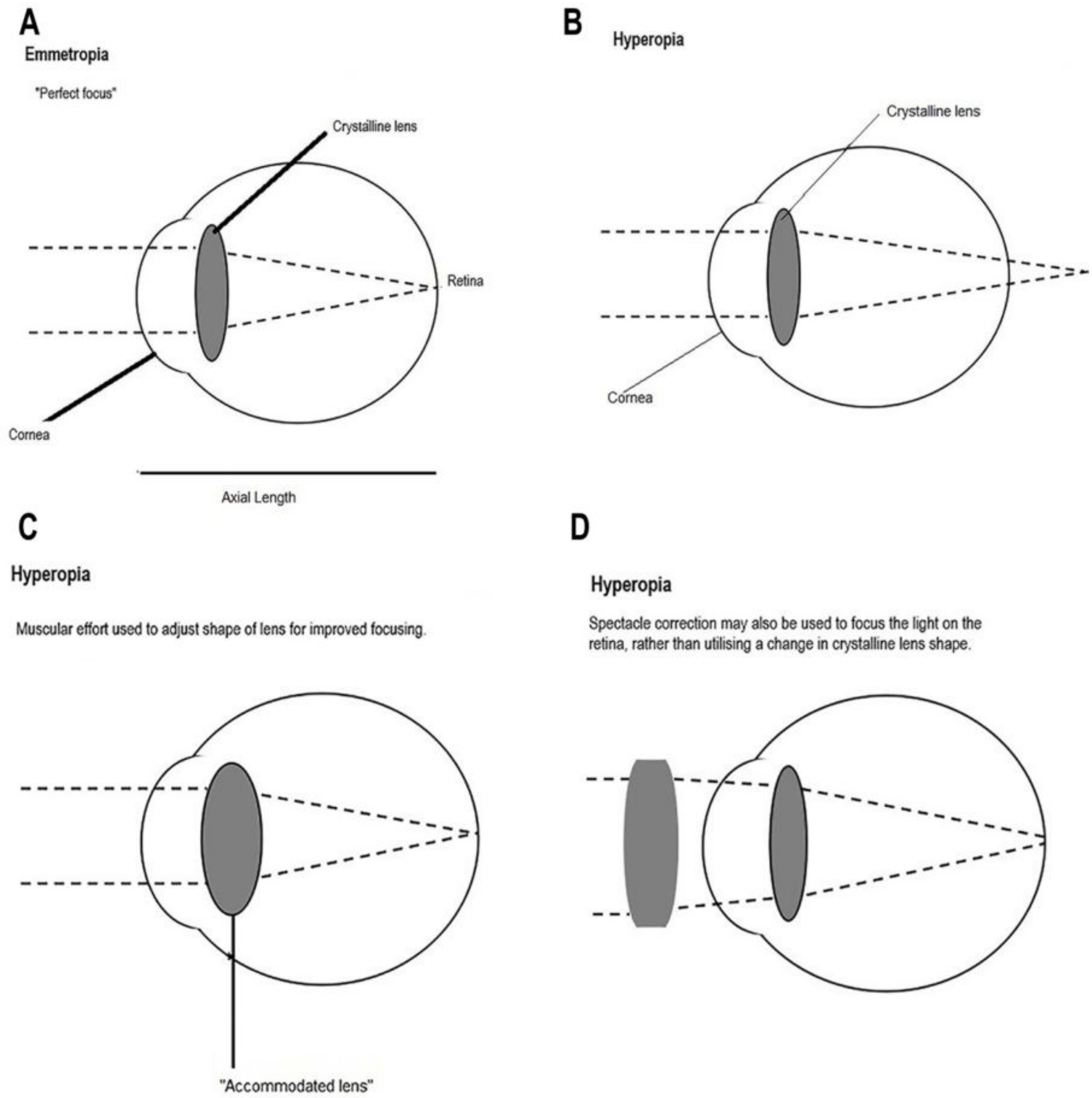


Figure 1.1 Schematic diagrams explaining: (panel A) Perfect focus of an object with accommodation relaxed (during far viewing); (panel B) Image focussed behind the retina in hyperopia with accommodation relaxed; (panel C) ciliary muscle effort employed to adjust shape of lens to achieve focussed rays of light on the retina; (Panel D) Convex (plus powered) spectacle lens correction enabling the eye to achieve 'precise focus' without the use of accommodation (Images courtesy Prof. K. Saunders).

1.2.1.2 Classification of hyperopia

Broadly speaking, two classifications exist for hyperopia: a clinical classification, and research-based classification. In most published studies, classification/definition of hyperopia has been based on the magnitude of hyperopia in dioptres. These definitions are approximately:

1. Low hyperopia: <+1.50 D (Kleinstein *et al.* 2003; Zadnik *et al.* 2003; Ip *et al.* 2008b; Krantz *et al.* 2010; Wu *et al.* 2016).
2. Moderate hyperopia: >= +1.50 D (Rosner and Rosner 1997); >= +2.00(Ip *et al.* 2008b; Wen *et al.* 2013), >=+3.00 D (Kulp *et al.* 2014; Ciner *et al.* 2016), >=+3.25 D (Kulp *et al.* 2014).
3. High hyperopia: >= +4.0 D (Dobson and Sebris 1989); > +4.50 D (Williams *et al.* 2005); or > +5.00 D (Kassem *et al.* 2012).

However, in clinical terms, hyperopia could be classified as (Augsburger 1987; Moore *et al.* 1997):

i. Simple hyperopia; which results when there is variation in the relationship between the axial length of the eye and its optical components.

ii. Hyperopia based on the role of accommodation, including *facultative hyperopia*, where accommodation can be used to overcome the refractive error; and *absolute hyperopia* where accommodation cannot be used to correct the refractive error. Similarly, *latent hyperopia* and *manifest hyperopia* are terms used to describe the amount of hyperopia hidden by accommodation but revealed through cycloplegic refraction, and the amount of hyperopia present during routine refraction without cycloplegia respectively.

iii. Pathologic hyperopia; a rare form which develops secondary to congenital malformations of the eye such as in microphthalmia, or from ocular disease or injuries such as paralysis of accommodation.

1.2.1.3 Prevalence of hyperopia

Hyperopia is a common refractive condition in young children (Ip *et al.* 2008b; Leat 2011). Although many studies have reported on the prevalence of hyperopia in different populations, deriving a summary estimate of hyperopia from the literature is constrained by variations in the study protocols of published studies. Such variations include: (i) differing age of participants between studies, (ii) different definitions for hyperopia (iii) different refractive analysis, including the use of least hyperopic meridian, most hyperopic meridian, spherical equivalent, (iv) different refraction protocols i.e., with or without cycloplegia, and (v) different sample sizes (Tarczy-Hornoch 2007; Castagno *et al.* 2014).

The use of cycloplegic agents is a particularly important factor in consideration of a study's data; as it is likely that true hyperopia may be masked by accommodative function if refractive error is measured under non-cycloplegic conditions. This can lead to under-estimation of the magnitude of hyperopia in the study population (Morgan *et al.* 2015; Hashemi *et al.* 2016; Feldman *et al.* 2017)

Despite differences in studies outlined above, the consensus from the data is that there is an age-dependent relationship in hyperopia prevalence (Ip *et al.* 2008b; O'Donoghue *et al.* 2010; Castagno *et al.* 2014). In a meta-analysis of 40 cross-sectional studies of hyperopia by Castagno *et al*. (2014), a summary prevalence of 5% at age 7, 2-3% for 9 and 14 years, and 1% at age 15 were reported. However, a higher prevalence of hyperopia has been reported in predominantly Caucasian populations; including a 26% and 15% prevalence in children aged 6-7 and 12-13 years respectively, in Northern Ireland (O'Donoghue *et al.* 2010); and 16% and 7% in 6 and 12 years respectively, in a study conducted in Australia (Ip *et al.* 2008b). The age and ethnic distributions of hyperopia appear to be partly related to the axial length of the eye, being shorter in younger and Caucasian children (Ip *et al.* 2008a; Ip *et al.* 2008b). Furthermore, ethnic differences in corneal curvature have also been implicated in the hyperopia-ethnicity association (Ojaimi *et al.* 2005; Ip *et al.* 2008b), though this has not been consistently reported across studies (Uretmen *et al.* 2003; Ip *et al.* 2008b). Table 1.1 summarises the variation in hyperopia prevalence found in key studies across the world.

Some published studies have reported a female preponderance in hyperopia (Wen *et al.* 2013; Castagno *et al.* 2015): however, this observed association is inconclusive, as other studies have reported contrary findings (Naidoo *et al.* 2003; Ip *et al.* 2008b). Observed gender differences in ocular biometric measures (i.e. females have a slightly smaller eye) amongst some studies could account for the differences in findings between gender and hyperopia. Ip *et al.* (2008a) whose study did not find any female preponderance, reported more hyperopia in boys than girls in their refractive error study of 2353 children, aged 11-14 years, with boys having a flatter cornea than girls. However, O'Donoghue *et al.* (2010) found no association between ocular biometry and gender in their study of children aged 6-7 years and 12-13 years (n=1053) in Northern Ireland.

Other proposed associations between hyperopia and factors such as parental education and socioeconomic status, geographic location (in terms of urban versus rural), have been deemed largely insignificant (Castagno *et al.* 2014). However, there is emerging evidence that children's engagement with outdoor activities may influence the distribution of refractive errors because of exposure to light during outdoor activities (Read *et al.* 2010; French *et al.* 2013). Also, low demand on accommodation during outdoor activities may potentially reduce the stimulus for ocular growth (Rose *et al.* 2008).

Table 1.1 Table showing the study protocols and the prevalence of hyperopia from selected studies by geographic location.

Study (Country)	**Sample size (N)**	**Age (years) and Gender**	**SE Definition of hyperopia**	**Refractive method**	**Prevalence (%) (95% CI)**
Asia					
(He *et al.* 2004) **China** (Asian participants)	4364	5-15 Boys Girls	≥+2.00D	Cyclo Auto & Ret	**4.6**(4.4 – 4.9) No gender breakdown for hyperopia prevalence
(Fan *et al.* 2004) **Hong Kong** (Asian participants**)**	7560	5-16 Boys Girls	≥+2.00D	Cyclo Auto	**4.0** (95% CI (N/A) 3.9% 4.2
(Pi *et al.* 2010) **China** (Asian participants)	3070	6-15 Boys Girls	≥+2.00D	Cyclo Ret	**3.26** (2.6 – 3.9) No gender breakdown of hyperopia prevalence, †P=0.08.
(Zhao *et al.* 2000) **China** (Asian participants)	5884	5-15 Boys Girls	≥+2.00D	Cyclo Auto & Ret	**2.7** (95% CI (N/A) 8.8% in 5yrs 19.6% in 5yrs
(Murthy *et al.* 2002) **India** (Indian participants)	6447	5-15 Boys Girls	≥+2.00D	Cyclo Ret	**7.4** (6.0 – 8.8) Hyperopia associated with female gender (OR=1.72, (95% CI:1.05- 2.81)
(Pokharel *et al.* 2000) **Nepal** (Nepalese participants)	5067	5-15 Boys Girls	≥+2.00D	Cyclo Auto & Ret	2.1 (95% CI (N/A) Similar % prevalence (1-2%) for boys and girls

Australia					
(Ip *et al.* 2008) **Australia** (Multi-ethnic)	4094	6-12	≥+2.00D	Cyclo Auto	**13.0% 6yrs, 5.0 12yrs** Girls more hyperopic at 6yrs, no gender difference at 12yrs
(Robaei *et al.* 2006) **Australia** (Caucasians)	2353	12	≥+2.00D	Cyclo Auto	**5.0%** Gender specific prevalence unstated
Middle East					
(Fotouhi *et al.* 2007) **Iran** (Iranians)	3673	7-15	≥+2.00D	Cyclo Auto	**16.6** (13.6 – 19.7) No significant differences in gender prevalence
(Ostadimoghaddam *et al.* 2011) **Iran** (Iranians)	639	5-15	≥+2.00D	Cyclo Auto	**19.05** (15.7 – 22.4) No significant differences in gender prevalence
Europe					
(O'Donoghue *et al.* 2010) **Northern Ireland, UK** (Caucasians)	1053	6-7 12-13	≥+2.00D	Cyclo Auto	**26** (20 – 33) **14.7** (9.9 – 194) No significant differences in gender prevalence
(Gronlund *et al.* 2006) **Sweden** (Caucasians)	143	4-5	≥+2.00D	Cyclo Auto	**9.1** (95% CI N/A) No significant differences in gender prevalence
Americas					
(Kleinstein *et al.* 2003) **USA** (Multi-ethnic)	2523	5-17	≥+1.25D Boys Girls	Cyclo Auto	**12.8** (11.5 – 14.1) 12.6% 13.1%, P<0.05
(Zadnik *et al.* 2003) **USA** (Multi-ethnic)	2583	7-12	≥+1.25D	Cyclo Auto	**8.6** (95% CI (N/A) No significant differences in gender prevalence
(Castagno *et al.* 2015) **Brazil** (Hispanics)	1032	6-16	≥+2.00D	Cyclo Auto	**13.4** (11.2-15.4) Girls more hyperopic, OR=1.39(CI:1.02-1.90)
(Maul *et al.* 2000) **Chile** (Hispanics)	5303	5-15	≥+2.00D	Cyclo Auto	**19.3** (95%CI (N/A) Girls more hyperopic, OR=1.21(95% CI: 1.03-1.43)
Africa					
(Naidoo *et al.* 2003) **South Africa** (Africans)	4890	5-15	≥+2.00D	Cyclo Auto	**2.6** (95% CI (N/A) No significant differences in gender prevalence

CI – Confidence Interval; Cyclo Auto – Cycloplegic autorefraction; Cyclo Ret – Cyclo retinoscopy; OR – Odds ratio; SE- Spherical Equivalent refraction; P-value represents the probability of Chi-squared test of association between gender and hyperopia being statistically significant.

1.3 Accommodation and Hyperopia

Accommodation and vergence functions are initiated by the eye in order to achieve a clear, single binocular vision during near viewing (Tondel and Candy 2008). The pupils also constrict during the process and in combination, these three elements are sometimes referred to as the "near response triad" (Myers and Stark 1990; Suryakumar *et al.* 2007) (Figure 1.2). These three processes occur simultaneously due to neuronal coupling at the level of the mid-brain (Zhang *et al.* 1992; Judge 1996; Gamlin 1999), and innervation by the third nerve for medial recti extraocular muscles (for vergence), iris sphincter (for pupil constriction), and ciliary body (for accommodation). A good understanding of accommodation-vergence interaction requires a prior discussion of the individual mechanisms of accommodation and vergence.

A

B

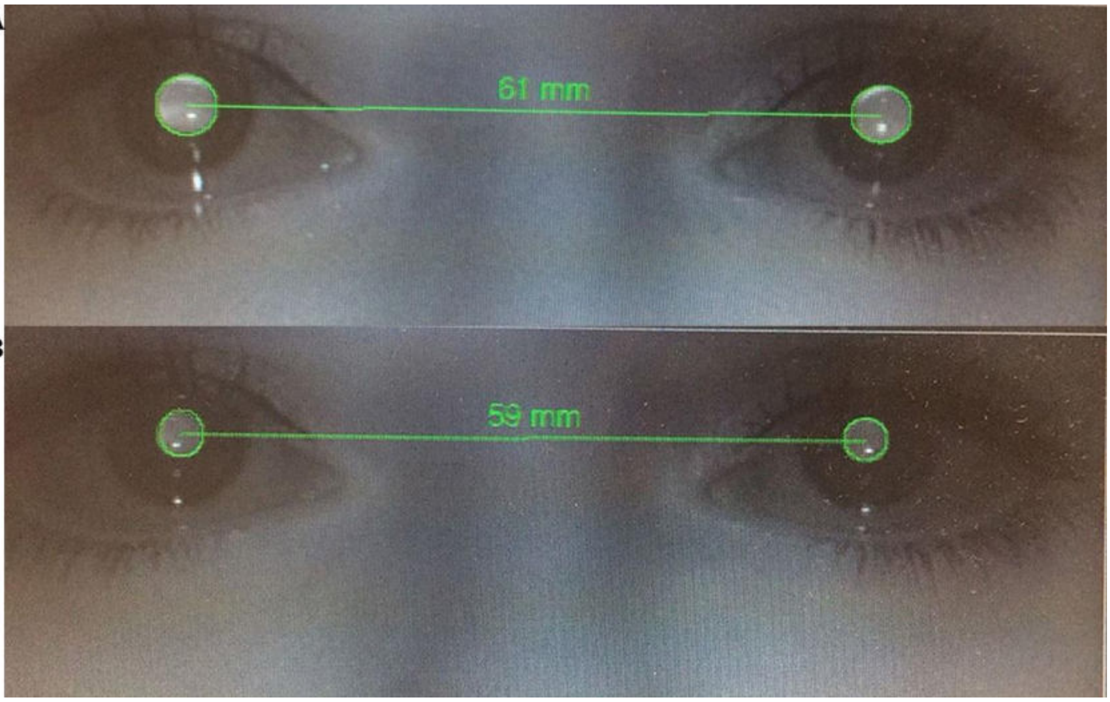


Figure 1.2 The near triad as captured by an infrared, eccentric photorefractor, the PlusOptix PowerRef 3™. In Panel A, as the subject views an object at far, there is less convergence, evidenced by large interpupillary distance (IPD) of 61cm. Note also, the large pupil sizes. In panel B, where the subject fixates an object at near, there is increased convergence, evidenced by smaller IPD (59cm), and small pupil sizes.

1.3.1 Mechanism of Accommodation

Accommodation is an oculomotor mechanism by which the eye increases its refractive power through adjustment in the shape of the eye's crystalline lens to allow changes in focus from a distant object to a near object (Schor 1999). This dynamic mechanism ensures that a clear retinal image is maintained at all times; and also includes when the eye makes changes in fixation from near to far; termed 'negative' accommodation or disaccommodation (McBrien and Millodot 1987; Glasser 2011).

In theory, changes in the refractive surface of any of the optical components of the eye could result in changes in the focusing power of the eye. For example, changes in corneal curvature could result in changes in focusing power (Atchison 1995). However, this has been discounted as a dynamic accommodative mechanism with empirical evidence from some studies showing that there is little to no change in corneal curvature during accommodation. For example, a study in nine emmetropic subjects aged 20-38 years, measuring ocular surface radii of curvature, axial separation and alignment in the accommodated and relaxed states using autokeratometry, A-scan ultansonograpahy, and video ophthalmophakometry at 25 cm (4D), and cycloplegia in the relaxed state, did not find any difference in the mean corneal curvature during relaxed and accommodated states of the eye (Kirschkamp *et al.* 2004). The vitreous body has also been purported to contribute to accommodation with Coleman and Fish (2001) contending that there is a continuous intra-ocular pressure difference between the aqueous and the vitreous humour during accommodation (Coleman and Fish 2001). They proposed that this difference causes a change to the anterior surface of the lens during accommodation. However, a study using ultrasonographic data to simulate a model of accommodation did not reveal any refractive surface power change consistent with the hypothesis of Coleman and Fish (Martin *et al.* 2005). Further, if the vitreous plays a significant part in the accommodative process, then it would be expected that little or no accommodation will occur in an eye without vitreous humour. Interestingly, some studies have observed accommodation in eyes without vitreous (Fisher 1983).

The debate on the exact mechanism of accommodation is far from over. However, our current understanding of the mechanism of accommodation is based on the widely accepted theory of accommodation developed by Helmholtz von (1924). This theory is based on lenticular changes, primarily changes in the lens and its capsule, which occur during accommodation. Further published studies have corroborated Helmholtz's theory and contributed to our current understanding of the mechanism of accommodation, (Gullstrand 1924; Glasser and Campbell 1999). In this theory, the crystalline lens of the eye which is held in place by zonular fibres, attached at the equatorial region of the lens, is relaxed during distant viewing (Glasser and Campbell 1999; Glasser 2001; Glasser 2011). During distant viewing, the ciliary muscles are relaxed, and traction from the posterior zonular fibres cause stretching of the anterior zonular fibres. The tension on the anterior zonular fibres causes the lens to assume a flattened shape at distance (Figure 1.3). However, when the eye changes fixation from distant to near, the ciliary muscles contract, which results in a forward and inward movement, releasing the tension on the zonular fibres, to cause the lens and its capsule to increase in convexity (Figure 1.3). This produces increased power for near viewing. The changes in the radius of the curvature of the surfaces of the lens from the released tension are greater for the anterior lens surface than the posterior surface (Rosales *et al.* 2006), partly because of the increased effect of the change associated with the anterior zonular fibres (Charman 2008). Additional lenticular changes observed during accommodation include: increase in the axial thickness and an apparent forward movement of the lens (Drexler *et al.* 1997; Strenk *et al.* 2005; Bolz *et al.* 2007), and a decrease in the equatorial diameter (Wilson 1997; Glasser *et al.* 2006). The distance from the posterior surface of the cornea to the posterior lens surface remains fairly constant despite the increase in the curvature of the anterior lens surface (Koretz *et al.* 2002).

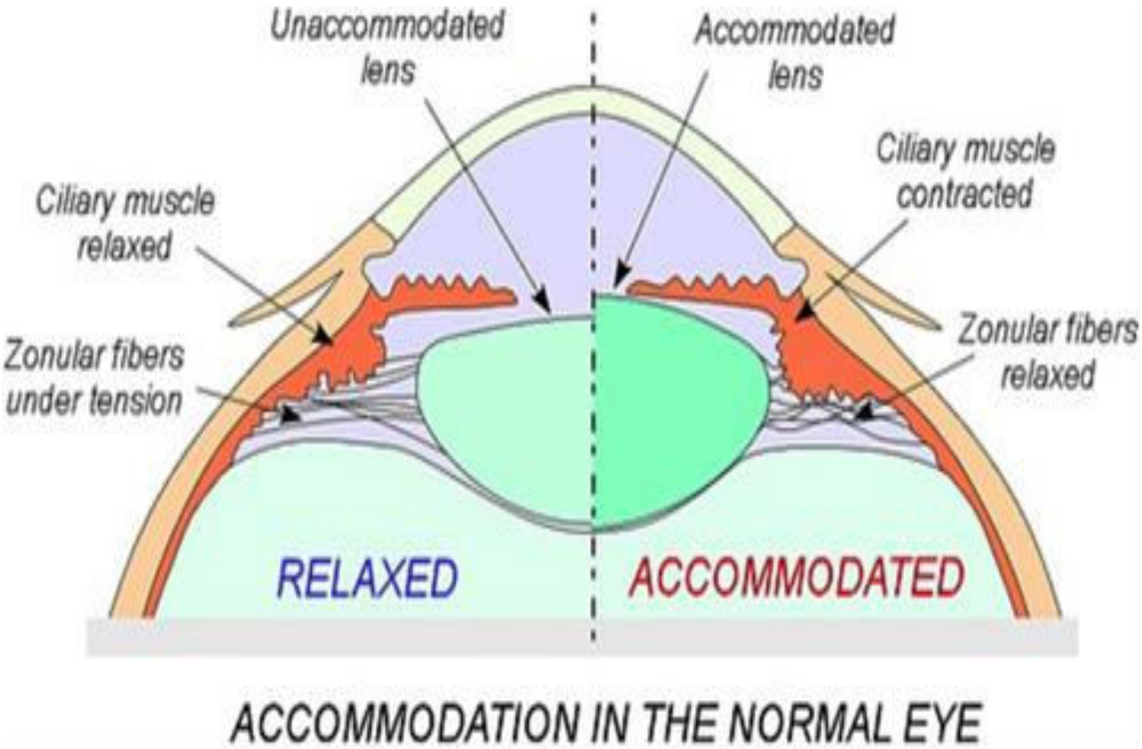


Figure 1.3 The mechanism of accommodation in the normal eye, shown through a cross-section of the anterior segment of the eye. The lens in an unaccommodated eye (left side of figure) is flattened due to the exertion of pressure (tension) by the zonular fibres. However, during accommodation (right side of figure), the tension exerted on the lens by the Zonular fibres is released, allowing the lens to assume a more convex shape, resulting in increased dioptric power. Reproduced from Azar et al. (2006).

A number of studies have challenged the Helmholtz theory of accommodation and have proposed a variant theory (Tscherning 1900; Schachar *et al.* 1993; Schachar 2000). Tscherning (1900) was of the view that when the ciliary muscles contract, there is rather an increased zonular tension which causes flattening at the lens periphery and a steepening of the central lens in the pupillary region. Tscherning's theory has been corroborated by Schachar's published studies (Schachar *et al.* 1993; Schachar 2000; Chien *et al.* 2003), who proposes that during accommodation, when the ciliary muscles contract, they exert a force on the zonules which cause an increase in the lens equatorial diameter, flattening of the peripheral surfaces and steepening of the central surface. However, a different study using similar methodology (numerical analysis) as Schachar's, found results consistent with the Helmholtz theory of accommodation (Burd *et al.* 1999). Additionally, arguments for equatorial lens diameter increases have been rejected by some studies which used imaging technology such as gonio videography (Glasser *et al.* 2006), and magnetic resonance imaging (Sheppard *et al.* 2011) and found a decrease in equatorial lens diameter during accommodation.

1.3.2 Components of Accommodation

The accommodative response generated is a function of the nature of the cue presented to the eye (Horwood and Riddell 2008; Babinsky and Candy 2013). Four components of accommodation have been identified to drive the accommodative responses (Heath 1956). These are blur, disparity, proximity and the accommodative resting state of the eye, known as tonic accommodation. These are often referred to as cues.

Also referred to as reflex accommodation (Heath 1956), the blur cue has traditionally been viewed as the primary driver of accommodation in adults (Phillips and Stark 1977). Under binocular viewing conditions, there is contribution from all cues, which provides information on depth. However, because accommodation is a negative feedback controlled system, it uses blur as the primary *error correcting* cue to effect errors arising from the other components of the accommodative response (Babinsky and Candy 2013). Once the eyes detect a change in the luminance contrast of the retinal image (through the process of error signalling by the retinal ganglion cells) – *retinal defocus*, the accommodative system uses a negative feedback mechanism to adjust the response until a point of maximum luminance contrast and smallest blur circle diameter is achieved

(Rucker and Kruger 2001). Blur as a driver of accommodation can thus be removed once feedback is opened through the use of pin-holes, total darkness, or low spatial frequency targets or difference of Gaussian (DoG) filters to remove higher spatial frequency content. The perception of blur depends on the integrity and or sensitvity of the visual system, as well as the spatial content of the stimulus (Babinsky and Candy 2013). Consequently, blur perception could be impeded by the presence of significant refractive errors, amblyopia, media opacities of the eye and insults to other parts of the visual pathway (Horwood and Riddell 2008). Blur perception is also less efficient with low spatial frequency targets (Charman and Tucker 1977). The role of blur as the primary driver of accommodation has been challenged. Judge (1996), and other published studies (North *et al.* 1993; Horwood and Riddell 2008) have challenged the primary role of blur-driven accommodation in both adults and infants. These studies have proposed disparity as a significant driver of total accommodative response along with blur. Moreover, in infants and children, the efficient use of the blur cue is poorly understood as infants have limited resolution and thus are more sensitive to low spatial frequency targets (have low blur sensitivity) (Green *et al.* 1980; Roberts *et al.* 2018b).

Under binocular viewing conditions, the image of an object is expected to fall on corresponding retinal points of the two eyes. When the image of the object falls outside these points, this gives rise to retinal disparity, which serves as a cue to correct this error. Contribution of the disparity cue to the accommodative response is quantified by the cross-link interaction between convergence and accommodation (CA/C ratio) due to the neuronal coupling of accommodation and convergence functions (Judge 1996). The disparity cue has been put forth as a significant driver of the accommodative response (Semmlow and Wetzel 1979; North *et al.* 1993; Judge 1996; Horwood and Riddell 2008). Horwood *et al*. (2008) in their study of 32 participants, aged 8-24 years, reported disparity cue to be the main driver of both accommodation and vergence. They observed that the accommodative response was significantly reduced when disparity was removed, compared to the effects observed when blur or proximity was removed. Similar work from their laboratory also purports that disparity is a 'weightier' visual cue to accommodation, and consequently may be adapted to aid the relaxation of accommodation (Horwood and Riddell 2009). Babinsky and Candy (2013) speculated that hyperopic infants and children who primarily use this cue to drive accommodative response (thus those with high CA/C ratio) might be less likely to develop strabismus secondary to excessive use of blur to drive accommodation. In most research studies, the contribution of the disparity cue has been evaluated by removing blur cues by either using blurred targets (e.g. DoG targets) (Horwood and Riddell 2008; Tondel and Candy 2008), a pin-hole or dark experimental setting (Weiss *et al.* 2004), and then using prisms to drive vergence-accommodation binocularly. However, the disparity cue is absent under monocular viewing conditions (vergence open-loop) such as in the presence of strabismus. The question of which cue drives the accommodative response in the face potential conflict between blur and disparity, as would occur in an eye with heterophoria, has produced inconsistent results (Okada *et al.* 2006; Bharadwaj and Candy 2009). Okada *et al.* (2006) report that in such a conflict situation, disparity-driven accommodation was the main driver of the responses whereas Bharadwaj and Candy (2009) did not find any strong preference for disparity or blur in such situation. Bharadwaj and Candy (2009) tested 140 infant subjects aged (2 months to 40.8 years) whereas Okada *et al.* (2006) evaluated five young adults aged 21-24 years. Differences in target detail could also account for the differences in results.

The awareness of the nearness of an object – proximity, has also been shown to drive accommodation (Heath 1956; Horwood and Riddell 2009; Babinsky and Candy 2013). In research studies evaluating the individual contribution of proximal cue to the accommodative response, proximal cues have been presented as a looming object (both scaled and unscaled for distance), motion parallax or contour overlay of objects (Currie and Manny 1997; Horwood and Riddell 2008). It remains unclear whether the proximal cue drives accommodation directly or it drives convergence and through the cross–coupled convergence–accommodation, accommodation is stimulated (Rosenfield *et al.* 1990). If its contribution is via convergence-accommodation, then it could be a potential pathway for avoiding the development of strabismus, while the contrary scenario could be a risk factor for the development of strabismus in hyperopia (Babinsky and Candy 2013). Compared to blur and disparity, the role of proximal cue in driving accommodation may be minimal (Horwood and Riddell 2008).

In the absence of any apparent visual stimuli, as it would be in a completely dark room or "empty field", the eye assumes a resting or baseline accommodative state referred to as tonic accommodation (TA) (Heath 1956). It has also been referred to as dark focus (Miller 1978b; Rosenfield *et al.* 1993; Miwa and Tokoro 1994; Rosenfield *et al.* 1994). Accommodative values produced at this resting state of the eye have been reported to be in the range of 0.5D to 1.5D (Heath 1956; Rosenfield *et al.* 1993; Glasser 2011). Tonic accommodation has been put forth as an explanation for the phenomenon of nocturnal or night myopia (Rosenfield *et al.* 1993). The true TA level has been measured in studies after excluding the effects of spherical and chromatic aberrations through the use of pin-holes (Miller 1978a), and monochromatic light (Wald and Griffin 1947; Jenkins 1963). In using pin-hole to measure TA, however, a distant target must be used as any near target has the potential to introduce proximal cues (Rosenfield *et al.* 1993). Even though total darkness or "empty field" would remove blur, disparity, and proximal cues and potentially give true TA values, it has been noted that the degree of cognitive activity such as the awareness of the immediate surrounding (*surround propinquity*) can affect measurement (Rosenfield and Ciuffreda 1991). TA has been reported to show variations between individual subjects (Leibowitz and Owens 1978; McBrien and Millodot 1987) despite being a stable component of the accommodative response (Miller 1978a). Furthermore, a number of studies in children have reported differences in TA levels for different refractive groups (McBrien and Millodot 1987; Rosner and Rosner 1989; Gwiazda *et al.* 1995), with hyperopes reportedly exhibiting high TA responses (e.g. 1.33±0.49D vs. 0.92±0.61D for hyperopes and myopes (early onset) respectively in McBrien and Millodot (1987) study; and 1.73±0.40D vs.1.36±0.46D for hyperopes and myopes respectively in Rosner and Rosner (1989)). In adult hyperopic participants, TA levels are similarly high compared to adult myopes (Maddock *et al.* 1981). It has been suggested that sympathetic innervation is responsible for distance accommodation (resting focus), whereas the parasympathetic system is for near accommodation; therefore, the high TA levels in hyperopes may be due to a higher sympathetic innervation in hyperopes, compared to the low sympathetic tone in myopes – which may explain the observed differences in TA levels in different refractive groups (McBrien and Millodot 1987).

An important aspect of TA, which has been a subject of prolonged interest due to its possible role in near-work induced myopia, is the apparent change in the tonic accommodation levels following sustained periods of fixation. This change has been referred to accommodative adaptation in the literature (Rosenfield *et al.* 1994). It has been noted that the level of pre-task TA differs from post-task TA following a sustained period of fixation, with the magnitude of change reported to being in the range of 0.34D to 1D (Rosenfield and Gilmartin 1988; Ebenholtz 1992). The magnitude of the adaptation is related to the refractive error of the subject, with hyperopes observed to exhibit small adaptive shifts compared to emmetropes and myopes (McBrien and Millodot 1988; Rosner and Rosner 1989; Gwiazda *et al.* 1995). An explanation for this observation has been linked to the magnitude of baseline (pre-task) TA levels in the different refractive groups, where individuals with higher baseline TA tend to exhibit small adaptive shifts (McBrien and Millodot 1987; Rosenfield *et al.* 1994).

Another characteristic of accommodative adaptation is the time it takes for the adaptation to decay. Typically, the adaptation decay occurs between 60 – 90 seconds (Rosenfield *et al.* 1994). The time of decay depends on a number of factors including the method used to open-loop accommodation for measurement of TA, and the fixation distance. A previous study noted less decay when a target blurred with DoG grating was used in combination with a 0.5mm pin-hole compared to when accommodation was open-looped with a totally dark room (Schor *et al.* 1986).

Tonic accommodation and accommodative adaptation have been implicated in refractive development and progression, particularly in myopia (McBrien and Millodot 1988; Gwiazda *et al.* 1995). However, the focus of this review is to look at how these two accommodative characteristics may function within the cross-link interactions in the model of accommodation and vergence described by Schor and Kotulak (1986), which will be discussed shortly. Before that, a brief discussion of the characteristics and components of vergence is presented.

1.3.3 Components of Vergence Stimulus-Response

Disjunctive movements of the eyes, during which the eyes move in opposite directions are known as vergence (Quaia and Optican 2011). It is measured in degrees or prism dioptres (ΔD) or meter angles (MA). Preference for the metre angles unit is because it allows for a direct comparison between accommodation and convergence (Schor 2011). One MA is equal to the reciprocal of a viewing distance of 100 centimetres. The MA unit can be converted into prism dioptres or degrees by incorporating a subject's IPD. Four components of vergence have been identified similar to accommodation (Morgan 1980). These are disparity-driven vergence, blur-driven vergence, proximally-induced vergence, and tonic vergence. It is thought that these cues provide weighted contribution to the total response (Horwood and Riddell 2008; Horwood and Riddell 2009; Babinsky and Candy 2013; Wu *et al.* 2016). Retinal disparity, defined as the relative angular displacement of images from corresponding retinal points of the two eyes when viewing objects binocularly (Babinsky and Candy 2013), has been thought of as the primary cue driving vergence during binocular viewing of an object (Horwood and Riddell 2008). Disparate retinal images of an object in space initiates vergence eye movements, wherein the visual axes of the two eyes move in opposite directions to realign on the images of the object of regard, such that the retinal images in the right and left eyes fall within Panum's fusional area (Judge 1996; Schor 2011). The mechanism of vergence, which is also based on the negative feedback control like accommodation, uses disparity as an error-correcting cue (Sweeney *et al.* 2014). As previously discussed, due to the coupling of accommodation and vergence, gain in accommodation (A) can drive accommodative-convergence (AC). This is quantified by the AC/A ratio and can be measured under open loop conditions.

Proximal cues also drive vergence response. It has been reported that this cue component can provide a significant drive for larger changes in vergence (Schor *et al.* 1992). Proximal cues may be contained in monocular depth cues such as size, texture, and motion (Schor 2011; Wu *et al.* 2016). A final component of the vergence stimulus-response is that vergence response elicited due to the normal tonus of the extraocular muscles, i.e. that which would be observed in the absence of any visual stimulus. In the absence of any stimulus, it has been reported that vergence response assumes an intermediate value of 0.25 – 0.8MA (Rosenfield and Gilmartin 1988), but its magnitude tends to be age-dependent, due to differences in convergence demand – being small in children due to small IPD (Rosenfield 1997; Wong *et al.* 2001; Bharadwaj and Candy 2009).

Vergence adaptation, which represents the changes in the baseline tonic vergence following a sustained period of near fixation is an important characteristic of the vergence mechanism, which may have clinical implication particularly in children at risk of binocular vision dysfunctions (Schor 1979; Wong *et al.* 2001). Rosenfield (1997) in his review of tonic vergence and adaptation, suggests that the change observed post-task does not necessarily reflect a true change in the baseline tonic vergence, but that it may be the slowly decaying component of fusional vergence (fusional vergence is the reflex response to retinal disparity cue). The relationship between vergence adaptation and age has produced inconsistent results. Wong *et al.* (2001) reported higher vergence adaptation (0.45 MA change) in children aged 5.5 – 11.7 years compared to adults (0.11 MA change), which is inconsistent with other studies (Wu *et al.* 2016; Babinsky *et al.* 2016). Participants in Wong *et al.'s* (2001) study were older children, compared to the participants used in the other two studies. Wong *et al.* (2001) also used a target positioned at 15cm, with measurement made for five minutes. Published studies have reported on vergence adaptation pattern in children with myopia (Ehrlich 1987; Hung and Ciuffreda 1999; Sreenivasan *et al.* 2014), however, there is no such data for a representative sample of hyperopes, although some of the subjects described in Wu *et al.* (2016) included low hyperopes. Wu *et al.* (2016) speculated that vergence adaptation may play a role in binocular alignment for hyperopic children undergoing developmental changes and emmetropisation, but evidence of this is yet to be adduced. Further studies are required to understand vergence adaptation in the uncorrected hyperope.

1.3.4 Accommodation-vergence interaction

As previously discussed, the accommodative and vergence systems ensure that the eyes see a clear, single binocular image of an object during fixation. This is due to the cross-coupling of their neural responses. Cross-link interactions are important to ensure that both accommodation and vergence systems respond to a visual stimulus at the same time. Currently, a model of cross-link interaction widely accepted, and used in the literature is based on the work by Schor and Kotulak (1986). This model has been described as *dual-interactive controller* and consists of the *phasic* or *fast* acting components, and a tonic or slow acting component (Schor and Kotulak 1986; Schor 1999), and is drawn in Figure 1.4.

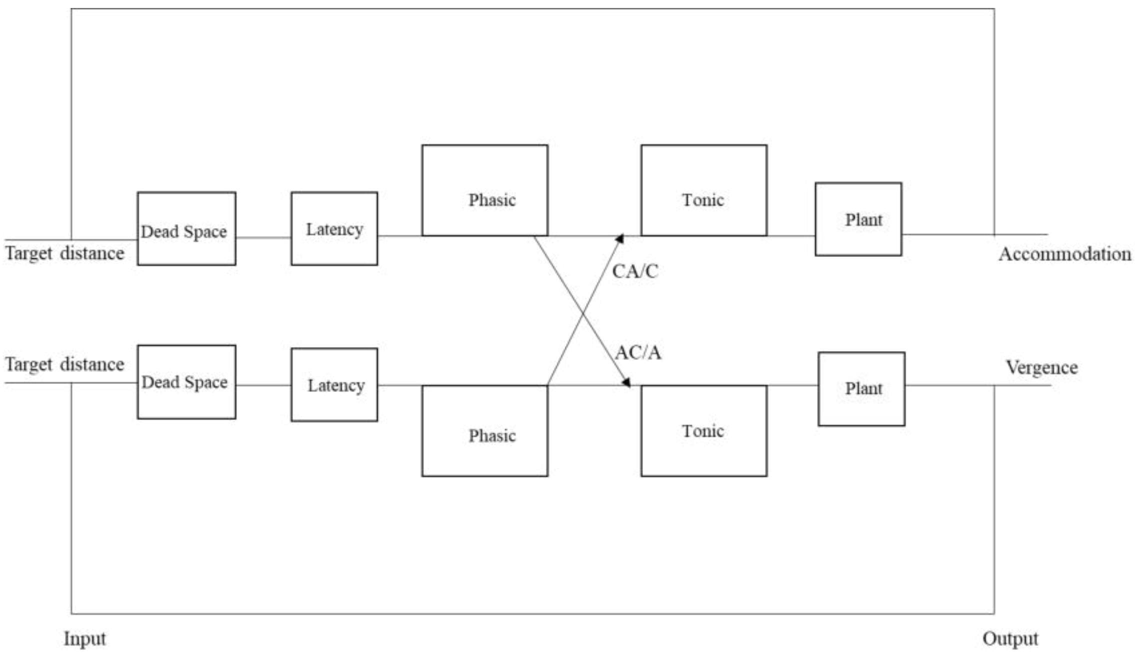


Figure 1.4. The dual – interactive model of accommodation and vergence control systems drawn from the model developed by Schor & Kotulak (1986). The dead space represents the depth of focus and Panum's fusional area respectively. The input signal must hit a threshold to set off a response, after a delay (latency period) for the two systems. The phasic and tonic components represent the controllers. The phasic component represents the fast component of the response, while the tonic component represents the slow, sustained response. The plant represents the dynamics of the ciliary body-lens (accommodation), and extraocular muscles (vergence). Cross-link interactions are represented by the AC/A & CA/C ratios.

The *controllers* are the neurological systems that provide the impulse for accommodation and convergence, while the *accommodative plant* is the ciliary muscle-lens, and extra ocular muscles that execute the accommodation and vergence respectively. The phasic component ensures rapid responses to external stimuli such as blur and disparity (horizontal disparity) are generated whereas the tonic component allows for sustained responses until adaptation to the intrinsic activity of the phasic component occurs. Furthermore, the phasic component is allowed to remain inactive, while the tonic component controls the response until a stimulus change occurs (Schor 1992). The model also has a cross-link component, whose function is to coordinate the responses of accommodative and vergence system under open-loop conditions. The cross-link interactions are quantified by the AC/A and CA/C ratios which represent the amount of convergence associated with a unit change in accommodation (Metre Angle / Dioptre or prism dioptres/Dioptre; ΔMA/D or ΔD/D), and the accommodation associated with a unit change in convergence (ΔD/ MA) respectively. The cross-link interactions can be estimated with the stimulus as reference – stimulus AC/A and CA/C ratios or relative to the response – response AC/A or CA/C ratios. Many investigators tend to use the response ratios, citing more accurate results with this method (Babinsky and Candy 2013; Sweeney *et al.* 2014). The cross-link interactions are thought to be stable over time and reciprocally related – a high AC/A may be associated with low CA/C (Schor 1992).

In the model described by Schor and Kotulak (1986), the cross-link interactions are located before the tonic component, but after the phasic component (Figure 1.4), which means that the cross-link interaction occurs before tonic component takes control. There are several experimental observations that have been adduced to support the location of the cross-link interaction. First, aftereffects of both accommodation and vergence can be stimulated by either blur or disparity suggesting that the tonic component responds to direct stimulation from the phasic component and the cross-link interaction (Schor and

Tsuetaki 1987). Another evidence for the placement of the cross-link interaction before the tonic component is the observation that decay of tonic aftereffects (accommodation adaptation and vergence adaptation) is different for the two motor systems. If the tonic component occurs before cross-link interaction, the decay would be expected to be the same (Schor and Kotulak 1986). Finally, the amplitude of the cross-link interaction at different velocities accounts for the locations of the different components of the model. At low velocities, the output of cross-link has been shown to be low, and this has been attributed to the slow tonic component of the model which does not directly stimulate the cross-link component (i.e. at low velocities, accommodation adaptation will cause the output of the accommodative convergence to reduce, while the prims adaptation will cause the output of vergence accommodation to reduce). However, at higher velocities representing the response from the phasic component (blur and disparity driven), the outputs of cross-link interactions are high (Schor and Kotulak 1986).

The observations described in the model by Schor and Kotulak (1986) were made in adults. However, it is plausible to assume that similar observations will exist in children, and thus this model could be used to explore alternative mechanisms underlying the accommodative and vergence motor systems in children with hyperopia, besides factors such as family history of strabismus, and anisometropia. Understanding the two motor systems in hyperopia is important as the question of why some hyperopic children become strabismic, and others do not, is poorly understood (Babinsky and Candy 2013).

First, given the reported inverse relationship between the AC/A and CA/C ratios, and the imbalances in tonic adaptability, one could posit that hyperopes who are poor tonic adapters with high AC/A ratios will drive excessive convergence when they attempt to achieve clear vision. This could put them at risk for development of esotropia (Babinsky and Candy 2013). A challenge to this view may relate to the fact that some published studies report of lower AC/A ratios in uncorrected hyperopia compared to myopia (Mutti *et al.* 2000), which may make this hypothesis less likely. Nonetheless, it may be possible to have a subset of hyperopes at risk of strabismus because of high AC/A ratios. Further application of Schor's model, at least in theory, would mean that there is a potential for some hyperopic children, with low vergence adaptation to developing refractive esotropia in their quest to achieve clearer vision; and in the case of those with high vergence adaptation to obtain clearer vision with any such outcomes. However, to date, there is no current data on the vergence adaptation of hyperopic children to further investigate this hypothesis.

1.3.5 Characteristics of Accommodative Response in Hyperopia

Accommodation is an important aspect of visual function as it largely dictates the quality of retinal image during fixation (Charman 2008). The use of accommodation to overcome blur, particularly in low to moderate hyperopia, results in extra accommodative demand on the hyperopic eye during near work (Candy *et al.* 2012). However, the measurement of accommodative response rarely exactly matches the demand in terms of distance of object of regard. Thus, accommodative response to a target demand is often described as the "lag" or "lead" of accommodation. The lead of accommodation occurs when the accommodative response produced is larger than the demand, while the lag of accommodation occurs when the response produced is lower than the demand. Normative data shows that children tend to demonstrate a lag of accommodation (McClelland and Saunders 2004). Compared to myopia, there are a few published studies on the accommodative response in hyperopic children. However, of the few published studies, the consistent finding is that children with hyperopia tend to hypoaccommodate to targets at near (Horwood and Riddell 2011; Kulp *et al.* 2014; Suh *et al.* 2016; Ciner *et al.* 2016), with hypoaccommodation increasing with increased hyperopia. Candy *et al.* (2012), using

Nott retinoscopy for a target at 50 cm (2.00D demand) in children aged 3.7 – 90 months (n=111) without prior optical correction, reported a lag of less than 2.00D when subjects' hyperopia was <= +4.00D. However, in subjects with greater levels of hyperopia (> +4.00D), the lag increased and became more variable. A similar finding of increased hypoaccommodation in higher magnitudes of hyperopia (whether corrected or not) has been reported by Horwood and Riddell (2011) who investigated 94 hyperopic participants (consisting of infants aged 6-26 weeks, and children aged 5-9 years) with some participants wearing full correction and others without correction. Large lags of accommodation in hyperopic children may relate to their poor use of retinal defocus/ blur to drive accurate accommodative response (Candy *et al.* 2012). Blur is the primary error-correcting cue in a closed-loop system, which implies that failure of the sensorimotor system to detect and utilise the right amount of blur might result in large errors or lag of accommodation (Yao *et al.* 2010). Thus poor blur sensitivity in children (Ingram *et al.* 1994; Rosenfield and Abraham-Cohen 1999; Schmid *et al.* 2002) may be a plausible explanation for large lags of accommodation in this population. Poor blur sensitivity in children with hyperopia has been reported in some studies (Nathan *et al.* 1985; Roberts *et al.* 2018b). Besides the sensorimotor system's sensitivity to retinal defocus/blur, it is possible that large lags of accommodation exhibited by some hyperopes may also be due to the inflexibility of the accommodative-vergence interaction to which the hyperopic child must make a preference – either for a single vision or a clear vision. In this hypothesis, the hyperopic child who chooses single vision to avoid excessive blur-driven accommodation is likely to have a large lag of accommodation (Babinsky and Candy 2013), while those who sacrifice double vision for clear vision may efficiently use blur to reduce lag, but over-converge in the process, potentially leading to double vision (followed by suppression), and to give rise to esotropia.

Although the findings of hypoaccommodation in hyperopic children discussed above are useful as they offer insights into the accuracy of the response, the question of sustained accommodative performance or the stability of the response is still unknown. It is possible that a hyperope could exhibit a relatively accurate response during a short response duration, but exhibit increased or variable accommodative lags over time. The significance of assessing sustained accommodative response in hyperopic children also reflects a natural use of accommodation during prolonged school work such as reading, and recreational activities as such as time spent on tablets or E-readers. Roberts *et al.* (2018a) have recently published results of their study on sustained accommodative response in children and adults. They reported no statistically significant difference between sustained accommodative response and refractive error. They measured accommodative response during a 10-minute duration in 54 children aged three to less than 10 years with refractive error ranging from -0.37 to +4.58D mean spherical equivalent. All children and adult participants of their study were not habitual spectacle wearers. Children performed an "active task" where they read story passages or answered questions about displayed shapes and a "passive task" where subjects looked at letters or shapes placed at 33cm. While their study provides useful insight into sustained accommodative response in hyperopia, it is not without limitations. First, there is not much difference between the "active" and passive "tasks" in terms of visual content as they both are likely to contain same spatial frequency contents (words/letters). The target distance may also not reflect the typical near working distance children engage in at school (Rosenfield *et al.* 2001). Further studies are needed to investigate sustained accommodative response in uncorrected hyperopic children using a robust study design which includes a large sample size. The relationship between sustained accommodative response and vergence has not been reported yet, as well as the effect of optical correction on the two measures.

Determining the stability of accommodative response in children is also important as retinal image quality depends not only on the accuracy of the response but its stability too (Candy and Bharadwaj 2007). The stability of the response during performance of sustained near task in uncorrected refractive error has received little attention (Harb *et al.* 2006). The stability of the accommodative response has been characterised by variations exhibited during viewing of a stationary target – what has been termed as *steady-state* fixation. It has been reported that the accommodative response exhibits small oscillations or variations in power of typically 0.50D during steady state viewing. This has been referred to as the *accommodative microfluctuations* (Charman and Heron 2015). While their exact role in the accommodative response control is yet to be fully understood, the current consensus is that microfluctuations serve as an 'error' cue to quantify the magnitude and direction of the mean defocus level to help maintain appropriate accommodative responses (Kotulak and Schor 1986; Charman and Heron 2015; Metlapally *et al.* 2016). A strong correlation has been reported between microfluctuations of accommodation and the objective depth-of-focus (Yao *et al.* 2010). The objective depth-of-focus quantifies how the accommodative system uses the smallest changes in blur to initiate a response. Thus, a correlation between the objective depth-of-focus and microfluctuations indicates its potential role in the accommodative response. Analysis of fluctuations in the accommodative response has been undertaken in both time and frequency domains. Describing the microfluctuations in the time domain using the root mean square (RMS) deviation, several authors have reported increased microfluctuations with decreased luminance (Gray *et al.* 1993b; Day *et al.* 2009b), and small pupil sizes (Gray *et al.* 1993a; Day *et al.* 2009b) in adult subjects. Candy and Bharadwaj (2007) have also reported larger RMS values (i.e. increased instability of microfluctuations) in infants (n=63, aged 8-30 weeks) compared to 8 pre-presbyopic emmetropic adult subjects. Roberts *et al.* (2018a) study described earlier in this section also found larger microfluctuations in children compared to adults which are similar to the results of Candy and Bharadwaj (2007). Results of Roberts *et al.* (2018a) study showed that large variabilities in the accommodative response were dependent on the type of task. They found significantly larger RMS in the passive task compared to active tasks and attributed this to differences in cognitive demand of the two tasks

In the frequency domain, two frequency components have been identified to characterise the microfluctuations associated with the accommodative response (Figure 1.5). These are described as the low-frequency component (LFC; <0.6Hz), and the high-frequency component (HFC; occurring between 1 to 2.3 Hz) (Kotulak and Schor 1986; Winn and Gilmartin 1992; Charman and Heron 2015). The HFC's role in the accommodation control system is unclear, with some authors suggesting that it may be accommodative noise originating from the mechanical and elastic properties of the lens (Winn *et al.* 1990). Also, the magnitude of HFC does not appear to have any relationship with depth of focus (DoF), as it does not respond to conditions which can alter the DoF such as changes pupil sizes, luminance and spatial frequency of the target (Gray *et al.* 1993a; Day *et al.* 2006; Day *et al.* 2009b). The HFC component also demonstrates large inter-subject variability (Charman and Heron 2015). A relationship between the HFC, ciliary body thickness and systemic arterial pulse has been reported (Schultz *et al.* 2009). Schultz *et al.* (2009) postulate that thicker ciliary bodies may dampen the effect of pulse on accommodation, thus reducing the HFC values measured. Their work also reported high powers for HFC in participants who were hyperopic (n=49, aged 8-15 years).

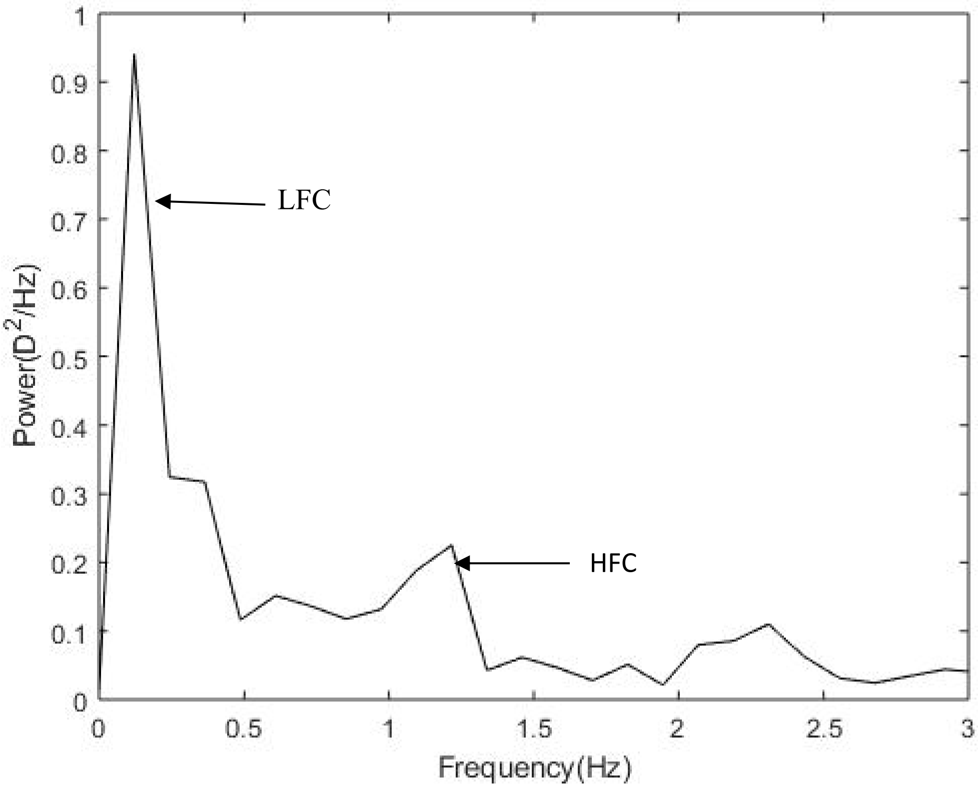


Figure 1.5. Graph showing the major frequency components of accommodative microfluctuations (0.3 Hz for LFC & 1.3Hz for HFC) of a hyperopic subject who took part in this PhD study. Subject fixated on a 4D target.

The LFC has been suggested to be an inherent component of the accommodative system (Charman and Heron 1988), playing an active role in maintaining an appropriate steady-state response (Charman and Heron, 2015). The magnitude of the LFC component has been shown to change with changes in factors which affect the DoF (Gray *et al.* 1993a; Day *et al.* 2009b). The LFC increases with smaller pupil sizes (Gray *et al.* 1993a; Day *et al.* 2009b), low target luminance (Gray *et al.* 1993b) and low and high target spatial frequencies (Day *et al.* 2009a) . Day *et al.* (2009a), using pinholes of diameter <2mm and very low target luminance (0.002 cd/m^2) found increased microfluctuations in the accommodative response in both myopes and emmetropes. It has been suggested that low luminance of target and small pupil sizes produce shallower contrast gradient in the cortical image due to a reduction in maximum spatial frequency available in the target (Day *et al.* 2009a). Therefore, larger alterations (increased microfluctuations) are required to allow the accommodation controller to detect changes in contrast in order to initiate a response (Day *et al.* 2009a). The contrast gradient has been defined as the difference in contrast between two points in a target divided by the space between the two points (Day *et al.* 2009b). Regarding the spatial frequency of targets, it has been suggested that mid or broadband spatial frequency targets produce steeper contrast gradient in the cortical image, so that small changes are sufficient to signal the accommodative controller to respond, unlike low and high frequency targets which produce shallower contrast gradients (Day *et al.* 2009b).

Although large inter-subject variabilities in microfluctuations have been reported, several studies have found myopes to exhibit larger microfluctuations than emmetropes (Seidel *et al.* 2003; Seidel *et al.* 2005; Day *et al.* 2006; Day *et al.* 2009a; Day *et al.* 2009b; Langaas and Riddell 2012). Myopes have been shown to have larger DoF compared to emmetropes (Rosenfield and Abraham-Cohen 1999; Vasudevan *et al.* 2006), and this increased DoF in myopes has been ascribed to reduced sensitivity to high spatial frequency targets (lower/lesser blur sensitivity) (Radhakrishnan *et al.* 2004). In the case of hyperopic refractive error, there is a paucity of data on the characteristics of microfluctuations with only recent work by Roberts *et al.* (2018a) available during a systematic literature search. Robert *et al.* (2018a) reported increased microfluctuations of accommodation in children (n=54, aged three to <10 years) with a varying range of refractive errors (-0.37 to +4.58D mean spherical equivalent). They observed statistically significant association between increased hyperopia and large accommodative microfluctuations. However, their work is limited by smaller sample size for both hyperopic and emmetropic controls and did not include a rich mix of high hyperopes (the highest amount of hyperopia reported was +4.58D). Further work is required to examine microfluctuations in a carefully sampled population of hyperopia. Additionally, it will be interesting to know whether accommodative microfluctuations in hyperopia is affected by optical correction, which is currently unknown.

1.3.6 Measurement of Accommodation

In clinical practice and research studies, the amplitude of accommodation (AA) and the accuracy of the accommodative response (AR) are the parameters often measured, although other aspects of the accommodative function such as velocity and accommodative facility can be measured too. While the accommodative amplitude represents the maximum amount of accommodation the eye is capable of when an object is progressively moved closer to the eye (McClelland and Saunders 2003; Win-Hall and Glasser 2008), the AR, also called errors of accommodation, measures the subject's plane of focus with respect to the accommodative target (Antona *et al.* 2009a). The accommodative facility measures the responsiveness of the accommodative system to changing stimuli over time, often involving the use of flipper lenses (plus and minus lenses) to stimulate and relax accommodation (Pandian *et al.* 2006). Correlations between these measures of accommodation functions have been reported (Allen and O'Leary 2006).

Traditionally, the subjective Push–Up/Push–Down (Push Away) technique has been used to measure AA in both research and clinical practice. This method of measuring AA is fast, simple and requires minimal equipment to use. It is usually performed by positioning a near reading chart or other targets at the subject's customary working distance, typically at 40 cm (2.5 D), and gradually moving the target towards the subject (Push–Up) until the subject reports a sustained blurring of the line of letters viewed. It is then moved closer, and then drawn back away from the subject (Push–Down/Away) until the target is reported as clear again. The AA can be an average of these two points, or the point at which blur is first reported, depending on the clinical protocol. The reciprocal of the distance of the chart (in metres) where blur was reported is recorded as the subject's amplitude of accommodation (Ostrin and Glasser 2004; Antona *et al.* 2009b). The measurement can be taken monocularly, and/or binocularly, and is typically performed with the patient's habitual spectacle correction in place.

Although this technique is widely used in both research and clinical settings, it suffers some inherent limitations; notably, its overestimation of the accommodative amplitude (Win-Hall and Glasser 2008; Antona *et al.* 2009b). This could be due to the influence of depth of focus (Ostrin and Glasser 2004), which is a reason AA has been obtained in presbyopes without any residual accommodation. Also, the subjective nature of the task and response biases from subjects can affect measurement. The fact that the method depends on verbal responses from the subject also means that it cannot be employed for use in infants and individuals with impaired communication (McClelland and Saunders 2003). Finally, this method of measuring the accommodative amplitude does not reveal the typical dioptric changes in refraction that occurs as the eye accommodates.

Objective measurement of the accommodative response amplitude can also be obtained. These objective measurements include using the technique of dynamic retinoscopy, employing an autorefractor to measure refractive error for different target distances, or infra-red eccentric photorefraction (Win-Hall and Glasser 2008). For autorefractometry and photorefraction techniques, the difference between baseline refraction values when a subject fixates a target at distance, and near becomes the objective response amplitude. Win-Hall and Glasser (2008) found lower values of accommodation for the two objective instruments (WR-5100K Gran-Seiko autorefractor and I Trace aberrometer) compared to the values obtained with the subjective push-up method.

The dynamic retinoscopy technique has been used often in both clinical practice and research to measure the accommodative response, particularly in children because of the rapidity with which results can be obtained (McClelland and Saunders 2004; Tarczy-Hornoch 2009). It has been shown to be a valid and repeatable technique for assessing the accommodative response (McClelland and Saunders 2003; Tarczy-Hornoch 2009).

There are two main ways of performing dynamic retinoscopy which includes either using Nott retinoscopy (Nott 1925; McClelland and Saunders 2003) or the Monocular Estimate Method (MEM) (Rouse *et al.* 1982; Locke and Somers 1989). In Nott retinoscopy, AR is measured by having a subject fixate a near target placed at a fixed distance and examining the retinoscopy reflex, moving the retinoscope closer or farther away from the subject until a neutral reflex is achieved (McClelland and Saunders 2003). The reciprocal of the point at which neutrality is achieved in meters is the AR. The MEM technique, which is also performed with the subject fixating on a near target, involves the use of spherical lenses to neutralise the retinoscopic reflex, which is fixed at the distance of the near target, instead of the relative movement of the examiner. Despite the potential difficulty that could be associated with the introduction of a series of lenses before a young child, it has been successfully used to assess the AR in children (Tarczy-Hornoch 2009). Dynamic retinoscopy, although a straightforward and objective technique, also suffers from a potential observer bias, which can arise from the judgement of neutrality due to the knowledge of the target position (demand) (Manny *et al.* 2009).

The use of automated instruments such as autorefraction and eccentric infrared photorefraction for the measurement of the accommodative response have been widely reported (Seidemann and Schaeffel 2003; Win-Hall and Glasser 2008). Open-field autorefractors are best suited to enable different target distances to be utilised, and they have been used to measure mean accommodative performance in different refractive populations (Day *et al.* 2006; Day *et al.* 2009b). It can also be adapted to a dynamic mode where it offers a continuous measurement of the accommodative response monocularly (Day *et al.* 2006). Eccentric, infrared photorefractors have also been used extensively in recent times to quantify different aspect of the near triad as it allows simultaneous, binocular measurement of accommodation, vergence and pupil size (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Horwood and Riddell 2011; Doyle *et al.* 2016;

Doyle *et al.* 2017; Roberts *et al.* 2018). Its remote positioning at one metre, also makes it ideal for use in younger subjects who are more likely to cooperate (or be less distracted by) an instrument that is not proximal to them (Choi *et al.* 2000). Earlier generations of the instrument used a sampling rate of 25Hz, but 50Hz versions are also commercially available and have been used in research studies. Just like the autorefractor, the eccentric, infrared photorefractors require individual calibration for both defocus and gaze positions, as the device uses a population average software, whose use has been shown to produce wide inter-subject variability (Choi *et al.* 2000; Bharadwaj *et al.* 2013). This PhD project used the 50Hz PlusOptix PowerRefractor 3™ (Nuremberg, Germany), to investigate sustained accommodation and vergence in children with and without hyperopia. In Chapter 2 of this PhD work, an extensive study on the calibration of the PowerRefractor 3™, exploring different gaze position calibration techniques will be presented.

Theoretical predictions of the accommodative response from anterior segment biometric changes which occur during accommodation have also been reported (Ramasubramanian and Glasser 2015). Ramasubramanian and Glasser (2015), predicted the AR using linear regression of the ocular biometric changes measured during accommodation. Anterior segment biometric changes were measured with ultrasound biomicroscopy. However, this method and its reliability and validity in measuring AR would need much further evaluation before its adoption for use.

1.4 Hyperopia and Other Visual Function Measures

Visual function measures such as visual acuity and stereoacuity have often been used as criteria for referral during refractive error screening, and to enable optical management of refractive errors (Horwood and Riddell 2011; Kulp *et al.* 2016).

1.4.1 Visual Acuity

Visual acuity (VA) is one of the most important visual function measures often used to diagnose, monitor disease progression and treatment outcomes (Anstice and Thompson 2014). Published normative data for visual acuity in children have often been limited to the pre-school years (Salomao and Ventura 1995; Pan *et al.* 2009; Leone *et al.* 2014). Often, an assumption of a good VA has been defined as 6/6 Snellen, but children and adults tend to score better than that. In children with uncorrected hyperopia, an inverse relationship between the level of vision and the magnitude of hyperopia has been reported, where greater levels of hyperopia are associated with reduced VA (Kulp *et al.* 2014; Ciner *et al.* 2016; Suh *et al.* 2016). Some studies also observe reduced VA in low to moderate amounts of hyperopia, contrary to what would be expected; given that uncorrected hyperopes can potentially use accommodation to improve the level of vision (O'Donoghue *et al.* 2010). It is possible that individuals with low to moderate amounts of uncorrected hyperopia, with reduced distant VA may have deficient accommodation, and hence may require correction for clear vision (Horwood and Riddell 2011; Bruce *et al.* 2018). Similar to distance vision, some studies have reported a dose-response relationship between near VA and uncorrected hyperopia; wherein, increasing hyperopia results in decreasing vision at near (Ciner *et al.* 2016). The uncorrected hyperope must accommodate at far to achieve a clear retinal image and further effort is required for near tasks such as reading optotypes, which may be difficult to achieve for some.

1.4.2 Stereoacuity

Stereoacuity is an important visual function with associations to other ocular parameters such the quality of near vision (Suh *et al.* 2016; Ciner *et al.* 2016). A higher magnitude of uncorrected hyperopia in children is often associated with increased risk of strabismus and amblyopia (Robaei *et al.* 2007; Kulp *et al.* 2014; Ciner *et al.* 2016). These outcomes will, in turn, affect stereo function to a greater or lesser extent depending on the type and extent of the deficit (Robaei *et al.* 2007; Kulp *et al.* 2014). Poor stereoacuity has also been reported in moderately uncorrected hyperopic children without any strabismus or amblyopia (Yang *et al.* 2012; Kulp *et al.* 2014; Ciner *et al.* 2016; Kulp *et al.* 2016; Suh *et al.* 2016). The finding of poor stereoacuity scores in uncorrected hyperopes may be due to blur from uncorrected refractive error which may affect the ability to resolve details in the stereo targets (Westheimer and Mckee 1980).

Hyperopic anisometropia is a significant factor which contributes to impaired stereo function (Robaei *et al.* 2007; Yang *et al.* 2012). Robaei *et al*. (2007), found anisometropia to be independently associated with stereoacuity scores in subjects without amblyopia or strabismus. Foveal suppression in the more hyperopic/poorer seeing eye, as well as reduced contrast and density of fusional detail, have been put forward for the association between anisometropia and reduced stereoacuity (Simpson 1991). Evidence of poorer stereoacuity scores in uncorrected hyperopic children at risk of developing strabismus and amblyopia (Suh *et al.* 2016; Ciner *et al.* 2016), may suggest its use as part of the criteria for evidence-based prescribing in children with hyperopia.

1.5 Educational Attainment and Uncorrected Hyperopia

Vision plays a significant role in the learning process (Narayanasamy *et al.* 2016). Consequently, anomalies of vision such as hyperopic refractive errors have the potential to reduce the efficiency of visual skills required for learning. Some studies have investigated the impact of uncorrected hyperopia on measures of academic performance in natural, uncorrected hyperopes (Rosner and Rosner 1997; Williams *et al.* 2005; Shankar *et al.* 2007), as well as subjects with simulated hyperopia (Narayanasamy *et al.* 2014; Narayanasamy *et al.* 2015). Increased emphasis on formal literacy skills (Kulp *et al.* 2016); increasing duration of classroom tasks, mostly at near (Ritty *et al.* 1993; Narayanasamy *et al.* 2016); and growing use of portable electronic devices such as tablets and E-readers for prolonged periods of time both at school and in the home all have the potential for an increased burden on the accommodative-vergence system (Collier and Rosenfield 2011; Benedetto *et al.* 2013). Thus, the hyperopic child, with already increased pressure on the accommodative-vergence system could be particularly disadvantaged with regard to their education and learning.

An association between hyperopia and poorer early literacy skills (including: print knowledge, which measures the child's ability to identify letters or written words; definitional/receptive vocabulary, which evaluates the child's ability to name and describe an object or to map a visual stimulus to spoken words; and phonological awareness, which assesses the child's ability to hear, recognise, and manipulate the sounds of language) have been reported in pre-schoolers (Shankar *et al.* 2007; Kulp *et al.* 2016). Similarly, studies of the association between hyperopia and literacy scores or reading performance in older children have been reported (Rosner and Rosner 1997; Williams *et al.* 2005). Earlier studies, using large population-based samples (n= 200 and 1910 respectively), however, reported no or weak association between the two (Blika 1982; Helveston *et al.* 1985). In the study by Kulp *et al.* (2016), hyperopia ≥3.00D to ≤6.00D, which was associated with reduced binocular near VA (≤20/40 (6/12) or reduced near stereoacuity (≤240 seconds or arc), in children aged four to five years (n=244), was linked to poorer performance on tests of early literacy. They found significant differences between hyperopes and emmetropes in print knowledge scores, definitional vocabulary, but no differences in phonological awareness. The worse performance of hyperopic pre-schoolers in the study by Kulp *et al.* (2016) is consistent with the work of Shankar *et al.* (2007) despite differences in their study methods including small size (n=13), test instruments and age of participants (4–7 years) in Shankar *et al.* (2007) work. In older children, the trend of study results are the same as in pre-schoolers: there is a poorer reading performance in hyperopes compared to emmetropic or myopic individuals (Rosner and Rosner 1997; Williams *et al.* 2005).

While these studies suggest an association between uncorrected hyperopia and poorer academic performance, no study has yet investigated causality. Causality has yet to be established due to several confounding variables which can interact with the effect of hyperopia on literacy scores. These include: visuocognitive, visuomotor and attention deficits; intelligence quotient (IQ) of the child; socioeconomic status of child's family, reading environment at home, amount of hyperopia present, the effect of crowding on the type of test administered (Atkinson *et al.* 2002; Atkinson *et al.* 2004; Shankar *et al.* 2007). Atkinson *et al.* (2002) have argued that deficits in visuocognitive and visuomotor domains in hyperopic children are responsible for the observed poorer academic performance. They attributed these deficits to poor neural processing due to hyperopia and hence postulated that they may not be remedied by hyperopic spectacle correction. Some published studies which have observed an association between impaired ocular growth (as may be the case in hyperopia) and cerebral development lend support to the hypothesis of Atkinson *et al.* (2002), (Miller 1992; Wallman and Winawer 2004). However, there is contrary evidence that optical correction may improve cognitive abilities in ametropic children, which would contradict the neural deficit hypothesis (Roch-Levecq *et al.* 2008). Furthermore, reduced academic performance in simulated hyperopia (Narayanasamy *et al.* 2015), as well as the findings in some early literacy tests, where hyperopia was associated with tests requiring only visual but not auditory skills (Shankar *et al.* 2007; Kulp *et al.* 2016), contradict a simple neural deficit hypothesis.

It is also possible that poorer performance of hyperopes on these academic tests could be due to lower IQ. However, evidence from a longitudinal study on measures of IQ, reading and refractive error in children aged seven to 11 years suggests that IQ alone cannot explain differences in literacy performance (Williams *et al.* 1988). William *et al.* (1988) found that although differences existed in IQ when participants were assessed at baseline (age seven) and later at age 11, there were no differences in reading scores at either age suggesting a lesser influence of IQ on the reading scores.

Interaction between hyperopia and the effect of the home environment (parental influence at home and educational engagement of the child), as well as the socioeconomic status of families, have also been identified as potential influencing factors to the association between hyperopia and academic performance (Hoff 2003; Rindermann and Baumeister 2015). Children in high socio-economic status homes tend to have better productive vocabulary scores than those in lower socio-economic homes (Hoff 2003). Parental educational behaviour at home including the number of words spoken to the child at home, and the quality of communication experienced by the child, have been reported to be greater in higher socio-economic homes than in lower socio-economic home (Hoff 2003; Rindermann and Baumeister 2015). If hyperopia is associated with the socio-economic status of parents, or the educational level of parents, then, all these could be potential confounders in assessing the relationship between literacy and hyperopia. However, this has not been extensively studied, and Castagno *et al.* (2014) did not find any evidence of a relationship between hyperopia and socio-economic status or parental educational level in their meta-analysis of hyperopia prevalence.

Visual function measures which may explain the impact of uncorrected hyperopia on literacy outcomes include blur and ocular alignment/vergence. Blur from deficient accommodation in uncorrected hyperopia could make identification of letters and words more difficult. In support of this, Kulp *et al*. 2016, reported deficient accommodation (larger lags of accommodation), and poorer binocular near VA in their hyperopic pre-schoolers. Moreover, work by Chung *et al.* (2007) in 19 subjects (aged 22-29 years), where dioptric blur was induced by placing plus lenses before a fixed pupil size, found 3.00D of blur to significantly impair reading performance. Prolonged blur from sustained near work would further compound the effect of blur on reading performance (Narayanasamy *et al.* 2014). It is worth noting that pupil sizes will influence how blur impacts on reading performance due to depth of focus (Campbell and Gregory 1960; Chung *et al.* 2007; Xu *et al.* 2016), though this effect will not be necessarily peculiar to a particular refractive error (Orr *et al.* 2015). If blur is a major explanation for the poorer literacy performance in uncorrected hyperopes, then the role of spectacle correction will be of interest to all stakeholders of the child. Recent studies report that spectacles wear may improve literacy scores particularly in subjects who are adherent to spectacle wear (van Rijn *et al.* 2014; Bruce *et al.* 2018).

Besides blur, the binocular status of the uncorrected hyperopia may affect academic performance (Simons and Gassler 1988). In their meta-analysis of studies on vision anomalies and reading skill, Simons and Gassler (1988) suggested that below average reading scores in uncorrected hyperopia may be due to the extra accommodative effort required for near tasks such as reading which may also affect the vergence system, due to the neural coupling between the two systems. This observation is consistent with recent studies, which have reported associations between poorer academic scores and vergence dysfunctions (Shin *et al.* 2009; Narayanasamy *et al.* 2014). The accompanying asthenopic symptoms such as headaches, inability to sustain focus, fatigue and binocular anomalies such as esophoria at near could make reading difficult. This could also produce aversion for reading and other near work activities, and the attending sequelae of poorer reading skills – bearing in mind that increased reading can improve vocabulary and conceptual knowledge (Shankar *et al.* 2007), so if the child does not engage frequently, the poorer they become.

While more evidence is needed to aid a better understanding of the impact of uncorrected hyperopia on educational attainment, it is important to stress that future studies need to apply robust methodologies by way of subject sampling (large samples to enhance statistical power), inclusion and exclusion criteria, definition and measurement of hyperopia, and the type of literacy or academic test administered. Some of the methods for determining hyperopia for inclusion criteria lacked robustness, for example, the use of results of fogging lenses test as inclusion criteria for hyperopic status (rather than cycloplegic assessment of refractive error) (Williams *et al.* 2005), could potentially have underestimated the true number of hyperopes in the sample. The application of standardised, uniform measures to assess academic performance should also be considered, such that results can readily be compared across studies.

To ensure all children have equal opportunities to perform well in their educational pursuits, the hyperopic child needs both visual attention and educational support, particularly in pre-schoolers whose early literacy experiences may be predictive of later literacy ability in older children (Levy *et al.* 2006).

1.6 Management of Hyperopia

Diagnosis of hyperopia is a combination of patient symptom presentation, assessment of visual function such as distance and near VAs, stereoacuity, and retinoscopy, preferably cycloplegic retinoscopy, especially for initial assessment. These are procedures routinely performed in clinical eyecare practice, and with the emerging evidence from poorer scores on near VA tests, stereoacuity, and dynamic retinoscopy, the diagnosis of hyperopia may be easily arrived at. However, the majority of children do not attend for routine eye examinations that include refraction. In the UK, the National Screening Committee (NSC) recommends vision screening at school entry for children aged four to five years to identify children with significant refractive errors, and at risk of amblyopia and strabismus (The UK NSC policy on Vision defects screening in children, 2013 available at: https://legacyscreening.phe.org.uk/vision-child). The screening protocol is distance visual acuity alone and thus many hyperopes will not be detected, given a screening criteria of <=0.2logMAR. Beyond screening and detection, the management of hyperopia is a subject of varied discussion in the literature. Management of hyperopia includes: no intervention, spectacle correction, contact lenses correction, and refractive surgery. Spectacle correction remains the traditional, most cost-effective, and least complicated treatment option especially in children (Morjaria *et al.* 2016).

There exist considerable intra- and inter-professional differences in the approach to spectacle correction of childhood hyperopia between optometry and ophthalmology (Lyons *et al.* 2004; Cotter 2007). The American Optometric Association has a clinical guideline for the care of the patient with hyperopia, but it falls short of giving cut-off points at which hyperopia should be corrected (Moore *et al.* 1997). Similarly, the American Association of Pediatric Ophthalmology and Strabismus have a preferred practice pattern built on clinical consensus for the spectacle correction of hyperopia in children, with a pattern towards optical correction of only higher levels of hyperopia

(Table 1.2). However, many would consider these conservative criterions, which do not take other clinical considerations such as VA, near binocular status and accommodative performance, into account. A review by Leat (2011) using evidence available then, summarised key considerations that should inform prescribing in children with uncorrected hyperopia, which includes the age of the child, the role of emmetropisation, amblyogenic factors, and visual function measures. She created a set of guidelines for clinicians to use to aid hyperopia management. However, as Leat (2011) recognises, not all her guidelines are supported by evidence, and still have elements of clinical opinions. For example, she recommended prescribing full non-cycloplegic subjective refraction for school-aged children. However, the evidence of the benefit of this recommendation is lacking, meanwhile, other clinicians prescribe full cycloplegic refraction for hyperopic children (Horwood and Riddell 2011). The optical management of the hyperopic child is an area which requires continuing research to generate robust evidence which will support cost-benefit analysis.

Table 1.2. Preferred practice guidelines for refractive correction in infants and young children developed by the American Academy of Ophthalmology.

Condition	Refractive errors (dioptres) Age <1-year	Age 1-2 years	Age 2-3years
Isometropia			
Myopia	-5.00 or more	4.00 or more	-3.00 or more
Hyperopia (no manifest deviation)	+6.00 or more	+5.00 or more	+4.50 or more
Hyperopia (with esotropia)	+2.50 or more	+2.00 or more	+1.50 or more
Astigmatism	+3.00 or more	+2.00 or more	+2.00 or more
Anisometropia (without strabismus)			
Myopia	-4.00 or more	-3.00 or more	-3.00 or more
Hyperopia	+2.50 or more	+2.00 or more	+1.50 or more
Astigmatism	2.50 or more	2.00 or more	2.00 or more

Consideration for spectacle prescribing in infants, and those children in the age group 3-6 years, depends on the magnitude of the child's error, and how it compares with age-matched normative data (Moore *et al.* 1997; Leat 2011). Infants and younger children whose refractive errors are within the normal range for their age are expected to emmetropise (Ehrlich *et al.* 1995; Ehrlich *et al.* 1997; Mutti *et al.* 2005; Mutti *et al.* 2009), with the rate of emmetropisation thought to be related to the initial refractive error (Saunders *et al.* 1995; Mutti *et al.* 2005). Those with initial large errors have an increased rate of change compared to those with little or moderate errors, so that infants/children with high magnitude of hyperopia can and do emmetropise (Mutti *et al.* 2005; Horwood and Riddell 2011). Emmetropisation, the process by which a balance is achieved between ocular growth (axial length increases) and the other optical components of the eye (Mutti *et al.* 2009), may be active in the early months after birth, reaching peak levels at about age 3 years (Mutti 2007). The decision to prescribe or not to prescribe in this cohort presents a trade-off: whether to allow the potential for normal emmetropisation to occur in the developing child or to intervene and potentially halt the emmetropisation process when spectacles are given (Mutti 2007). With the quality of visual signal or feedback purported to provide stimulus for ocular growth (Troilo 1992; Mutti 2007), spectacle correction of low to moderate uncorrected hyperopic infant could impair this process and hence may be unwarranted. Two previous randomised, controlled trials evaluating the effect of spectacle correction on emmetropisation in infants have yielded conflicting results (Atkinson *et al.* 2000; Ingram *et al.* 2000). Atkinson *et al*. (2000), found no difference in emmetropisation between infants (n=148, age range 8-9 months at the start of the study) treated with partial spectacle correction and those who were not after 36 months of follow-up. However, Ingram and Lambert (2000), reported that partial spectacle correction (subjects were given 2.0D less than their cycloplegic refraction) impeded the process of emmetropisation in hypermetropic infants (n=289, aged 6 months at the start of the study) who were followed for an average period of 44 months. In Ingram and Lamberts' cohort, constant spectacle wearers who failed to emmetropise also developed strabismus. Differences in the findings could be attributed to the different levels of partial corrections offered in the study (2D less for Ingram and Lambert, and 1D less for Atkinson and colleagues) which could affect the magnitude of defocus available. Also, Ingram and Lambert (2000) attributed differences in the results to the failure of Atkinson *et al.'s* (2000) study to separate those with strabismus from those without strabismus during analysis. For infants with higher levels of hyperopia associated with poor VA, who are likely candidates to fail the emmetropisation process (Mutti *et al.* 2009), it would seem sensible to prescribe spectacle correction, since it may confer protection against the development of strabismus and/or amblyopia.

In older, school-aged children, typically above 6 years of age, the emmetropisation process is mostly completed by this time (Gwiazda *et al.* 1993; Jones *et al.* 2005). Consequently, the fear of optical correction interfering with emmetropisation is considered less important. However, a combination of symptom presentations, as well as the impact of hyperopia on important visual function measures such as visual acuity, stereoacuity, accommodation, and vergence findings; and other educational measures should dictate the need to or not prescribe correction. However, the opportunity to use these factors other than emmetropisation to prescribe is constrained by the paucity of evidence on the role of optical correction in improving these visual function measures, particularly in low to moderate levels of hyperopia, whose clinical management remains a grey area. Mutti (2007), using data from the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study (CLERRE study) argues on the effect of refractive correction on distance visual acuity, stating that visual acuity typically improved by 0.05 to 0.15 logMAR with optical correction. Recent work by Bruce *et al.* (2018) also reports of improved VA with spectacle correction for participants who were adherent to spectacle wear. On the contrary, the evidence of the role of optical correction on the accommodative function, where large and variable lags have been reported even in moderate levels of hyperopia (Horwood and Riddell 2011; Roberts *et al.* 2018a), is yet to be ascertained. Further, more insightful evidence would be to determine the effect of correction on accommodation and vergence outputs during engagement in sustained near visual tasks. It is the aim of this project to contribute to this discourse.

1.7 Chapter Summary

- There is a high prevalence of uncorrected hyperopia in young children. There is a growing body of evidence of the impact of uncorrected hyperopia on the visual, and educational outcomes of children.
- Key amongst the visual measures affected by uncorrected hyperopia is accommodation. The accommodation system allows the eye to see at different object distances, and due to neural coupling with convergence and pupil size: these mechanisms can also be affected by uncorrected hyperopia.
- Hyperopes have been reported to exhibit larger and variable lags of accommodation. However, the current evidence available is limited to relatively short response duration. The accuracy of sustained accommodative response and other characteristics such as its stability in hyperopia could contribute to the knowledge of when hyperopia requires correction. We currently know little about these dynamics.
- Measurement of the accommodative response critically depends on the accuracy of the measuring device. While dynamic retinoscopy provides a quick clinical means of assessing accommodation at a single point in time, this technique would not provide sufficient information for sustained responses. Modified autorefractors can provide the means to capture responses over time but only operate on a single eye at any one time. Thus, the eccentric, infrared photorefraction is a child-friendly, safe and an appealing technology for measurement of the accommodative response in this population, yielding binocular measurements and also providing pupil size and vergence information. However, the accuracy of measurements depends on the individual calibration of the device. Therefore, in the next chapter, a thorough investigation of calibration protocols for this device is explored for its later use in this PhD work.

Chapter Two: Calibration of the PowerRefractor 3™ for Measurement Defocus and Gaze Position Estimates

2.1 Introduction

In this chapter, a background of the principle of photorefraction is presented. The PowerRefractor III (PlusOptix, Nuremberg, Germany), subsequently referred to as PowerRef 3™ for the rest of this chapter and other chapters of the thesis, was used as a model of current version of slope-based, eccentric infrared photorefractors. Prior to its utilization in the main study, the instrument was fully investigated to determine the accuracy and repeatability of calibration techniques for defocus and gaze position estimates of the device. The chapter is organised in the outline below:

- Background to photorefraction
- Recruitment and experimental set-ups for calibration techniques
- Results and discussions
- Chapter discussion and summary

2.2 Background to photorefraction

The eccentric infrared photorefraction technique, on which the PowerRef 3™ operates, allows simultaneous refraction of the two eyes, using a camera or other image-capturing technology, typically positioned one meter from a subject (Roorda *et al.* 1997; Choi *et al.* 2000; Blade and Candy 2006; Howland 2009; Bharadwaj *et al.* 2013). The photorefractor has an interesting history of being invented and used for military communication in the earlier versions (Howland 2009). The current versions, however, are mostly for clinical and research applications – including assessing accommodation measurements in animals (Glasser *et al.* 2006; Howland 2009; Bossong *et al.* 2009), and humans (Choi *et al.* 2000;

Blade and Candy 2006; Bharadwaj and Candy 2008; Doyle *et al.* 2016); and for screening for refractive errors in children (Hunt *et al.* 2003; Satiani and Mutti 2011). The wider acceptance of photorefraction in both research and clinical settings is due to the advantages offered by this technology. Such advantages include: a remote working distance which makes photorefraction suitable for use in subjects with less attention span like infants and children who can be examined whilst sitting on the lap of a parent (Blade and Candy 2006; Howland 2009; Bharadwaj and Candy 2009), and animals (Glasser *et al.* 2006). In addition, the subject positioning does not have to be precisely fixed, as long as the eyes are in the field of the camera (Howland 2009). With a high sampling rate (e.g. 50Hz for the PowerRef 3™), data can be obtained quickly. Furthermore, video-based recording results in the production of a permanent record of the measurements which can be stored for future use/reference.

The optics of the photorefraction technique involves a "double passage" of light through the optical system of the eye (Roorda *et al.* 1997). A centralised light source at a fixed distance, measured from the limiting aperture of a camera is projected onto the retina. Light returning from the retina is captured by the camera which is focused on the plane of the pupil producing a crescent-shaped reflex (Figure 2.1), which has different characteristics depending on the refractive status of the eye (Roorda *et al.* 1997). In the initial stages of photorefraction technology white light sources were used, until the introduction of infra-red (IR) light emitting diode (LEDs) into later versions, which have the advantages of minimal illumination allowing optimal pupil sizes, and minimal distraction from fixation targets. The light source can be a single spot of light (zero eccentricity), or an extended source (or multiple sources) of light located at a fixed distance from the camera's aperture (Roorda *et al.* 1997; Choi *et al.* 2000). Earlier eccentric photorefractors, based measurement of the refractive state of the eye on the size and orientation of the crescent reflex observed within the pupil (Figure 2.1). However, current eccentric models estimate the eye's refractive state using a slope-based calibration of the light intensity profiles in the pupils, which can be referred to as the *defocus calibration factor* (Sravani *et al.* 2015). The eccentric light sources generate a combined linear, luminance profiles in the pupil from which a linear regression fit can be used to quantify the magnitude of defocus of the eye. It has been shown that the slope of the luminance profile in the pupil increases with increasing refractive error (Roorda *et al.* 1995; Roorda *et al.* 1997; Choi *et al.* 2000). The camera's light source concurrently produces a sharp, first Purkinje-image for simultaneous estimates of gaze position (Blade and Candy 2006). In addition, the device uses a contrast detection software, which can locate the pupils to provide simultaneous measurement of pupil sizes (Blade and Candy 2006). Thus, this instrument allows simultaneous, and continuous measurement of the near triad (accommodation, vergence, and pupil size), and can be employed during active human behaviour (Howland 2009).

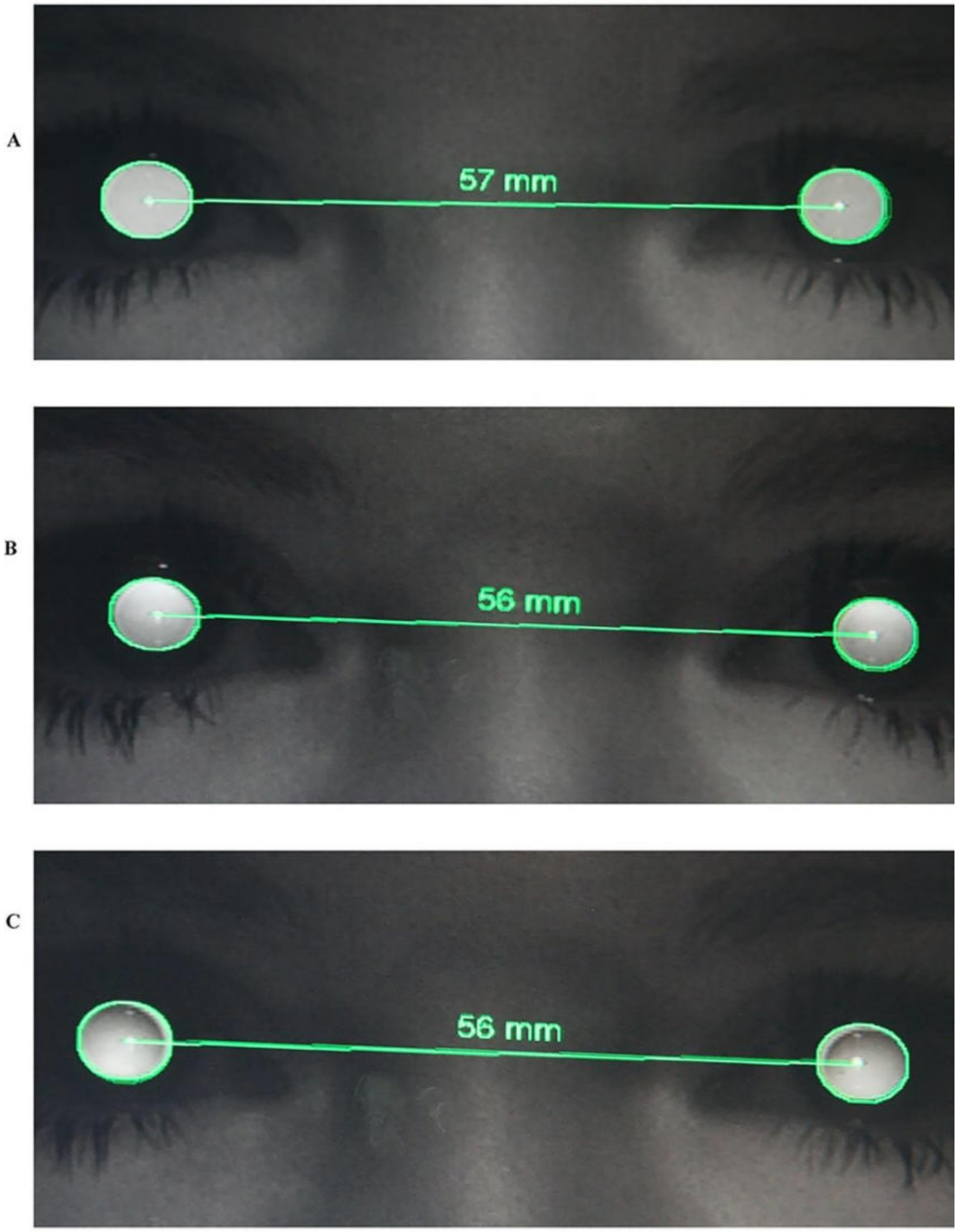


Figure 2.1 Figure showing the luminance profiles of IR light reflected through the pupils in different refractive conditions. In panel A, there is a uniform intensity of the distribution of light in the entire region of the pupils. This occurs in emmetropia. In panel B, there is a "myopic crescent" showing as intense distribution of light in the upper segment of the pupils. This occurs when the eyes are focused in front of the plane of camera aperture, and due to the arrangement of the IR lights in the upper portion of the aperture, the intensity of the light distribution in the pupils is greater in the same direction of the pupils. Panel C shows luminance profiles in a hyperopic eye. The "hyperopic crescent" is located in the lower half of the pupils, with the principle behind this being opposite to what happens in myopia. Images obtained by the kind courtesy of Dr Lesley Doyle, Ulster University.

Variability in the slope of the luminance profile– *defocus calibration factor*, of individuals with the same amount of defocus, have been observed in previous studies (Schaeffel *et al.* 1993; Choi *et al.* 2000). This has been attributed to several factors including: the size of the pupils, the distance between the camera and the subject's eye, the degree of eccentricity of the LEDs (the number of light sources arranged eccentrically around the camera's aperture), refractive error of the eye, higher-order monochromatic and chromatic aberrations of the eye (Bobier and Braddick 1985; Schaeffel *et al.* 1993; Roorda *et al.* 1995). The reflectance properties of the retina have also been purported to affect the luminance profile distribution, suggesting that variabilities can be observed for different ethnic groups (Bharadwaj *et al.* 2013; Sravani *et al.* 2015). Consequently, individual calibration of the *defocus calibration factor* to reduce intersubject variability has been widely accepted and used in several studies employing the slope-based, eccentric photorefraction technique for the measurement of the refractive state of the eye. Individual calibration of the *defocus calibration factor* is, therefore, a critical step to ensure accurate estimates of refraction by the PowerRef 3™.

To estimate gaze position of the eye, modern photorefractors incorporate an eye -tracking tool, which uses a conversion factor to convert the millimetre separation between the first Purkinje Image (PI) and the entrance pupil centre (PC, the virtual image of the anatomical pupil as seen through the cornea and anterior chamber) to angular unit of degrees or prism dioptres (Brodie 1987; Barry and Backes 1997). The conversion factor, referred to as the *Hirschberg Ratio* (HR), is the change in angular rotation of the eye which corresponds to a millimetre displacement of the first PI relative to the PC, in unit of degrees per millimetre or prism dioptres per millimetre (Brodie 1987; Riddell *et al.* 1994; Schaeffel 2002; Jagini *et al.* 2014). The HR depends on two biological factors: the anterior corneal curvature, and the anterior chamber depth (ACD) (Brodie 1987), which varies between individuals. Consequently, using a population-average HR such as used by the PowerRef 3™ (11.82 °/mm), could result in over or underestimation of eye position. Previous studies have reported wide inter-subject variability in HR (Riddell *et al.* 1994; Schaeffel 2002; Jagini *et al.* 2014), which implies that individual calibration of the HR is a useful step towards obtaining accurate gaze position estimates.

Calibration of different models of the PowerRef using *eccentric viewing, prism-based and theoretical calibration techniques* have been reported in the literature (Brodie 1992; Bharadwaj and Candy 2008; Jagini *et al.* 2014). However, a comprehensive comparison of the relative accuracy, repeatability, and agreement between these techniques is yet to be reported. The overall aim of the present study was to investigate the repeatability of the lens calibration technique for the built-in calibration factor; and to compare the accuracy, repeatability, and agreement between the three techniques previously used for calibration of gaze position estimates. A parallel experimental set-up for gaze position calibration techniques was carried out on an Indian cohort, at the LV Prasad Eye Institute in India, which have resulted in a joint manuscript (under revision) for publication in the journal 'Optometry and Vision Science'.

2.3 Techniques for calibration of defocus estimates

Two calibration techniques for estimates of defocus have previously been reported for the PowerRef. These are the *absolute* and *relative* calibration techniques (Blade and Candy 2006). In the *absolute* calibration technique, the photorefractor reading is compared with a gold-standard technique (such as retinoscopy) simultaneously (Blade and Candy 2006). For example, using the absolute calibration technique, Blade and Candy (2006), investigated the validity of an earlier version of the PowerRef (Multichannel Systems PowerRefractor, 25Hz) by simultaneously comparing the PowerRefractor's reading with the retinoscopy reflex in adults and infants. Using the plane of the camera aperture, and the plane of the retinoscope, allows measurement and comparison of the PowerRefractor reading with the retinoscopy reflex. For example, if the eye is focused on the plane of the camera aperture (at 1m), a myopic reading of -1D would be expected from the PowerRefractor and an against movement of the retinoscopy reflex. Results of the study by Blade and Candy (2006) found that the PowerRefractor recorded an offset range of -0.43 and 0.05 (mean -0.28D±0.22D of standard deviation) in four adults' participants. Their study, like others (Seidemann and Schaeffel 2003; Allen *et al.* 2003; Jainta *et al.* 2004) have reported that the PowerRefractor mostly recorded <1D of myopia when the retinoscopy reflex was found to be neutral with distance static retinoscopy. Although the absolute calibration technique is a robust option for calibrating photorefractors, it can be strenuous for use as a routine calibration technique, as simultaneous comparison with retinoscopy findings must be made. Furthermore, conducting the absolute calibration routine, ideally, requires stabilizing accommodation by the use of a cycloplegic agent which could make it potentially time-consuming, especially in studies employing large samples.

In the relative calibration technique, the photorefractor's ability to measure a change in the eye's refraction per dioptre change in defocus is assessed (Marran and Schor 1998; Choi *et al.* 2000; Blade and Candy 2006). Because of the use of lenses to induce defocus in this protocol, it has also been referred to as 'lens calibration'. A combination of known full aperture, trial frame lenses are used to induce defocus in one eye, and the anisometropic difference between the two eyes is plotted against the lenses presented. The slope of the linear regression fit on the data represents the calibration factor for an individual. This calibration factor is relative to the built-in calibration value of the device. The calibration factor derived is a unitless quantity. Crucially, to prevent inadvertent stimulation of accommodation by the introduction of lenses in front of one eye, an IR transmitting filter is placed on the eye on which the lenses are introduced (Bharadwaj *et al.* 2013). The relative calibration technique has been the mainstay technique used for defocus estimate calibration in most studies employing the PowerRef for measurement of accommodation or refractive errors. However, different lens ranges have been employed by different studies including a 10-lens protocol (-5D to +5D in steps of 1D or -6D to +6D in 2D steps) (Schaeffel *et al.* 1993), six lens protocol (-1D to +5D in 1D steps) (Suryakumar *et al.* 2007) and a five-lens protocol (+1D to +4D, and -2D) (Bharadwaj and Candy 2008). The decision on which lens protocol to use appears to centre on the age of subjects and their cooperation (smaller lens ranges can be completed quickly, for example, Gabriel *et al.* (2009) used a two-lens protocol (+2 D and +4 D) on their infant subjects. Also, the range of lenses which gives the best reliability or least variability when compared with the gold-standard estimation is another consideration. Bharadwaj *et al.* (2013), reported that a combination of lenses which span both positive and negative ranges tend to produce values which are less variable and approximate the gold standard protocol. Unlike the *absolute* calibration technique, the *relative* calibration technique can be carried out quickly, and easily, without cycloplegia and under naturalistic settings (e.g. no need to control pupil sizes) (Blade and Candy 2006; Bharadwaj *et al.* 2013).

2.4 Techniques for calibration of gaze position estimates

Three techniques previously used to calibrate gaze position in slope-based, eccentric photorefractors include the *eccentric viewing, prism-based* and *theoretical* techniques.

In the *eccentric viewing* technique, the individual's HR is derived by having the subject to look at a series of fixation targets placed at different angular eccentricities, which produces a separation between the PI and PC for each target eccentricity (Jagini *et al.* 2014). The reciprocal of the slope of the linear regression fit of the separation between the PI and PC against the target eccentricities gives the HR of the individual (Brodie 1987; Eskridge *et al.* 1988; Model and Eizenman 2011).

The *prism-based* technique works on the same principle of the "anisometropic" difference described previously in the lens calibration. With an IR filter on one eye, prisms of known base powers are used to induce gaze position (and thereby the separation between the PI and PC), and a with the reciprocal of the slope of the linear regression fit of the induced gaze changes against the range of prism powers correspondings to the individual's HR (Bharadwaj and Candy 2008). The induced gaze changes represent the "anisometropic" difference between the eye on which the prisms were held and the fixating eye. Previous studies have used prisms in the ranges of 0-16 ΔD (Doyle *et al.* 2017), and data from an Indian study (communication with Dr. Shrikant Bharadwaj) used 0-24ΔD in 4ΔD steps. In many respects, the HR derived from the prism-based and eccentric-viewing techniques operate under the same principle, except that prisms are used to change the millimetre separation between the PI and PC in the prism-based, while eccentric fixation targets are used to achieve the separation between the PI and PC.

The *theoretical* technique generates the individual's HR from two ocular biometric parameters: the anterior corneal curvature and ACD using a geometric optic formula previously described by Brodie (1987). The formula: $PI_{disp} = (CC+EP_{distance}) * \sin\theta$, (where PI_{disp} is the Separation between the PI and PC, CC is the corneal curvature in millimetres, $EP_{distance}$ is the distance between the entrance pupil and corneal apex (Jagini *et al.* 2014), was developed from the geometrical model by Brodie (1987). The decision on which technique to use for gaze position calibration depends on the characteristics, convenience, and the practical implications of each of these techniques (Table 2.1).

Table 2.1 Characteristics, advantages, and disadvantages of the three gaze position calibration techniques. PI – 1st Purkinje image, PC – Centre of the entrance pupil, AC- Anterior Chamber and HR – Hirschberg Ratio.

Technique	Characteristics	Advantages	Disadvantages
Eccentric-Viewing	• Subject fixates on targets placed at known angular eccentricities. • Separation between PI and PC for each target eccentricity is measured. • Reciprocal of the slope of linear regression fit of measured separation between PI and PC against target eccentricity gives HR. • Standard calibration routine in most eye trackers.	• Easy to perform in adults and healthy subjects. • Requires minimal technology.	• Assumes that subject is fixating accurately at the expected target location. • Unsteady head position can affect measurement. • Resistance to monocular occlusion in some subjects can make data collection difficult. • Data acquisition can be difficult in uncooperative subjects like infants and children.
Prism-based	• Involves the use of prisms of known base powers to create a separation between PI and PC while one eye is occluded with IR filter • A reciprocal of the slope of the linear regression fit of the separation between the PI and PC against prism power gives the HR.	• Requires minimal technology (loose prisms in a trial case can be used). • Requires minimal participation from subject. • Can be used in infants and children.	• Can be time-consuming (e.g. if reflections are present during measurements). • Resistance to monocular occlusion in some subjects can make data collection difficult. • Chance of binocular fusion if monocular occlusion technique is inappropriate.
Theoretical	• HR is derived from anterior chamber biometry of the eye (i.e. corneal curvature and AC depth). • Corneal curvature and AC depth converted into HR using a formula described by Brodie.[7]	• HR can be obtained more quickly than the other two techniques. • Less reliant on participant's cooperation. • Less reliant on gaze changes	• Dependency on the availability of technology for biometric measures. • Accuracy of HR estimates depends on the accuracy and repeatability of the biometric device.

2.5 Ethics, Sample Size Determination and Recruitment

2.5.1 Ethical Approval

Ethical approval for this study was obtained from the School of Biomedical Sciences Ethics Filter Committee of Ulster University prior to undertaking recruitment and data collection. Importantly, the study was conducted in accordance with the Declaration of Helsinki.

2.5.2 Sample Size Determination

The sample size for this study was calculated using the mean calibration slope of adults in the Blade and Candy (2006) study. A mean adult slope of 0.90 (±0.18 of standard deviation) was reported in that study. Using a 95% power, and 5% significance level, a sample size of 45 was derived for the study.

2.5.3 Recruitment

Participants recruited into the study consisted of staff and students of Ulster University, who met the inclusion criteria of the study.

2.5.3.1 Inclusion and Exclusion Criteria:

Individuals were recruited into the study if they were aged between 18-40 years. The lower age limit was chosen to allow individuals who could readily give consent once they understood the study to be recruited, while the upper age limit was imposed to allow recruitment of participants whose pupil sizes were within the operational range of the PowerRef 3™ (4-8mm). It is well known that pupil sizes decrease with age, and with presbyopia mostly setting in at approximately 40 years and above, an upper age limit of age 40 was considered appropriate cut-off point. Traditionally, the lens calibration protocol has been performed on eyes without correction, with most studies recruiting emmetropic participants. However, the use of contact lens correction in myopic subjects for clarity of vision (fixation on the target) have also been reported (Bharadwaj *et al.* 2013). Therefore, individuals were included in the study if they were either emmetropic (defined as spherical equivalent refraction of -0.50 D to + 1.25D) or were myopes. Myopes with contact lens correction wore them at the time of assessment, while those without contact lenses were temporarily provided with appropriate contact lens correction for assessments. Furthermore, all participants satisfied a <1.00DC of astigmatism, and anisometropia <1.00D. Finally, individuals who were recruited into the study had normal binocular vision, and an absence of any ocular pathology such as cornea opacities or cataracts which could affect data recording by the PowerRefractor 3™.

Participants aged below 18 years or over 40 years of age, with significant refractive errors which could not be corrected with contact lenses for testing were excluded in the study.

Similarly, participants who did not have normal binocular vision, and participants with ocular pathology involving the cornea, iris or lens of the eye that could inhibit photorefraction imaging were also excluded. These inclusion and exclusion criteria were applied for both the lens calibration protocol and the gaze position estimate protocol.

2.6 Methods

2.6.1 Baseline visual measures

A data recording form was designed to gather demographic, and visual information of each participant. Demographic data such was age, sex and ethnicity were collected. Visual information included in the study were: distance visual acuity, prism cover test, and autorefractometry.

2.6.2 Measurement of Visual Acuity:

The Bailey Lovie 6m LogMAR chart was used to measurement visual acuity (VA) at distance. The testing distance was 3 metres. Monocular measurements were made, first on the right eye, and then the left. Assessments were made over participants' habitual refractive correction. A correction factor was applied for the 3 metres testing distance during data entry.

2.6.3 Prism Cover Test

Assessment of ocular posture was made using the prism cover test. This was done while the patient fixated on a Maltese Cross Target at distance (6m), and on an accommodative optotype on a Budgie stick at near (40cm). Participants wore their habitual correction during measurement. A prism bar was used to measure the amount of deviation present during testing.

2.6.4 Autorefractometry

The refractive errors of participants were measured objectively, without cycloplegia, using the Shin-Nippon autorefractor ™. The process of assessment involved participants fixating on a Maltese Cross Target at distance greater than 6m, while a set of three measurements were made monocularly, beginning with the right eye. The average of the three readings was recorded as the refractive error of the eye.

2.6.5 Experimental set-up for lens calibration technique

The PowerRef 3™ set-up for the lens and prism calibration is presented in Figure 2.6.1. This set-up has been used previously to undertake calibration and to measure accommodation and vergence functions in special needs populations like children with Down Syndrome and Autism Spectral Disorders (Doyle *et al.* 2016; Doyle *et al.* 2017). Briefly described, the set-up consisted of the PowerRef 3™ camera sitting on a bench at 1m from the participant. The IR light of the camera was reflected into the eyes of the participant using a set of two mirrors – "hot" and "cold" mirrors which are inclined at 45 degrees towards each other (Figure 2.6.1). The "cold" mirror reflected the IR light from the camera to the "hot" mirror which redirects it into the eyes of the participant. There was a chinrest mount attached to the bench to ensure head stability and patient comfort during measurement. The whole bench was also encased in a box with a matte black surround covering it to reduce reflections and provided illumination levels required to achieve optimal pupil sizes during measurement. Although the PowerRef 3™ provides video output while measurements are ongoing, an additional video recording of each measurement session was included in the set-up to provide the option of video playback later on. The fixation target for the lens calibration protocol was a Maltese cross on an

LCD monitor, with a matte black surround attached around the screen to reduce illumination levels.

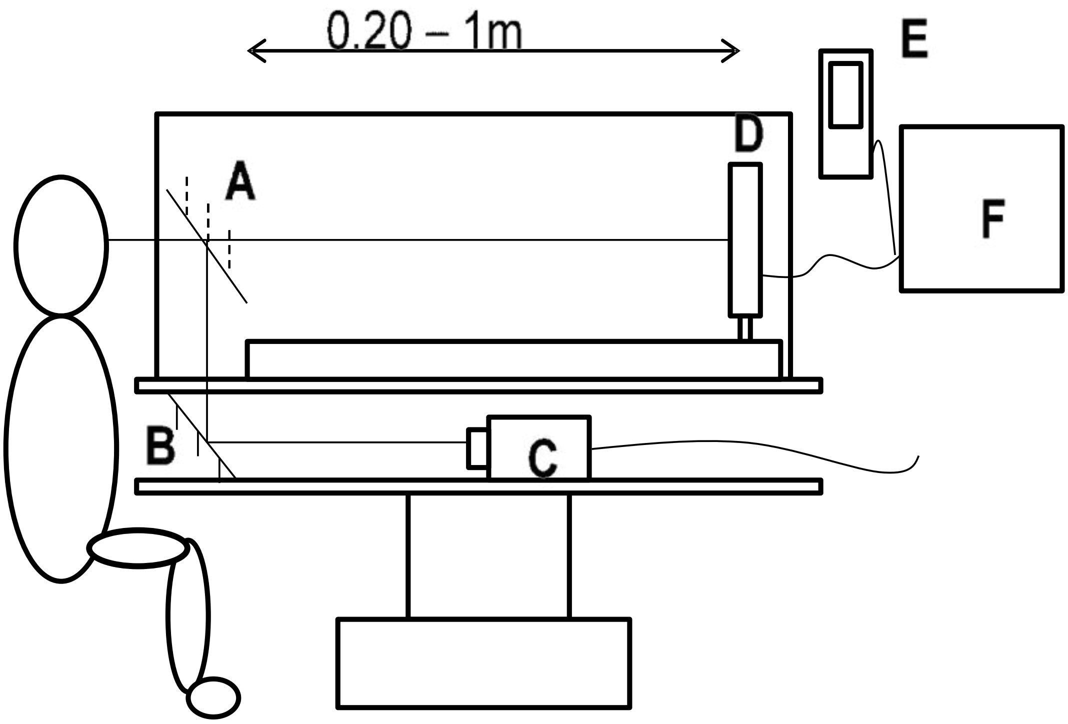


Figure 2.6.1. A schematic diagram of the PowerRef 3™ set-up for defocus and gaze position calibration. The part of the set-up labelled A, is the "hot mirror" which reflects the IR light from the "cold mirror" labelled B. The PowerRef 3™ camera is labelled C. D is the screen/target on which participants fixated; E is the PowerRef 3™ unit which is connected to a display monitor labelled F to record measurements in real time.

A six-lens protocol containing both plus and minus lenses was used in the present study. This lens range has been used previously in the same laboratory (Doyle *et al.* 2016). The lens ranged from: +4D to -4D (+4D, +3D, +2D, +1D, -2D, -4D). Lenses were introduced in front of one eye (non-dominant eye) for approximately four to six seconds worth of data while their dominant eye fixated on the Maltese cross target. See also Figure 2.6.2. The dominant eye of a participant was determined prior to the lens calibration measurement. This was determined while the patient fixated on a target at far and holding a card with a hole in it. The participant was asked to move the card with the hole into their line of sight and to move it towards their eyes. The eye on which the participant eventually placed the card, was determined as their dominant eye. Prior to the introduction of the lenses, the participant wore their contact lens correction if they were myopic, and a trial frame containing an Optcast long pass IR transmitting filter (Edmund Optics™, NT43-954, UK) was worn on the non-dominant eye (Figure 2.6.2). The introduction of the lenses commenced with the +4D lens, in decreasing steps until the last lens (-4D) was introduced. The lenses were held at a vertex distance of 10-14 mm. This distance has been reported to have practically little or no impact on the measurements (Bharadwaj *et al.* 2013). The participant was free to blink, and this was encouraged in contact lens wearers participant regularly, as this helped to reduce reflections. Measurements were carried out mostly in a dimly lit room to allow for optimal pupil sizes. However, where the pupil size was greater than the 8mm upper cut-off point of the instrument, the room illumination was varied.

To assess the repeatability of the lens calibration technique, participants returned within a week of the baseline (first visit) measurement. Measurement conditions remained the same as during the first visit.

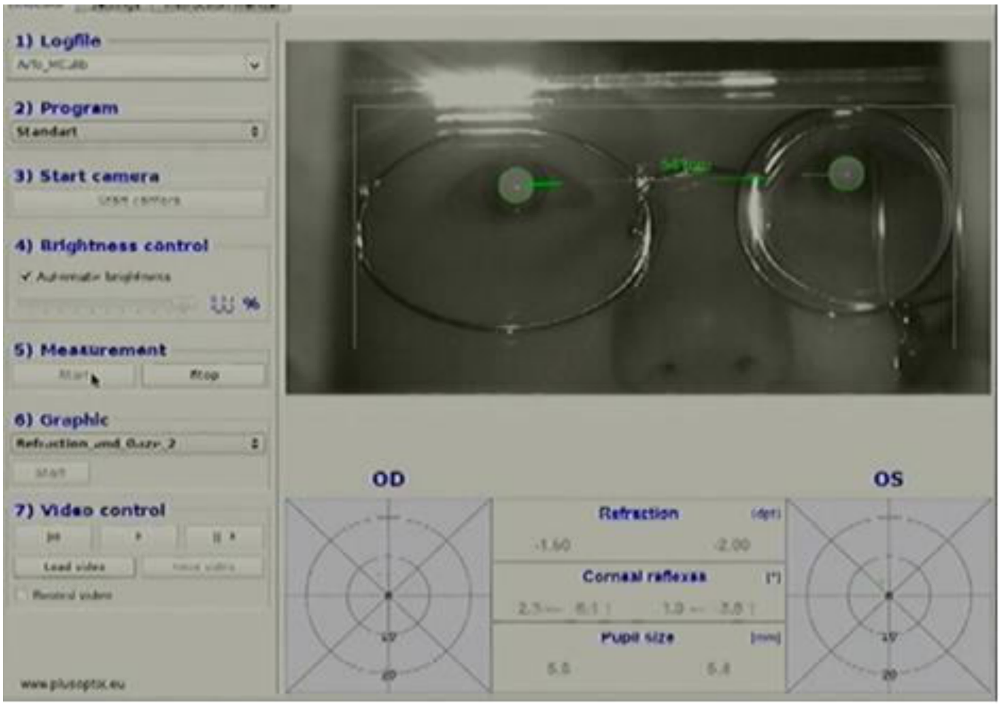


Figure 2.6.2 Figure showing the lens calibration technique as captured by the display monitor connected to the PowerRef 3™ unit. Details in the figure include a minus 2 DS lens introduced before the non-dominant left eye, which has been "occluded" with an IR filter while the dominant eye fixates on a Maltese cross target.

2.4.6 Gaze position calibration

The gaze position calibration techniques were measured subsequent to the lens calibration experiment.

2.4.6.1 Eccentric viewing calibration technique

In the eccentric viewing technique, the set-up included a series of six Maltese cross targets, numbering six, which were arranged horizontally (Figure 2.6.3). Each target subtended an angle of 4^o from the adjacent target. Together, these six targets produced $\pm 12^o$ of eccentricities which were well within the range of angular eccentricity ($\pm 25^o$) where a linear relationship exists between the PI displacement and angular eccentricity (Brodie 1992). Beyond $\pm 25^o$ of angular eccentricity, the relationship between the PI displacement and angular eccentricity becomes non-linear. Participants sat at 2m from these targets and fixated targets with their left eye while their right eye was occluded. Myopic subjects were assessed in this technique in their contact lens correction. The PowerRef 3™ camera was positioned at 1m from the participant's eye at the midline of the two eyes. Measurements were made in a dimly lit room. Repeatability measures were obtained when participants returned within a week for repeat measurement.

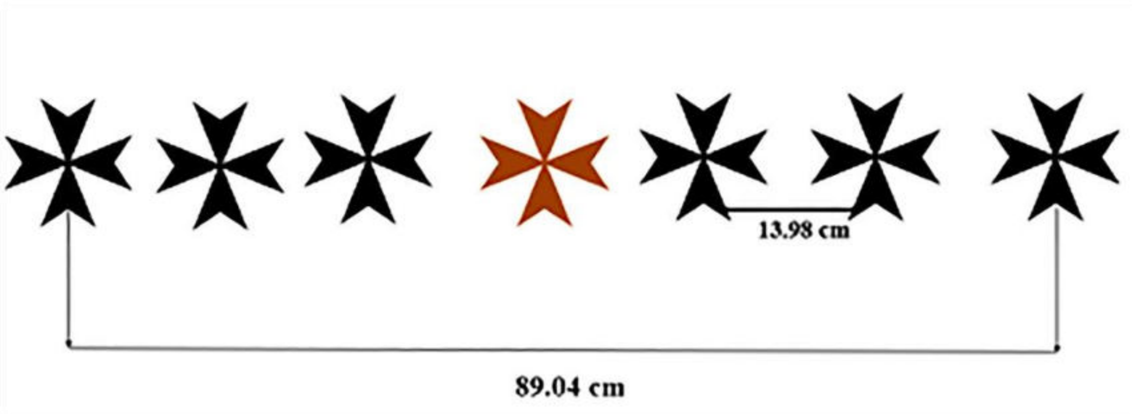


Figure 2.6.3 Schematic diagram of the fixation targets (Maltese cross) in the eccentric viewing technique. Participants were positioned at 2 m from the fixation targets while they fixated on the targets with their left eye. The entire targets subtended a total visual angle of ±12° from left to right corner, with each target separated from the adjacent one by 4° degrees.

2.4.6.2 Prism-based calibration technique

Assessment of the prism-based HR was carried out using the same PowerRef 3™ set-up described for the lens calibration routine. A four-prism calibration protocol was used in the present study. The prism powers used ranged from 4 ΔD to 16ΔD, which corresponded to 2.29° to 9.09°. The mathematical relation for deriving this conversion is: 1° = arctan (prism dioptres/100). These prims were introduced sequentially beginning with the 4 ΔD. The prism was held before the non-dominant eye, first in a base-in, then base-out orientation for four to six seconds worth of data at each base orientation, and at the same 10-14mm vertex distance as was used in the lens calibration technique (Figure 2.6.4). The measurements were also done over the contact lens correction of myopic subjects.

To assess the repeatability of the HR derived from the prism-based calibration, the measurement was repeated within a week of the baseline measurement (visit 1).

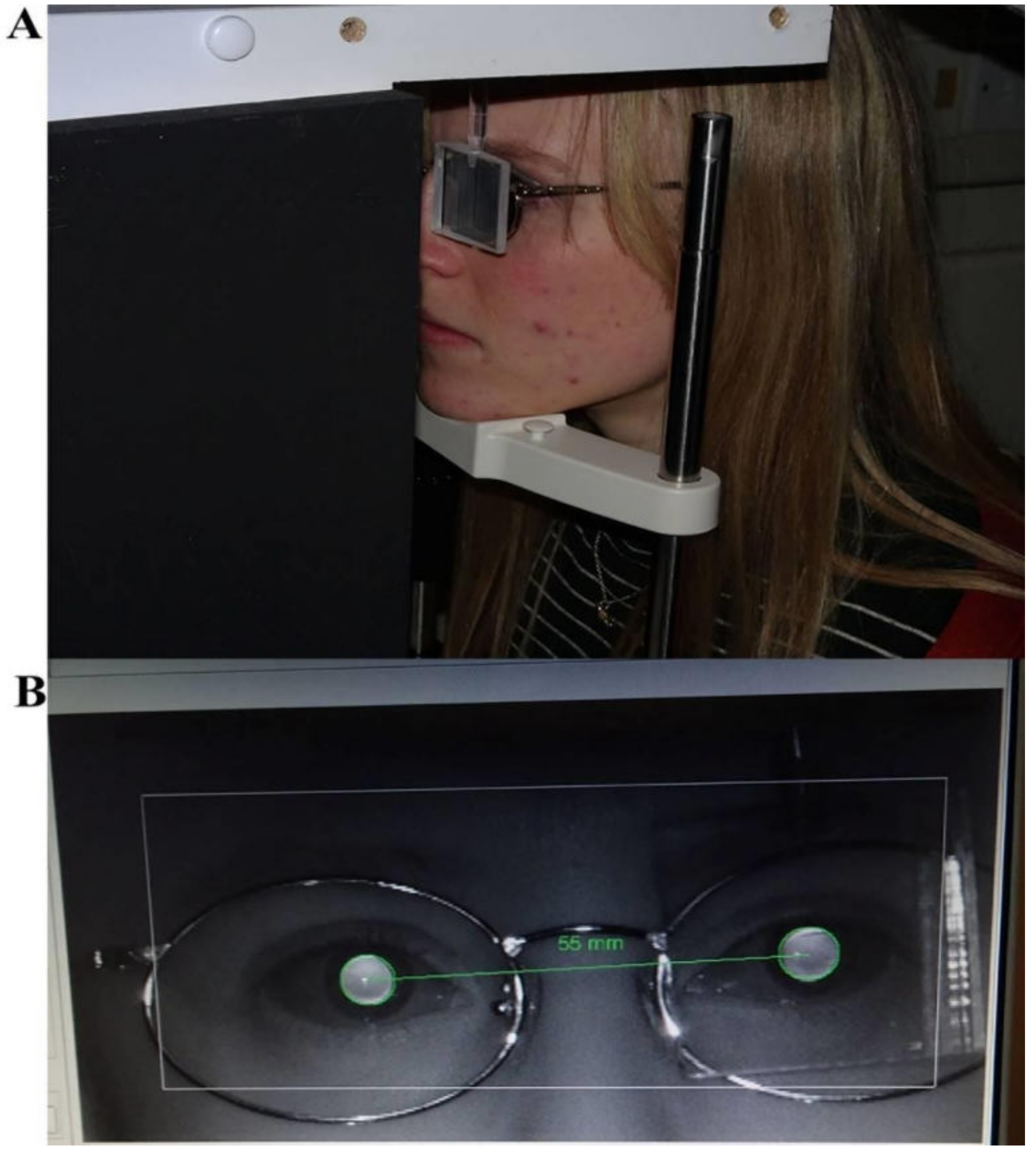


Figure 2.6.4 Figure showing (A) prism held base-in before a participant's non-dominant left eye in the prism-based calibration technique, (B) image of the set-up captured by display monitor connected to the PowerRef 3™ unit during prism base-out presentation. The non-dominant left eye was "occluded" with an IR filter.

2.6.6 Theoretical calibration technique

Hasebe *et al.* (1995) and (Jagini *et al.* 2014), have reported theoretical HRs which were derived from measures of a subject's corneal curvature and ACD. In a similar manner, theoretically derived HR in the present study was obtained from measures of the participants' horizontal anterior corneal curvature and ACD based on the geometric optics model described by Brodie, which states that the HR varies with the anterior corneal curvature and ACD. Horizontal corneal curvatures and ACD of participants were obtained using the Carl Zeiss IOL Master™ (Figure 2.6.5). The accuracy and repeatability of the IOL Master™ for measurement of these two ocular biometric measures have been previously reported (Lam *et al.* 2001; Wang *et al.* 2012). Three sets of measurements were made for the two biometric measures, and the average of three readings was recorded as the corneal curvature and ACD. A regression equation developed from Brodie's geometric model and described previously by Jagini *et al.* (2014) was used to compute the HR of each participant from the average corneal curvature and ACD measured in a custom-written script in Matlab®.

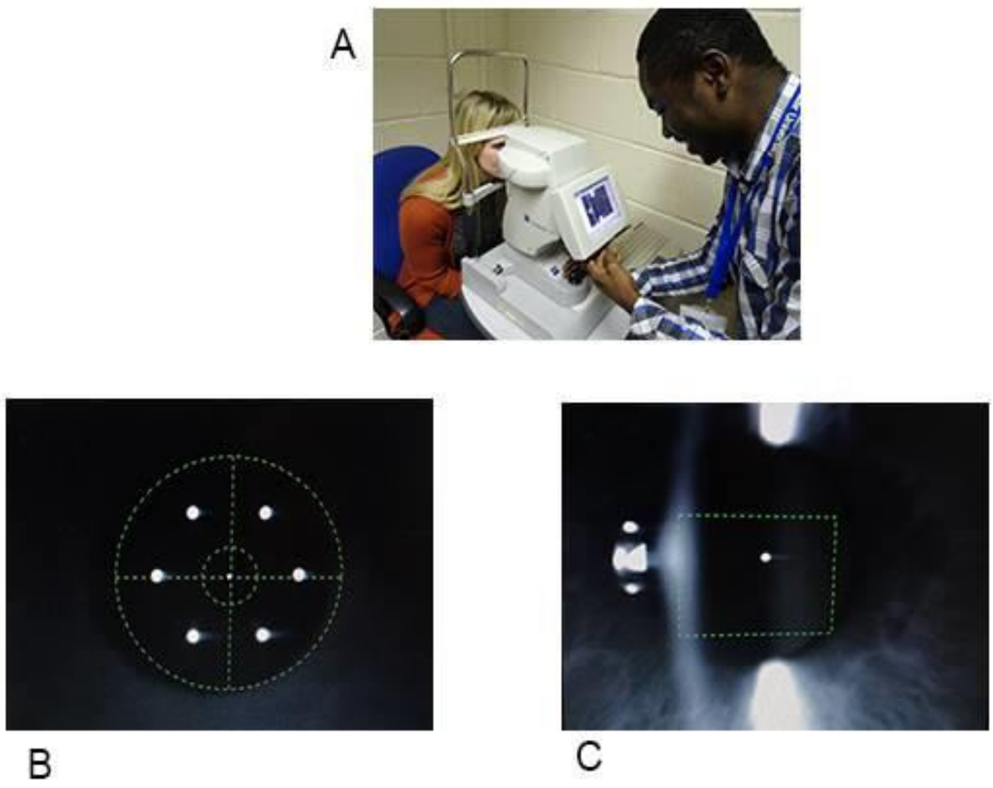


Figure 2.6.5 Figure showing (A) set-up for measurement of anterior corneal curvature and ACD of a participant's eyes (B) IOL Master™ configuration for measurement of corneal curvature (C) IOL Master™ configuration for measurement of ACD.

2.6.7 Data management and analyses

2.6.7.1 Data storage

A data recording form was designed for the entry of subjects' demographic and visual information. These were kept in a string-tie closure A4 file bags and stored in a locked cabinet with a locked office locker. The information contained on the data recording forms was also entered into Microsoft Excel on a password-protected computer for statistical analyses.

2.6.7.2 Data extraction of PowerRef 3™ output

Data extraction of the PowerRef 3™ output was carried out using Matlab™. Data points from the PowerRef 3™ recording were analysed using the criteria previously described in other studies (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Doyle *et al.* 2016):

- Exclusion of data points outside of the PowerRef 3™ operating range (+ 5D to - 7D)
- Exclusion of data points outside the horizontal range of the PowerRef 3™ (±15°).
- Exclusion of data points for pupil sizes less < 3mm and > 8 mm.
- Exclusion of blinks and missing data points.

Raw data traces for lens calibration, prism-based and eccentric viewing calibration techniques are presented in Figure 2.6.7. Defocus and eye movement data were plotted against time and scrutinised for a section of stable data, and two seconds worth of data (~100 samples) from each lens or prism power, or target position (eccentric viewing) was selected and averaged. Although two seconds worth of data have been frequently reported for lens, prism and eccentric calibration (Blade and Candy 2006; Bharadwaj *et al.* 2013; Doyle *et al.* 2016; Doyle *et al.* 2017), the decision to use two seconds worth of data in the present study was after extensive assessment of different sections of the data trace.

Results from this assessment showed that choosing two seconds of stable data was representative and reliable for the length of time during which a lens or prism was used or when eccentric fixations were made. For example, using the prism-based calibration technique data sampling, there was excellent agreement between choosing the start, and middle of the data traces [ICC: 0.97(95% CI: 0.94-0.99), P< 0.001]. Moreover, there was no statistically significant difference between averaging 100 samples (two seconds worth of data) or 300 samples (six seconds data), ($F_{(2,26)}$ =1.10, p=0.35, One-way ANOVA). These averaged defocus or gaze positions were plotted against the corresponding lens or prism power, and target eccentricity in the case of eccentric viewing technique. Linear regression analyses were performed to obtain lens and eye position calibration slopes. The calibration slope obtained from the lens, prism-based and eccentric viewing techniques is a unitless quantity describing the change in refraction or eye position recorded by the PowerRef 3™ for a unit change in lens or prism power, and target eccentricity. In the case of gaze position calibration, the slope of this linear regression equation provided an estimate of the subject's HR. The actual HR of the individual will be equal to the HR used by the PowerRef 3™ divided by the calibration slope of that individual obtained using these techniques. An eye position calibration slope that is equal to unity indicates an HR of 11.8°/mm (i.e. equal to the population average value used by the device). Eye position calibration slopes greater than unity correspond to HR <11.8°/mm (smaller than population average value) while calibration slopes smaller than unity correspond to HR >11.8°/mm (larger than population average value).

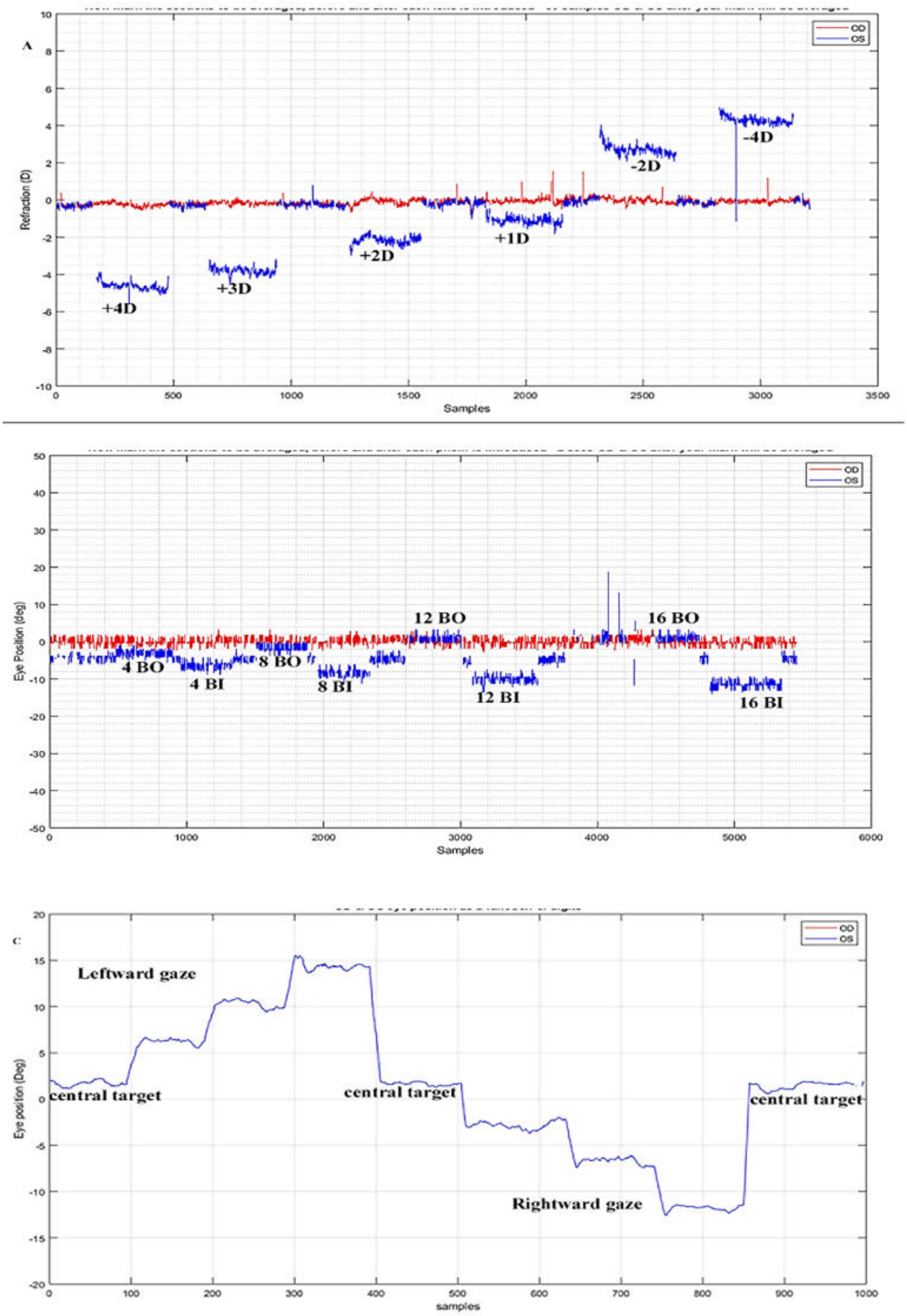


Figure 2.6.7 Figure showing (A) raw data traces for lens calibration recorded by PowerRef 3™ in a subject with lenses held before the IR occluded left eye, (B) raw data traces of eye position in prism-based technique for IR occluded left eye, (C) raw data traces of eye position in the eccentric viewing technique. The left eye fixated while the right eye was occluded in the eccentric viewing technique. In the eccentric viewing calibration technique, positive values in the y-axis represent leftward gaze position, while negative values represent rightward gaze position.

2.6.7.3 Statistical Analyses

Descriptive statistics including Mean±SD were used for normally distributed data, median (Interquartile range (IQR)) for non-parametric data, and frequencies for categorical data. Paired t-test was used to compute mean difference between repeated measures, from which Bland-Altman type plots were constructed (Myles and Cui 2007). Intraclass correlation coefficient test (ICC) was also used to also assess the agreement between variables or techniques. Statistical significance was considered a P-value of <0.05.

2.7 Results

2.7.1 Participants' Profile

A total of 46 subjects provided consent and took part in the study. Out of this number, 42 (91%) were Caucasians, three (7%) of Indian descent, and one of Arabian descent. However, statistical analyses were limited to the 42 Caucasian participants in both defocus and gaze position calibration, as the other racial groups were not sufficiently large enough to explore racial differences. Furthermore, a homogenous racial group was adopted for analyses to allow easy comparison with other studies conducted in different ethnicities. Out of the 42 Caucasian participants, one participant was excluded due to poor quality data arising as a result out of small pupil size, below the operational range of PowerRef 3™. The mean age of participants was 23.34±4.28 years (range: 18 – 34 years). There were more female participants 29 (71%) than males in the present study. Twenty-six (63%) of the participants were emmetropes, while 15 (37%) were contact lens corrected myopes. Participants' distance VA ranged from -0.20 to 0.24 LogMAR [median (25^{th} – 75^{th} IQR): -0.20 (-0.20 to -0.06 logMAR)] and -0.4 to 0.28 LogMAR [median (25^{th} – 75^{th} IQR): -0.18 (-0.20 to 0.00 logMAR)] for the right and left eyes respectively.

2.7.2 Accuracy and repeatability lens calibration technique

There was 98% success rate for assessment of accuracy and repeatability of the lens calibration technique.

At baseline (first visit), mean (±SD) of lens calibration slope was 0.93±0.14 (range: 0.69 to 1.44). Participants' R-squared values ranged from 0.89 to 0.99 (mean (SD): 0.97±0.03). Results of lens calibration slopes during baseline and repeat measurement (visit 2) are presented in Table 2.2. Across both visits, there was no statistically significant difference between the calibration slopes of emmetropes and contact lens corrected myopes (t=-0.55, p=0.58, and t=-0.40, p=0.69) for baseline and repeat measures respectively. See also Figure 2.7.1.

Table 2.2 A table of mean lens calibration slopes and R-squared values across two visits.

Refractive error details	**Slope 1 (Mean±SD)**	**R-squared (Mean±SD)**	**Slope 2 Mean±SD)**	**R-squared (Mean±SD)**	**Difference in slope (paired t-test)**
All participants (n=41)	0.93±0.14 (0.69 to 1.44)	0.97±0.03 (0.89 to 1.00)	0.93±0.13 (0.65 to 1.33)	0.98±0.04 (0.75 to 1.00)	0.00042 (t =0.02, p=0.98)
Emmetropes (n=26)	0.922±0.12 (0.69 to 1.12)	0.98±0.03 (0.89 to 1.00)	0.93±0.13 (0.65 to 1.14)	0.99±0.02 (0.92 to 1.00)	-0.0025 (t=-0.12, p=0.91)
CL myopes (n=15)	0.95±0.18 (0.72 to 1.44)	0.96±0.04 (0.89 to 1.00)	0.94±0.15 (0.71 to 1.33)	0.96±0.06 (0.75 to 1.00)	0.006 (t=0.14, p=0.89)
Difference (Independent t-test)	-0.03 t=0.55, p=0.58	0.01 t=1.26, p=0.22	-0.018 t=0.40, p=0.69	0.03 t=1.97, p=0.07	- -

CL – contact lens corrected

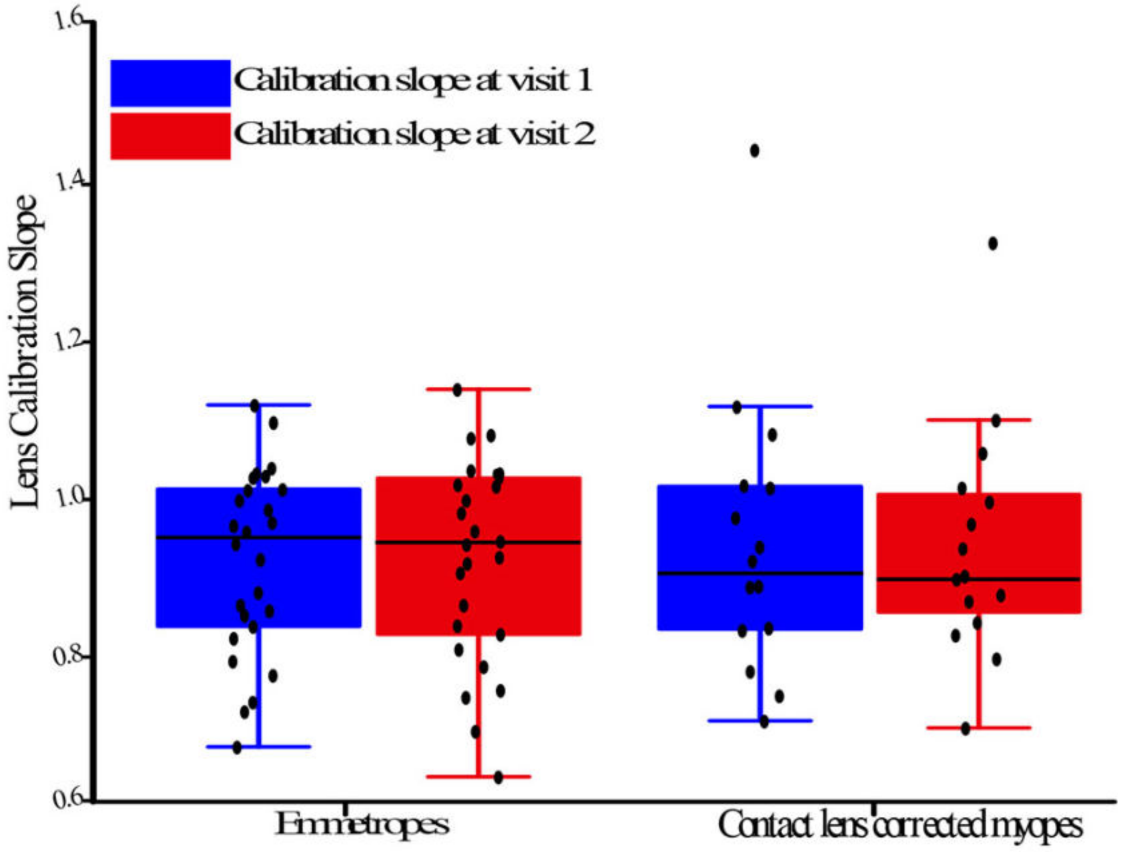


Figure 2.7.1. Box plot showing mean lens calibration slopes by refractive group across two visits. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

To assess repeatability of the lens calibration technique, Bland-Altman type plot was constructed using the mean difference between baseline and repeat measurements. The mean difference (95% limit of agreement (LOA)), between visit one (baseline) and visit two (repeat measurement) was 0.00042 (95% LOA: -0.24 to 0.24), t=0.02, p=0.98. See also Figure 2.7.2

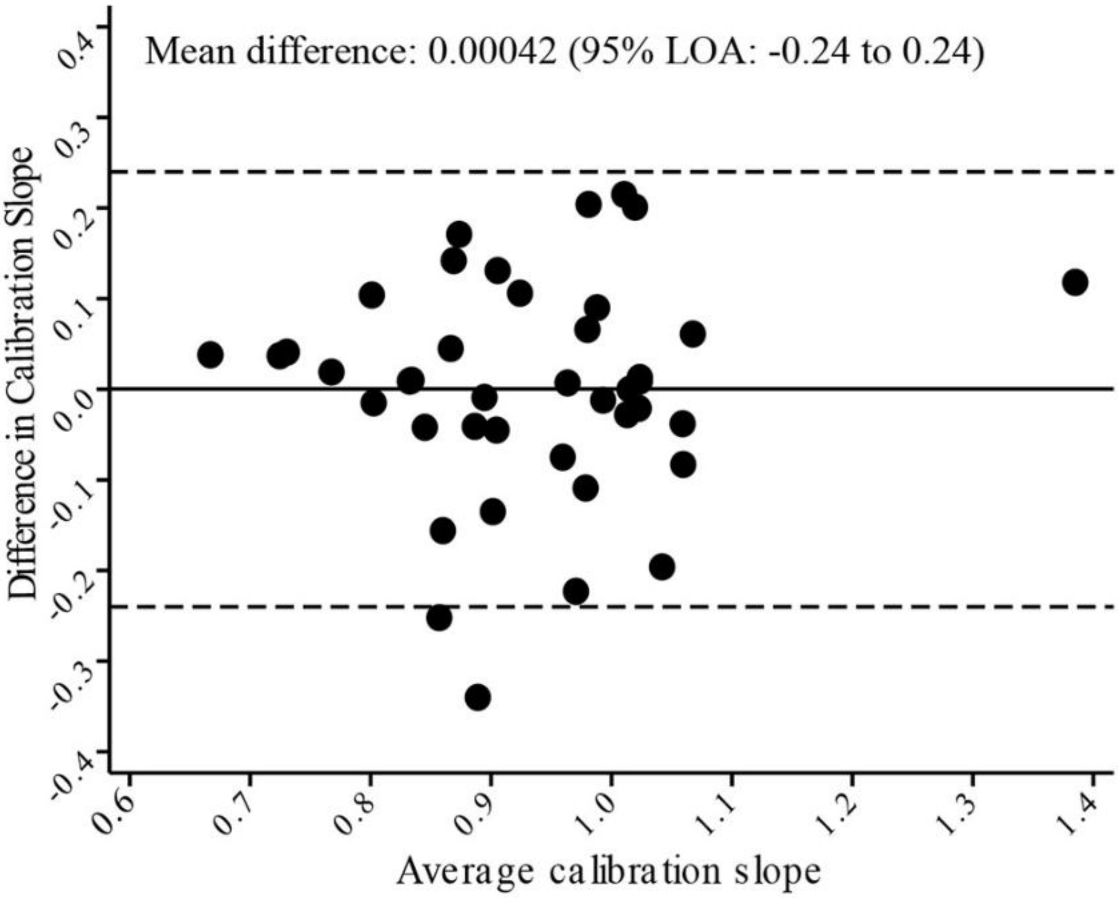


Figure 2.7.2 Bland-Altman type plot showing the agreement between the lens calibration slopes measured at baseline and during repeat visit. Difference in calibration slope represents the mean difference between visit 1 and 2 (inter-session difference in calibration). The solid black line in the figure indicates the mean difference between the two measurements while the dashed black lines indicate the 95% limit of agreement.

2.7.3 Accuracy and repeatability of three gaze position calibration techniques

Out of the 42 Caucasian participants who provided useable data traces for the lens calibration technique, only 28 were available for assessment of accuracy and repeatability of the three gaze position calibration techniques. Thirteen of the initial 42 participants, mostly final year undergraduate Optometry students were lost to follow-up. There was therefore a 67% success rate for assessment of the accuracy and repeatability of the three gaze position calibration techniques.

Baseline regression slopes ranged from 0.81 to 1.11 [mean ±SD: 0.97±0.08] for the eccentric viewing technique, and 0.70 to 1.03 [0.86 ±0.09] for the prism-based technique. The HR's calculated from these slopes ranged from 10.61 to 14.63°/mm [mean ± SD: 12.25±1.09 °/mm] for the eccentric viewing technique and 11.47 to 16.93 °/mm [13.88±1.53 °/mm)] for the prism-based technique (Table 2.4 and Figure 2.7.3, panel A). Baseline corneal curvatures and ACD ranged from 7.49 to 9.00 mm [mean ±SD: 8.03±0.41 mm], and 2.32 to 4.15mm, [mean ±SD: 3.45±0.41 mm] See also, Figure 2.7.3, panel B. These translated into theoretically derived HR ranging from 9.84 to 13.44 °/mm [mean ±SD: 9.84±0.96 °/mm] (Table 2.4).

Table 2.4 Repeat measures of mean(±SD) regression slopes, and HRs for three calibration techniques and Intraclass Correlation Coefficient (ICC) test of agreement between baseline and repeat measures. Baseline values represent first visit measurements. Intra-subject variability in each technique was calculated from the MEAN difference (95% Limit of agreement) between the baseline and repeat measurements.

	Regression slope (unitless) Mean±SD (range)	**Hirschberg Ratio (°/mm) Mean±SD (range)**	**Intra-subject variability** Mean difference (95% limits of agreement)	**Intraclass correlation Coefficient (ICC) rho (95% CI)**
Eccentric viewing				
Baseline	0.97±0.08 (0.81 – 1.11)	12.25±1.09 (10.61 – 14.63)	0.05 (-0.30 to 0.40)	0.99 (0.98-0.997)
Repeat measurement	0.98±0.08 (0.83 – 1.15)	12.19±1.04 (10.28 – 14.29)	(t=1.63, *P*=0.12)	*P*<0.001
Prism-based				
Baseline	0.86±0.09 (0.70 – 1.03)	13.88±1.53 (11.47 – 16.93)	0.09 (-1.91 to 2.08)	0.88 (0.74-0.944)
Repeat measurement	0.87±0.09 (0.66 – 1.04)	13.79 ±1.56 (11.34 – 17.83)	(t=0.44, *P*=0.66)	*P*<0.001
Theoretical				
Baseline	N/A	11.34±0.96 (9.84 – 13.44)	0.04 (-0.20 to 0.28)	0.99 (0.99-0.998)
Repeat measurement	N/A	11.29±0.93 (9.82 – 13.18)	(t= 1.93, *P*= 0.07)	*P*<0.001

t represents paired t-test of the mean difference between baseline measures and repeat measurement, and P represents the statistical significance.

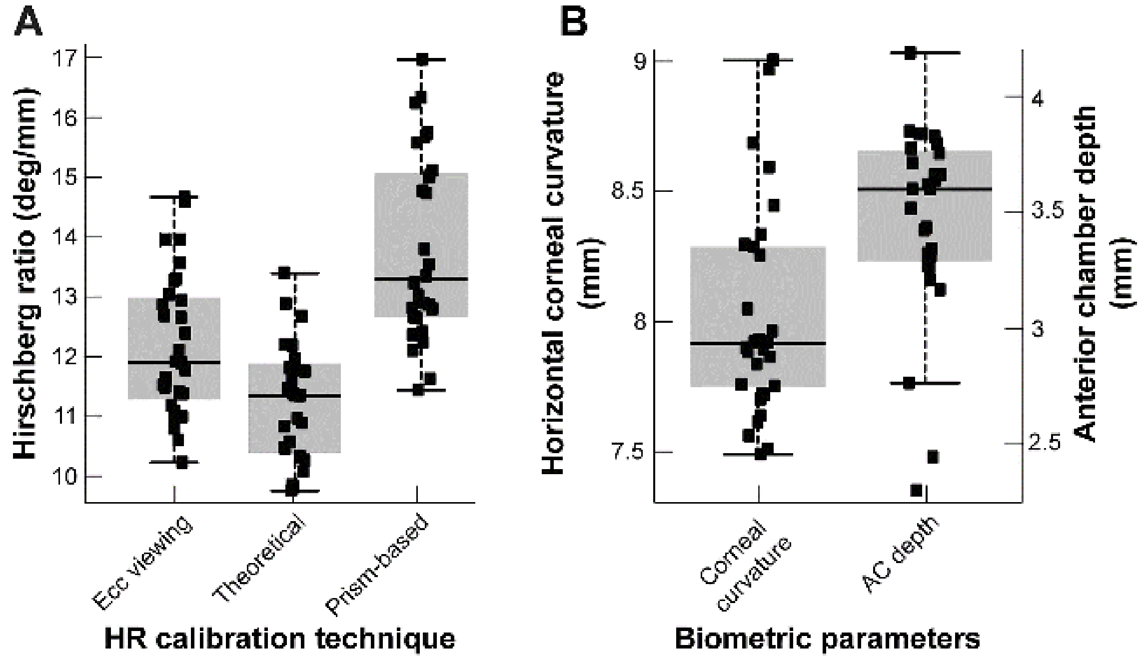


Figure 2.7.3 Box plots of the baseline Hirschberg ratios (HR) obtained using the eccentric viewing, prism-based, and theoretical techniques (panel A) and the anterior chamber biometric properties of the eye (panel B) for calculating the HR using the theoretical technique. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The squares represent individual data points.

2.7.4 Accuracy of the gaze position calibration techniques

To assess the accuracy of a calibration technique requires comparison with a gold-standard technique. In the present study, the eccentric viewing technique was considered the "gold-standard" technique because of its traditional use for calibrating the HR in most 1st PI-based eye trackers (Hasebe *et al.* 1995; Schaeffel 2002). This technique has also become a "legacy technique" from which the population-average HR has been derived in previous studies (Hasebe *et al.* 1995; Schaeffel 2002). Moreover, this technique uses angles anchored in space and is based on actual eye rotation, thus requires few assumptions. Table 2.5 shows the results of the relative inaccuracies of the prism-based and theoretical techniques compared to the "gold-standard" technique.

Table 2.5 A table showing relative inaccuracies in HR when the prism-base and theoretical techniques are compared to the gold-standard technique (eccentric viewing technique).

Technique	Gold-Standard (eccentric-viewing) 100 - ((individual baseline theoretical/prism HR) / individual eccentric HR) *100) **Average (range)**
Theoretical (28)	6.99%±8.30 (-6.35 to 32.75)
Prism-based (28)	-13.64%±11.27(-37.19 to 20)

2.7.5 Agreement between three gaze position calibration techniques

Agreement between techniques was assessed using the baseline HR (visit 1 HR) and constructing Bland-Altman type plots of the signed difference between techniques to show the spread of the data (Figure 2.7.4). However, to assess the possibility of range effects in HR, the mean absolute difference was also computed and presented with the mean signed difference (Table 2.6). Figure 2.7.5 also illustrates Bland-Altman plots using the mean absolute difference. Using the paired t-test, the mean absolute difference between prism-based and eccentric viewing techniques was 1.87°/mm (95% LOA: -0.27 to 4.01°/mm, P<0.0001), between the prism-based and theoretical techniques was 2.54°/mm (95% LOA: -0.32 to 5.40°/mm, P<0.0001), and between the eccentric viewing and theoretical techniques was 0.98°/mm (95% LOA: -1.22 to 3.18°/mm), P<0.001. To determine the effect of HR size on the mean difference (bias), linear regression analyses were performed on the absolute difference. Results of linear regression analyses revealed slopes that were statistically significantly different from zero between the prism-based and eccentric viewing techniques ($F_{(1,26)}$ =7.52, P=0.01), and between the prism-based and theoretical techniques ($F_{(1,26)}$ =6.98, P=0.01 (Figures 2.7.5, panels A & B show for this effect). However, there were no range effects on the mean difference between the eccentric and theoretical techniques ($F_{(1,26)}$ = 0.34, P=0.57) (Figure 2.7.5, panel C). Thus, the bias towards the prism-based technique with the difference between techniques appearing to increase with an increase in the size of the HR.

Table 2.6. Table showing results of mean signed and mean absolute difference between the three techniques. Paired t-tests were conducted, and P-values represent the probability of mean difference being statistically significantly different from zero.

Techniques	**Mean difference (signed) Mean °/mm (95% LOA)**	**Mean difference(absolute) Mean °/mm (95% LOA)**
Prism-based vs Eccentric viewing technique	1.63 (-1.17 to 4.43) *P*<0.001	1.87 (-0.27 to 4.01) *P*<0.0001
Prism-based vs Theoretical technique	2.54 (-0.32 to 5.40) *P*<0.0001	2.54 (-0.32 to 5.40) *P*<0.0001
Eccentric viewing vs Theoretical technique	0.91 (-1.40 to 3.22) *P*<0.0001	0.98 (-1.22 to 3.18) *P*<0.001

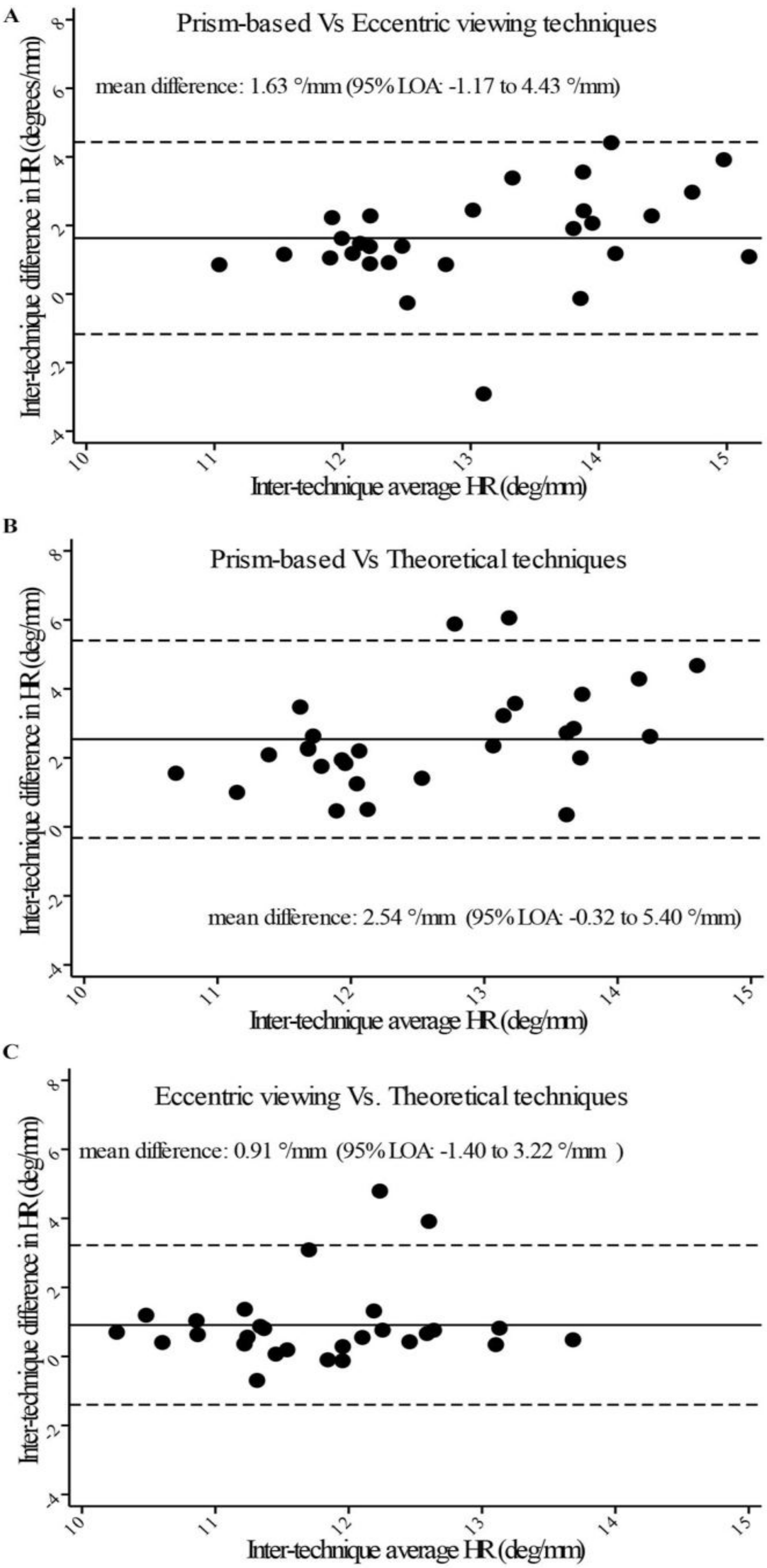


Figure 2.7.4. Bland-Altman type plots show the agreement between the HR's obtained using the three calibration techniques. Panel A shows the agreement between the prism-based and

eccentric viewing techniques, panel B shows the agreement between the prism-based and theoretical techniques and panel C shows the agreement between the eccentric viewing and theoretical techniques. The solid black lines in all panels indicate the mean difference between the two measurements while the dashed black lines indicate the 95% limit of agreement. The mean difference and the limits of agreement obtained for each comparison are also included in the figure panel. In this figure, the signed difference in HR presented. In Figure 2.7.5 below, the absolute difference in HR is presented for comparison of spread of the data.

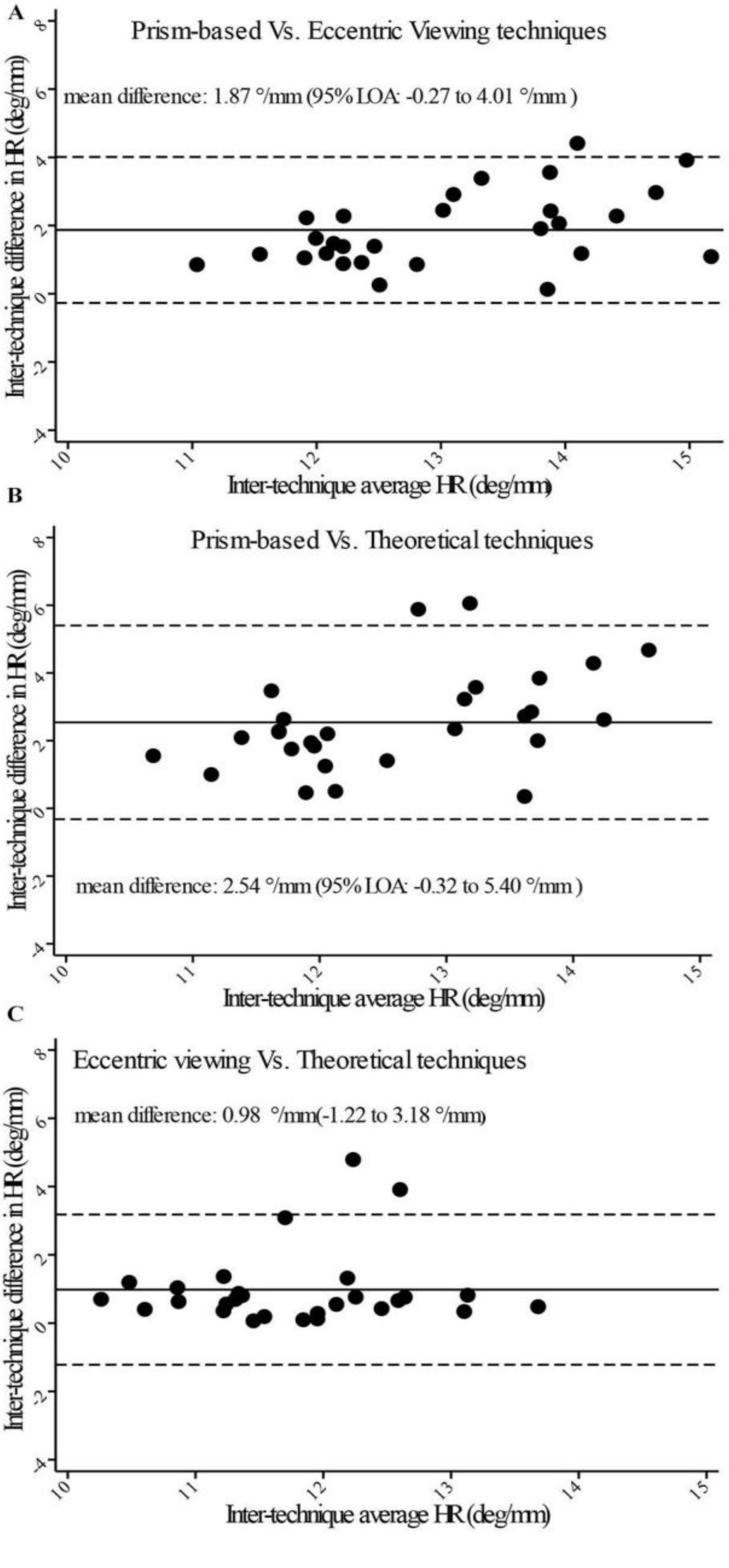


Figure 2.7.5. Bland-Altman type plots show the agreement between the HR's obtained using the three calibration techniques. Panel A shows the agreement between the prism-based and eccentric viewing techniques, panel B shows the agreement between the prism-based and

theoretical techniques and panel C shows the agreement between the eccentric viewing and theoretical techniques. The solid black lines in all panels indicate the mean difference between the two measurements while the dashed black lines indicate the 95% limit of agreement. The mean difference and the limits of agreement obtained for each comparison are also included in the figure panel. This figure presents the absolute difference in HR.

2.7.6 Repeatability of three gaze position calibration techniques

The intra-subject variability of the three gaze position calibration techniques was determined from the repeated measurement during the second visit. Bland-Altman plots were constructed using the mean difference of the baseline and repeat measurements (Figure 2.7.6). The mean difference (±95% LOA) in HR between the first and second measurements were: 0.05°/mm (95% LOA: -0.30 to 0.40°/mm) for the eccentric viewing technique (Figure 2.7.6, panel A) and 0.09°/mm (95% LOA: -1.91 to 2.08°/mm) for the prism-based technique (Figure 2.7.6, panel B). Repeat corneal curvature and ACD measures for calculating HR using the theoretical technique ranged from 7.46 to 9.08 mm [mean ±SD: 8.04±0.42 mm] and 2.28 to 4.12 mm [mean ±SD: 3.45±0.40 mm], respectively, and these translated into theoretically derived HR of range 9.82 to 13.18°/mm [mean ±SD: 11.29±0.93°/mm]. The mean intra-subject variability of the theoretically derived HR was therefore 0.04°/mm [paired t-test (95% LOA: -0.20 to 0.28°/mm)] (Figure 2.7.6, panel C). The mean difference between the first and repeat measures of HR for all three techniques was not statistically significantly different from zero ($t = 1.63$, $p=0.12$; $t = 0.44$, $p =0.66$; $t = 1.93$, $p= 0.07$) for eccentric viewing, prism-based and theoretical techniques respectively. Moreover, results of ICC revealed excellent repeatability in the eccentric viewing and theoretical techniques [0.99(95% CI: 0.98-0.997), $P<0.001$, and 0.99(95% CI: 0.99-0.998), $P<0.001$, for the eccentric viewing and theoretical techniques respectively] compared to the prism-based technique [0.88(95% CI: 0.74-0.944), $P<0.001$) Table 2.4.

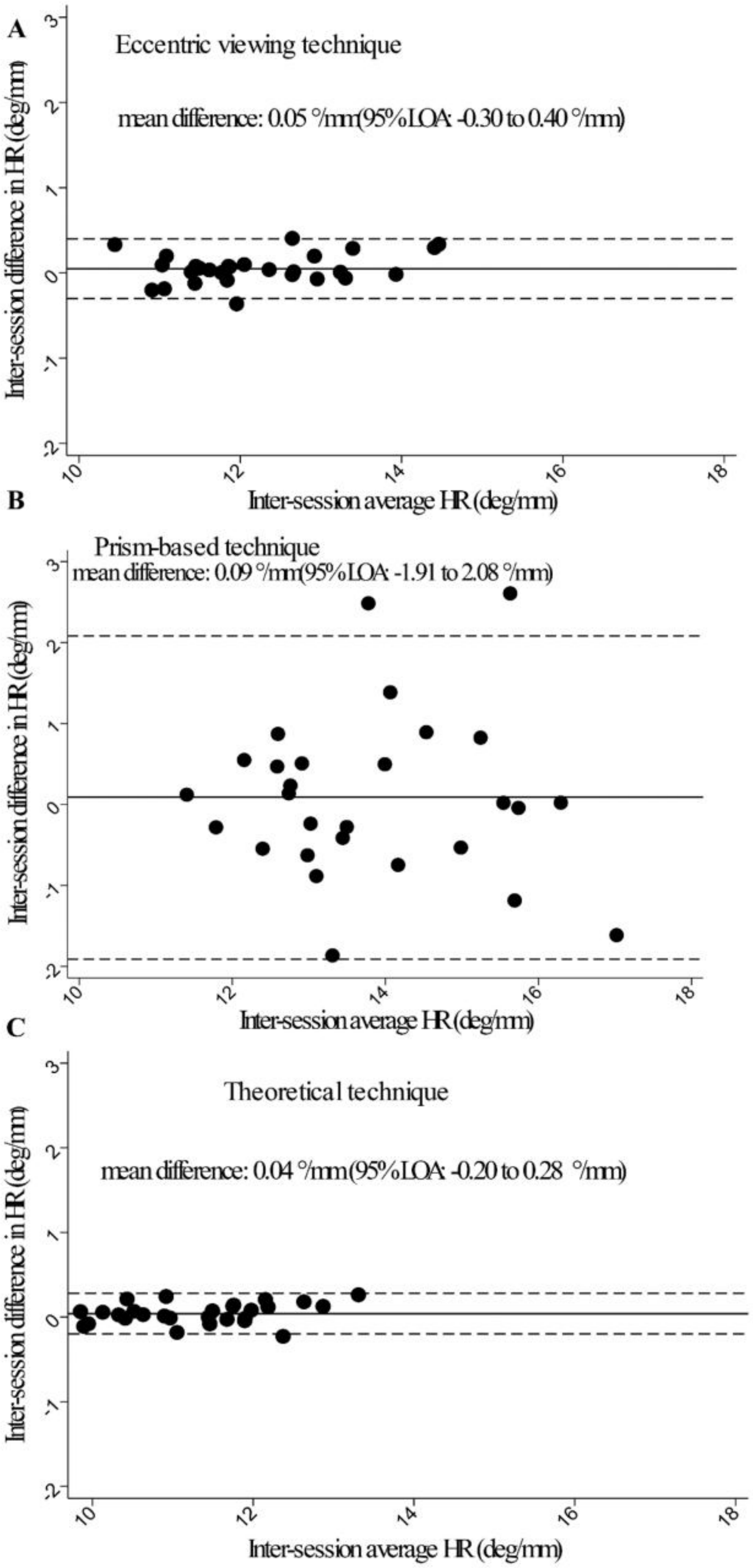


Figure 2.7.6. Bland-Altman type plots of repeatability of three calibration techniques. Panel A shows repeatability of the eccentric viewing technique, panel B shows repeatability of the prism-based technique and panel C shows repeatability of the theoretical technique. The solid black lines in all panels indicate the mean difference between the two measurements while the dashed

black lines indicate the 95% limit of agreement. The mean difference and the limits of agreement obtained for each comparison are included in the figure panel.

2.8 Discussion

2.8.1 Discussion of lens calibration results

In the present study, the built-in software of the PowerRef 3™ was calibrated using the lens calibration technique. There was a high success rate in this protocol, from which estimates of relative calibration using lenses were obtained despite challenges such reflections from the trial lenses employed.

Mean calibration slope for participants in this study was high, being closer to one, and nearly reaching the ideal 1:1 line or function (Blade and Candy 2006). The value recorded in this study is consistent with previous studies in Caucasian adults (Blade and Candy 2006; Bharadwaj *et al.* 2013). However, there was less inter-subject variability (indicated by the standard deviation of the mean calibration slope) in this study compared to the previous ones. It is possible that the lens range used for calibration in this study resulted in the higher mean calibration slope. Bharadwaj *et al.* (2013) reported that using a combination of positive and negative lenses could improve the results of relative calibration to that comparable with a gold-standard protocol. This study used a six-lens protocol spanning both plus and minus lenses, similar to that used by Bharadwaj *et al.* (2013). The built-in calibration software of the PowerRef 3™ was developed using Caucasian eyes (Sravani *et al.* 2015), therefore, results of this study which shows nearly perfect validation may suggest that using the built-in calibration software for an adult Caucasian eyes during photorefraction in situations where calibration may not be possible such as a subject with strabismus, or a media opacity problems in one eye, may not affect photorefraction estimates significantly. However, the inter-subject variability of the mean suggests that this may not always be appropriate for some individuals.

The lens calibration technique was highly repeatable within ±0.24 for participants in the present study. This range of repeatability is lower than the ±0.40 in the study of Bharadwaj *et al*. (2013). Bharadwaj *et al.* (2013) in their study used an older version of the PowerRef (Multi-Channel system PowerRef) with a sampling frequency of 25Hz in Caucasian adults (n=48) aged 19-55 years. A five-lens protocol (0D to +4D and a -2D) was used to assess repeatability in the study of Bharadwaj *et al.* (2013). These methodological differences could account for the observed differences between the two results. A calibration technique should not only be accurate but must also be precise for it to be relevant for use in calibration. Whereas retinoscopy may provide true, accurate and absolute estimates of refraction/accommodation, it may be fraught with precision challenges, for which reason, a more precise technique such as lens calibration may be preferred.

Recent published studies have reported that photorefractive estimates obtained while plus and minus lenses are held before the eyes can potentially affect findings Bharadwaj *et al.* (2018). These studies, however, found significant effect when these lens powers are greater than 4D. Reduced vertex distance also minimizes the effects of such magnification or minification due to the lenses. In the present study, a combination of plus (highest +4D) and minus (highest – 4 D) lens powers were used, at the constant vertex of 14mm, which would have minimized any potential effects.

The present study did not ascertain if non-contact lens wearers (spectacle corrected-myopes) had prisms in their spectacle prescriptions, which presents a limitation to the study findings.

2.8.2 Discussion of gaze position calibration results

The essence of calibrating an individual's HR in 1st Purkinje image-based eye trackers is to reduce the errors in gaze position estimates that may arise when using the population-average HR as the conversion factor (Riddell *et al.* 1994; Schaeffel 2002; Model and Eizenman 2011; Jagini *et al.* 2014). This problem is of real concern to commonly used eye trackers given the large inter-subject variability in HR that has been reported in the literature (Riddell *et al.* 1994; Schaeffel 2002; Model and Eizenman 2011; Jagini *et al.* 2014). The main aim of the present study was to examine the accuracy and repeatability of three gaze position calibration techniques previously employed for calibration.

Following the decision to use the subject's own HR to calibrate the eye tracker for improved accuracy, a second challenge is to determine which calibration technique is to be adopted for this purpose. The performances of three such techniques that have been used previously in the literature – *eccentric viewing*, *prism-based* and *theoretical* – were tested in the present study. To determine the accuracy of a given calibration technique, the values obtained by this technique need to be compared against a "gold-standard" measure. For the present analysis, the *eccentric viewing* technique is considered as the "gold-standard" technique simply because of its traditional use for calibrating the HR in most 1st PI-based eye trackers (Hasebe *et al.* 1995; Schaeffel 2002). This technique has also become a "legacy technique" from which the population-average HR has been derived in previous studies (Hasebe *et al.* 1995; Schaeffel 2002). Moreover, this technique uses angles anchored in space, and is based on actual eye rotation, thus requires few assumptions.

Compared to the eccentric viewing technique, the prism-based and theoretical techniques both demonstrated relative inaccuracies of 13% and 7% respectively when the mean values were compared [see Table 2.4 for mean values: (100- (13.88÷12.25) ×100) = 13%, and (100-(11.43÷12.25) ×100 = 7%)]. At the individual level, these inaccuracies ranged from 6% of underestimation of HR to 33% of overestimation in the theoretical technique, and 20% underestimation to 37% overestimation in the prism-based technique (Table 2.5). Similar relative inaccuracies for the two techniques, when compared to the eccentric viewing technique, have been observed for data from an Indian cohort. When the accuracies of the two techniques are considered in terms of the "coefficient of accuracy (COA)", which is defined as 1.96 times the standard deviation of the mean difference between the gold standard technique and the two other techniques (Elliott *et al.* 1997; Allen *et al.* 2003), the theoretical technique demonstrated a lower COA of 2.3 (1.96*1.17 of standard deviation of the mean difference between the eccentric viewing and theoretical techniques) compared to a COA of 2.8 (1.96* 1.43) for the prism-based technique. A ±2.3 COA for the theoretical technique means that if the HR of a subject was measured with the eccentric and theoretical techniques, 95% of the time, the difference between the HRs of the two techniques would be less than or equal to 2.3.

The present study also demonstrated the over-estimation of HR by the prism-based technique, relative to both the eccentric-viewing and theoretical techniques (Figure 2.7.5, panels A & B). This was particularly significant in the agreement between the prism-based technique and the theoretical technique, although there were range effects in the bias towards the prism-based technique; with the difference between techniques appearing to increase with an increase in the size of the HR (Figure 2.7.5, panels A&B). However, there was no such range effect between the eccentric viewing and theoretical techniques, and the mean difference between the two was closer to zero compared to the mean differences when the prism-based technique is considered. The Bland-Altman plots in Figure 2.7.5, and Table 2.6, also show that range effects in the data did not differ much whether the signed difference or absolute difference between techniques was used.

Assessment of a technique's usefulness and applicability would be limited if its accuracy is the only parameter considered. Particularly for calibration, where the aim is to enhance precision of individual estimates, the value of an individual calibration paradigm is undermined if the calibration technique exhibits considerable intra-subject variability (Bharadwaj *et al.* 2013). Therefore, in addition to accuracy, the calibration technique's repeatability also needs to be assessed to determine its usefulness in estimating the individual HR. The theoretical technique demonstrated the least intra-subject variability as the HR obtained with this technique was repeatable to within ±0.30°/mm in a subject, less than the 0.50°/mm previously reported by Jagini *et al.* (2014). This may be attributed to the more consistent, repeatable measures of corneal curvature and ACD (~ 0.01mm for both measures in this study, less than the 0.08mm reported previously (Lackner *et al.* 2005; Crawford *et al.* 2013; Jagini *et al.* 2014)) available in the present study. The HR obtained using the eccentric viewing technique was repeatable to within ±0.40°/mm in individual subjects; slightly less repeatable than the theoretical technique, but superior to the prism-based technique. Furthermore, there was improved intra-subject repeatability in the eccentric viewing technique in this study than previously reported (1.5 to 3.0 degrees/mm) (Quick and Boothe 1992; Hasebe *et al.* 1995). The use of different fixation target in the present study compared to previous work could explain the differences in the intra-subject repeatability reported as fixation target characteristics are known to affect the stability of eye movements (Thaler *et al.* 2013). Perhaps the use of Maltese cross fixation target in this study minimized micro-eye movements, thereby contributing to enhanced repeatability. The highest intra-subject variability in HR, with the lowest ICC, was observed in the prism-based technique. The HR measured in the prism-based technique was repeatable to within ±2.0°/mm. There are no previously published data with which to compare these findings, but when compared with the other two techniques in this study, the variability exhibited by the prism-based technique is high (Figure 2.7.6, panel B). Moreover, the lowest ICC was recorded in the prism-based technique demonstrating least agreement between the baseline and repeat measures. It is possible that the high variability in HR exhibited in the prism-based technique is inherent when using prisms for calibration. Variability in PI displacements which can arise from minimal variance in orientation and/or placement of the prisms before the IR-occluded eye during repeat measurements will influence the results (Thompson and Guyton 1983). Furthermore, variability in a subject's phoria adaptation at different measurement times (Toole and Fogt 2007), could lead to the high variability observed with the prism-based technique. Finally, in the prism-based technique, although one eye is occluded with an infrared transmitting filter, potential conflicts in fixation between the target presented to the non-occluded eye and the image of the IR LED's in the occluded eye could lead to additional variability in this technique.

Another way to quantify the precision of a technique is to compare the intra-subject and inter-subject variability of the technique. If the magnitude of intra-subject variability equals the inter-subject variability produced by the technique, then its usefulness for calibration could be questioned. In the case of theoretical technique, the intra-subject variability was 13% relative to the inter-subject variability [see Table 2.4, (for a -0.20 to 0.28°/mm of intra-subject variability, expressed as percentage of its inter-subject variability (9.84 to 13.44°/mm): 0.48÷3.6 × 100) =13%]. Similarly, the eccentric viewing technique exhibited 17% variability of the inter-subject value. However, the prism-based technique exhibited 73% variability relative to the inter-subject variability [e.g. (for a -1.91 to 2.08°/mm, expressed as percentage of its inter-subject variability (11.47 to 16.93°/mm): 3.99÷ 5.46 × 100) = 73%]. From these data, it is evident that the prism-based technique exhibited the greatest variability relative to the two other techniques. Despite the successful use of the prism-based calibration technique for calibrating gaze position estimates in infants and children previously (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009), the results of the present study in adults may indicate the need to exercise caution during its use for gaze position calibration of PI-based eye trackers.

2.9 Chapter Discussion

The use of the slope-based, eccentric, infrared photorefractor (predominantly PowerRef 2 or 3™) for measurement of accommodation and vergence, and/or refractive error screening in children, is increasingly being reported in the literature. However, a critical step in ensuring accuracy and reliability of measurements is calibration of the instrument. While previous studies have validated the device for refraction or accommodation measurements using different calibration protocols, this is the first study to comprehensively look at the different calibration techniques for gaze position estimates. This is a strength of the study – concurrent comparison of three gaze position calibration techniques. Although previous studies measuring accommodation and vergence in infants and children have employed the prism-based calibration technique for gaze position estimates (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Doyle *et al.* 2016; Doyle *et al.* 2017), the present study demonstrates the tendency of this technique to over-estimate the HR of subjects compared to the eccentric viewing and theoretical techniques. The prism-based technique also demonstrated poorer repeatability compared to the other techniques.

Reflecting on the role of this study for the overall PhD work, it can be said that the calibration of the PowerRef 3™, also afforded the opportunity to familiarise and understand the instrument, which enhanced confidence for data collection on sustained accommodation and vergence functions in children with and without hyperopia.

There were some participants who were lost to follow-up during the gaze position calibration assessments. While this may be labelled as a weakness of the study, about 70% of participants who sat in the lens calibration technique were available for the gaze position calibration measurements.

In the prism-based calibration technique, the range of prisms used was 4-16ΔD. This translates to a range of 2.29 to 9.09 degrees. However, in the eccentric-viewing technique, target eccentricity range was ±12 degrees. Although the range of induced gaze positions is different for the two techniques, this would less likely account for the observed difference in results between the two techniques. Data from an Indian cohort, which used a wider prism range 0-24ΔD revealed similar results in the prism-based technique as have been reported in this study (personal communication with Dr. Shrikant Bharadwaj).

The assessment of agreement between the eccentric viewing and prism-based techniques in the present study is limited by the fact that the non-dominant eye was assessed in the prism-based technique whereas the left eye was used in eccentric viewing technique. Regardless, participants had normal binocular function and wore optical correction during assessments, which would have minimized any possible effects. Additionally, there was a high intraclass correlation between the two ocular biometric measures of the two eyes [0.99(95% CI: 0.98-0.99), $P<0.001$ and 0.99(0.97-0.99), $P<0.001$] for the corneal curvature and ACD respectively. With this very high level of agreement, the HR of a subject, which depends on these two biometric measures, would not have been significantly different regardless of which eye was used in the prism-based technique.

2.9.1 Summary

- **Calibration slopes closer to unity were recorded in participants during lens calibration of the PowerRef 3™. However, inter-subject variability of the mean value was observed.**
- **The lens calibration technique was highly repeatable within ±0.24 in study participants.**

- **In the gaze position calibration techniques, the prism-based technique tended to over-estimate HR and showed the poorest repeatability**
- **Eccentric viewing and theoretical techniques showed superior repeatability in comparison to the prism-based technique.**

Having gained an insight into the relative accuracy and repeatability of various calibration modalities for the PowerRef 3™, the next chapter (chapter 3), describes the use of PowerRef 3™ to measure sustained accommodative and vergence functions in children with and without hyperopia. Prior to this assessment, baseline demographic and visual profile information were measured.

Chapter 3: Recruitment and Methods for the Assessment of Visual profile and Sustained Accommodative Performance in Children with and without Hyperopia

3.1 Introduction

This chapter describes the protocols which were followed to obtain demographic, and baseline visual information in children with and without hyperopia prior to undertaking the main assessment tasks (sustained accommodative and vergence performance). A detailed description of how data were collected for the main assessment tasks is also presented in this chapter (Figure 3.1). The chapter concludes with a discussion of the strengths and inherent limitations associated with the methods which were selected for data collection.

3.1.1 Study Aims

The main aim of the present study, which was the overall aim of this PhD work was to investigate the accuracy and quality of sustained accommodative effort in childhood hyperopia. Further, the study aimed to explore any relationships between accommodative and vergence performance and baseline visual characteristics of participants.

Primary research questions included:

- Are the characteristics of the accommodative response different in hyperopic children compared to emmetropic controls?
- Where inaccurate accommodative response exists in parallel with hyperopia, does correction of hyperopia restore accurate accommodation responses?

- Do children with poorer accommodative function also have deficits in vergence (eye coordination) performance?
- Is reading speed influenced by uncorrected hyperopia and/or poorly sustained accommodation?
- Does spectacle correction of uncorrected hyperopia improve reading speed?
- Does simulated hyperopia impair accommodative and vergence functions?

3.2 Recruitment

3.2.1 Sample Size Determination

The sample size required for this study was calculated using mean (±SD) accommodative response slopes previously reported for emmetropic controls 0.91 (±0.27) (Doyle *et al.* 2016), and a predicted mean accommodative response slope of 1.2 (±0.34) for the hyperopic group. The predicted mean for the hyperopic group was based on the findings of Horwood *et al*. (2010), who reported steeper accommodative response slopes (due to greater accommodative lags) in hyperopic infants compared with their emmetropic counterparts. Using a power of 90%, two samples (two-sided tail), and a sampling ratio of one (equal number of samples for hyperopic and emmetropic groups), these values yielded a sample size of 22 per group. In the hyperopic group, this translated to a sample size of 66 (22 * 3 groups), and 66 for the emmetropic controls.

3.2.2 Case Definition

A participant was defined as having hyperopia based on spherical equivalent refraction of ≥+1.00 D in the least plus eye after cycloplegic refraction. This definition was adopted to include varying levels of hyperopia from low (≥+1.00D to <2D), moderate (2D to 4D) and high hyperopia (>4D) so that assessment of the impact of different magnitudes of hyperopia on sustained accommodative and vergence functions could be explored. Hyperopia was classified using previously published studies as low (Kleinstein *et al.* 2003), moderate (Ip *et al.* 2008b), and high (Dobson and Sebris 1989).

3.2.2.1 Inclusion and Exclusion Criteria for Hyperopic Group:

Children aged 5–10 years were included in the study. This age range was chosen to ensure younger children who may have been acquiring their first hyperopic correction were recruited, and also to allow older children, whose educational and visual demands would have progressed through schooling, to be examined.

Previous findings from published works have highlighted the relationship between anisometropia and impaired visual function (Robaei *et al.* 2007; Yang *et al.* 2012). To explore the possible impact of anisometropia on sustained accommodative performance and other clinical data, subjects with anisometropia more than 1.00D were included in the study to allow a subgroup analysis. In the anisometropic group, hyperopia was categorised using the spherical equivalent refraction of the least hyperopic eye.

Subjects demonstrating with-the-rule astigmatism (most hyperopia in the vertical meridian), and whose astigmatism was 2.00DC or more were excluded. These exclusion criteria for subjects with astigmatism was adopted to reduce the possible impact of higher levels of astigmatism on accommodative performance (Harvey *et al.* 2014), and to allow measurement of refraction along the vertical meridian given that the PowerRef 3™ is designed to measure refraction in the vertical meridian only.

Additional exclusion criteria for the hyperopic group were the presence of ocular abnormalities such albinism, congenital cataract and nystagmus which obstruct the functional operation of PowerRef 3™. Moreover, children with developmental disorders such as cerebral palsy, Down syndrome, and Asperger syndrome, where sustained attention could be difficult to achieve, were also excluded.

3.2.2.2 Inclusion and Exclusion Criteria in the Emmetropic Control Group

Inclusion criteria for the emmetropic control group, included children aged 5-10 years with -0.25D to less than +1.00D of spherical equivalent refraction determined by cycloplegic retinoscopy, astigmatism less than 2.00DC, and absence of any ocular disease such as listed in the hyperopic group above. Similar to the exclusion criteria in the hyperopic group, children with ocular diseases and developmental disorders were excluded from participation.

3.2.3 Recruitment Pathways

Children were recruited from two pathways: from a local primary school (Millburn Primary School, Coleraine, UK); and from the Ulster University Optometry clinic, and a local Optometry practice (Kennedy Eye Care, Coleraine, UK). For children who were recruited in the school, a study pack containing parent information sheet (Appendix 1), consent form (Appendix 2), and a short eye and medical questionnaire (Appendix 3) were sent to parents via class teachers. Data collection took place on the school premises to allow for maximum participation while minimising disruption to school work. Children recruited from local optometry practice, and the University eye clinic were assessed at the Ulster University optometry and vision science research lab, accompanied by their parents. Eye and medical questionnaires were administered directly to parents at the time of assessment.

3.3 Ethical Statement

Prior to the commencement of recruitment and data collection, ethical approval for the study was obtained from the Ulster University Research Ethics Committee (UUREC) after submitting the study protocol first, to the School of Biomedical Sciences Ethics Filter Committee, before a final submission and approval by UUREC (see Appendix 4 for UUREC decision letter). The study procedures followed the Tenets of the Declaration of Helsinki.

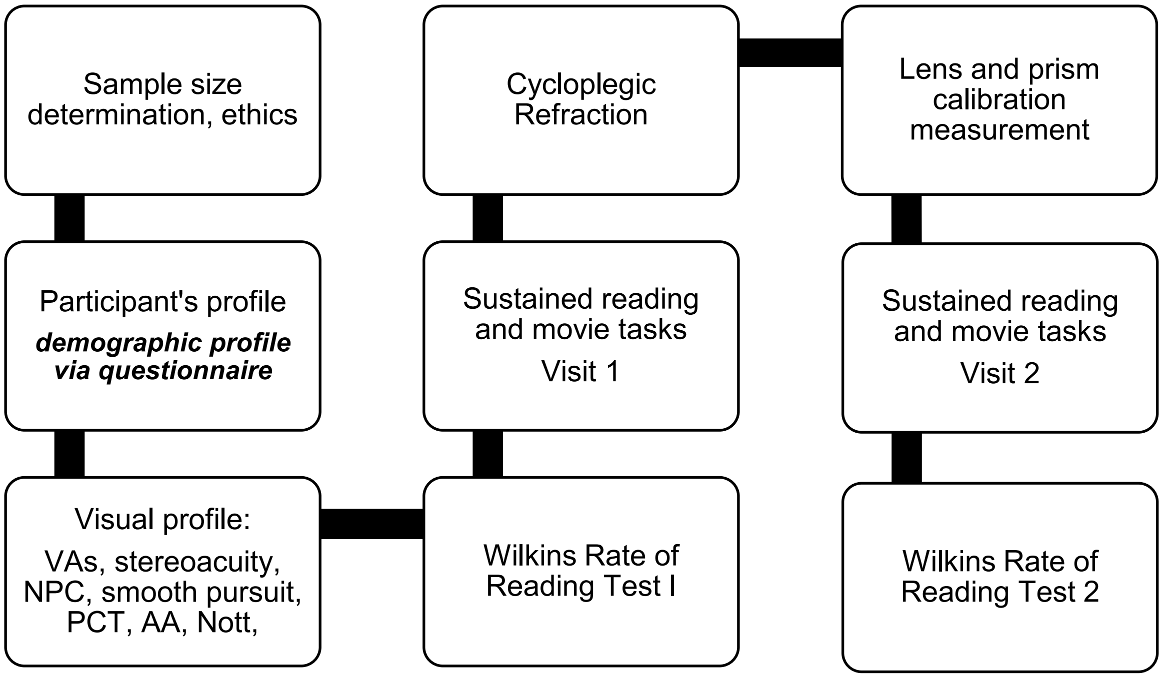


Figure 3.1; Diagrammatic presentation of the study protocol for the collection of demographics, visual profile, and sustained accommodative tasks data in children with and without hyperopia. VA – visual acuity; NPC – near point of convergence; PCT – prism cover test; AA – amplitude of accommodation; Nott – Nott retinoscopy.

3.4 Methods

3.4.1 Questionnaire for Demographic Data

A short eye and medical history questionnaire was developed for the collection of data on the child's eye and medical health (See Appendix 3) for details of questions in the questionnaires). The questionnaire also served as a tool to gather information on the child's demographic details: age, gender, class in school and the name of their local optometrist (if any). The short questionnaire was attached to the consent form, and the two were returned via a sealed envelope.

3.4.2 Measurement of Visual Acuity

Visual acuity (VA) has been defined as the spatial resolving power of the eye (Collin 2008). It is an important visual function measure used in both clinical practice and research studies. In a clinical setting, it is used to quantify the level of vision for the diagnosis, management, and follow-up or progression monitoring, while in a research setting it is often used as the primary outcome measure for hypothesis testing. In the present study, distance and near visual acuities formed part of the baseline clinical data collected to characterise participants in terms of their level of vision, and to explore possible relationships between their vision and sustained accommodative performance.

3.4.2.1 Presenting Distance VA

The Sonksen LogMAR Test (SLT) of VA was used to measure the visual acuity of subjects. The SLT is a tool commonly used to measure VA in children aged 2.5 years and above (Sonksen *et al.* 2008). The test uses LogMAR scaling and contour interaction, standard letter optotypes, and standard test protocols and has a high testability and reliability (Salt *et al.* 2007).

In the present study, measurements were made in the habitual refractive state. The distance VA was measured while the child was seated, with the examiner standing at 3m from the child. Measurement of distant VA commenced with presentation of the SLT single letter 'flip over' booklet (Figure 3.4.1, panel A) to the child at eye level, while they fixated binocularly. Testing with the single letter chart served as a 'level finding' protocol, to determine where to start during the crowded test. It also allowed comparison of single letter score with crowded letter score. Most children responded by naming the letter present, while a few of the younger children matched the letters presented to a handheld Keycard. Following the completion of the single letter test, the linear display booklet (crowded letters) was presented for the measurement of the binocular crowded acuity after which monocular measurements were made, starting with the right eye (Figure 3.4.1, panel C). Binocular crowded visual acuity was measured first so that if a child had limited cooperation with monocular occlusion and testing, data from binocular measurement could be used. There are two crowded letter booklets (booklets C and D); a different booklet was used to assess crowded acuity in each eye. In the present study, the child had to identify at least two letters to move onto the next line. Where a child could not identify the letters at 3m, the examiner moved to a closer distance of 2m or 1m, and a correction factor was incorporated into the visual acuity score. Scoring of visual acuity was by the number of letters identified, and credit given for each letter identified.

3.4.2.2 Presenting Near VA

Measurement of near VA was also made with the SLT near test chart (Figure 3.4.1, panel B). The examiner sat directly in front of the child and presented the near test chart at 40 cm binocularly, directing the child to identify the letters presented, line-by-line. A cord was used to check and maintain testing distance. Similar to the SLT crowded letters test scoring, scoring was made based on the number of letters which were correctly identified.

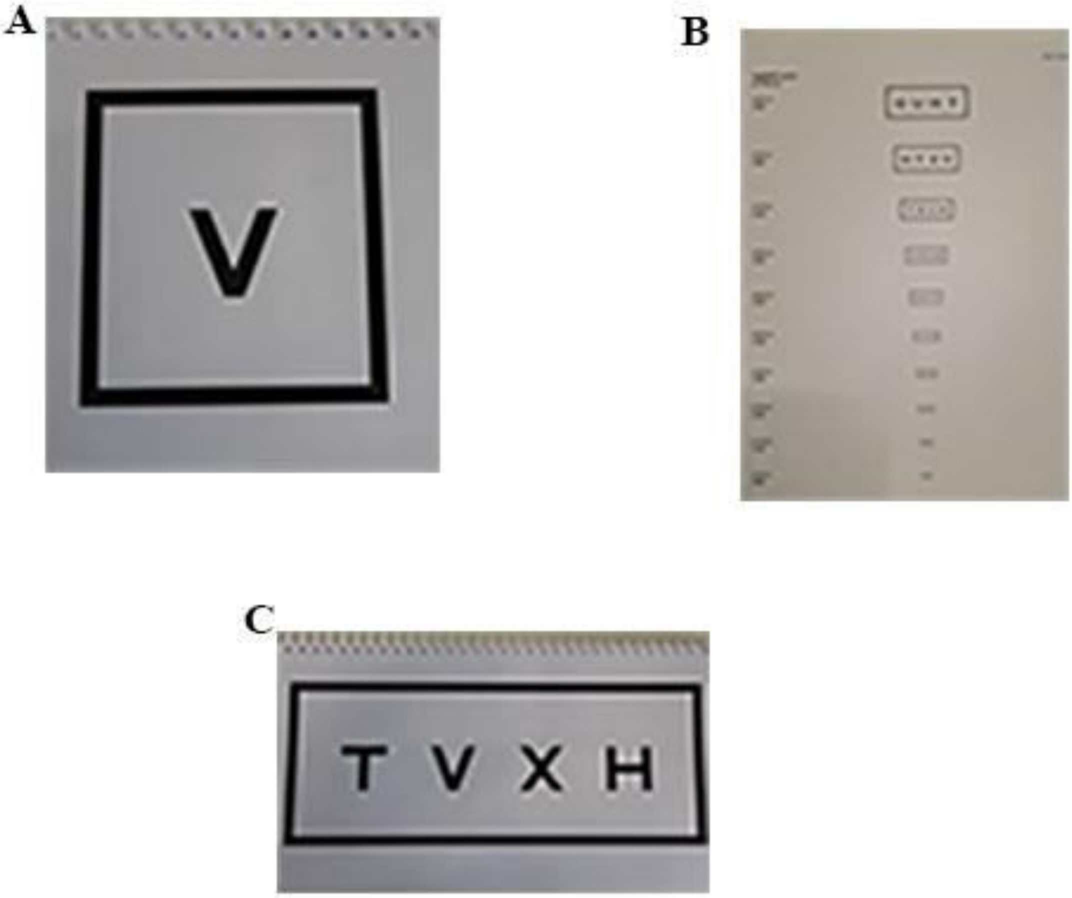


Figure 3.4.1 Image showing the Sonksen LogMAR Test chart types (A) Single letter display, (B) Near chart, (C) Linear display (crowded letter booklet).

3.4.3 Ocular Posture

Ocular posture allowed assessment of ocular alignment between the two eyes. In the present study, ocular posture was determined objectively by using the prism cover test (PCT) to determine the presence and direction of any deviation in the eye. The use of the prism cover test to detect and measure the amount of deviation in child participants have been previously reported (Deacon and Gibson 2001). Cover test was performed at distance (6m) while the child fixated on a cartoon target. The colourful target, containing a wide variety of gross and fine spatial detail, served to stimulate and sustain interest of the child for continuous fixation. The Cover/Uncover test was performed first to determine the presence of strabismus, after which the Alternating cover test was performed to determine the direction and the magnitude of the deviation using a prism bar. A similar measurement was made at near (40cm) while the child fixated an appropriately-sized letter accommodative target on a Budgie stick. For children who already owned spectacle correction and were wearing them at the time of assessments, measurements (both distance and near) were made with and without their glasses.

3.4.4 Ocular Motility

The role of visual tracking or eye movement in individuals with reading difficulty has been reported (Benfatto *et al.* 2016). To obtain gross quantitative estimates of smooth pursuit and saccadic eye movements in subjects, a visual tracking test (Nakajima 1990; Hain 1997), involving the use of a swinging pendulum was performed on each participant to gain an idea of the quality of their eye movement. The ball was swung in a back and forth pattern, as may be done when demonstrating the Pulfrich pendulum effect. With the examiner sitting directly in front of the participant, the participant was instructed to fixate on the ball which was stationary at the start and to follow the ball with their eyes without moving the head (Figure 3.4.2). The movement observed was graded as either excellent, fair, or poor. Three cycles of tracking were used to grade the quality of eye movements.

Figure 3.4.2 Image demonstrating gross estimation of the quality of eye movement using the pendulum ball in a participant.

3.4.5 Stereoacuity

Increasingly, stereoacuity is an important diagnostic tool for assessing hyperopic children at risk of abnormal visual development (Robaei *et al.* 2007; Yang *et al.* 2012; Kulp *et al.* 2014; Ciner *et al.* 2016). In the present study, the Frisby stereotest was used to assess stereoacuity. The Frisby stereotest is widely used in research, and particularly in child vision research (Anketell *et al.* 2013), as this free-space real-depth test doesn't require the use of red-green or polarising spectacles. The Frisby stereotest is made up of three Perspex plates of varying thickness (6mm, 3mm, 1.5mm). The plates can be presented on either side depending on whether the examiner is testing a *crossed* or *uncrossed* disparity. In addition to these advantages, it is simple to administer, light in weight, has a broad operating range, and easy to conduct at a range of distances.

Measurement of stereoacuity in this study followed the protocol used by Anketell *et al.* (2013). The test kit was positioned 80cm from the spectacle plane of the child at baseline, and the 6mm plate was first introduced (Figure 3.4.3). Uncrossed disparity was tested in the present study by asking the participant to identify a "hole" in one of the four squares. If the participant could correctly identify the "hole" in two of three presentations, the 3mm plate was introduced, and the process was repeated. The 1.5mm plate was introduced if the child could correctly identify the two of the three presentations. If all the three plates were correctly identified at the 80cm baseline distance, the test distance was increased to the 150cm and the whole assessment was repeated starting with the 3mm plate. Each participant's score was determined by referring to the table of scores provided with the testing kit and recorded in minutes of arc. However, if the child was unable to identify the "hole" in the 6mm plate at 80cm, the plate was moved closer towards the child at 10cm interval. If the "hole" on the 6mm plate was not correctly identified at 30cm, a fail was recorded, and the test was discontinued. All assessments were made over a child's spectacle correction, if they had any, and presented them at the time of testing. A metre rule was used to confirm and check test distance at several time points during testing.

Figure 3.4.3 Image showing assessment of stereoacuity in a participant. Assessment was made over a participant's habitual refractive correction.

3.4.6 Assessment of Amplitude of Accommodation

To assess each participant's accommodative amplitude, the present study used the Push-Up/Pull-Back method. This is a subjective assessment based on the child's response of reporting blur when a near target is presented. The Royal Air Force (RAF) near point Rule was used for the measurement of the accommodation amplitude. The RAF rule is essentially a 50cm rule, that has a slider which holds a rotating four-sided cubes. Assessments were made with the participant's habitual refractive correction in place. The RAF rule was rested on the cheekbones of the participant and they were directed to fixate on a single word on the smallest line of letters which could be seen clearly on one of the rotating four-sided cubes. The participant was instructed throughout the assessment to maintain clear vision and to report when the target first became "fuzzy" or blurred as it was moved closer to the participant. This point of reported blur was recorded as the amplitude of accommodation in dioptres. The target was then pushed close to the participant and then pulled back until the child reported the word was back in focus again. For each participant, three sets of measurements were made for each eye and then repeated binocularly. The average of the three readings was recorded as the amplitude of accommodation for the right eye, left eye and under binocular viewing conditions. A few of the youngest participants struggled to sustain attention required for monocular testing, so only binocular assessment was achieved in these cases. Testing was done through habitual refractive correction, if worn.

3.4.7 Near Point of Convergence

The near point of convergence (NPC) is the maximum convergence the eyes are capable of when the two lines of sight intersect on an object located in the median space in front of the face (Siderov *et al.* 2001). The NPC in this study was assessed using the RAF rule. This instrument and the technique applied has been used to measure the near point of convergence in typically developing children (Chen *et al.* 2000; Siderov *et al.* 2001). The near point of convergence was assessed subjectively and objectively by resting the RAF rule on the participant's cheekbones, while they fixated on a spot (with a vertical line through it) on one of the rotating four-sided cube faces. The participant was asked to report the point when the vertical line divided into two, with the examiner watching closely for the point when one of the eyes diverged. This point was noted as the break point and recorded in centimetres. Three readings were made on each participant and the average of the three reading was recorded as the near point of convergence. Testing was done through habitual refractive correction, if worn.

3.4.8 Assessment of Accommodative Response

Modified Nott dynamic retinoscopy was used to measure the accommodative accuracy of each participant. Using the Ulster-Cardiff Accommodation Cube, the present study followed the protocol previously used by McClelland and Saunders (2004) to measure the accommodative response of school-age children. The protocol consisted of testing the least hyperopic meridian of the right eye while the participant was instructed to binocularly fixate the smallest line of letters on one side of the rotating four-sided cube placed at 25cm (Figure 3.4.4). The 25cm testing distance was chosen to allow comparison to be made with the two near tasks (reading on a Kindle and a watching a movie) which were also tested at the same distance. The retinoscope was held as close as possible to the ruler while the examiner checked the reflex movement for neutrality. The examiner moved towards or away from the participant to achieve a neutral reflex. The target position remained stationary. The position at which neutral was seen with the retinoscope, was recorded in centimetres and subsequently converted into dioptres as the accommodative response. Testing was done through habitual refractive correction, if worn.

Figure 3.4.4 Image showing assessment of a participant's accommodative response by Nott retinoscopy.

3.4.9 Assessment of Reading Speed

Previously published work by van Rijn *et al.* (2014) reported that spectacle correction may improve reading speed in children with hyperopia. To further investigate the relationship between uncorrected hyperopia and reading speed, and the influence of optical correction using a different methodology, the Wilkins Rate of Reading (WRR) test was administered to measure the reading speed of participants. The WRR is a one-minute administered test, originally designed to be used in a population with reading difficulties (Wilkins *et al.* 1996) but for which normative data are available, describing the rate of reading in a typically developing population (Firth *et al.* 2007). The WRR test uses simple words and is not a conventional reading test for assessing reading ability: such tests are typically designed such that words become progressively more difficult to read. The test consists of a passage of 13 simple words presented and repeated in a random sequence which have no logical, contextual meaning or grammatical structure. The words are printed in nine-point Times font. The test has four versions (version A, B, C, and D), containing the same words (150 words) but with different arrangements, and a score sheet for each version. In the present study, the test was administered using the participants' habitual refractive condition at baseline (where the participant wore glasses, the test was administered while they wore their correction, and for those without correction, the test was administered unaided). The reading sheet (version A, B, C or D) was placed on a table with the participant comfortably seated (Figure 3.4.5). Prior to reading, the test was explained to the participant as follows: "this is a passage containing random words which do not make any sense when reading it. I want to measure how quickly you can read them. You will start reading when you hear the beep of the stopwatch and stop when the stopwatch beeps again. Please read the words aloud". The number of words read per minute was recorded as the rate of reading.

For younger children with less reading experience, brief training time was administered, and they were familiarised with the words prior to testing. If they demonstrated poor cooperation or were unable to read the words after training, the test was abandoned. However, the test was attempted on all participants at baseline, and a repeat measurement was made on the participants in the hyperopic group, with a "reversed" refractive condition (optical correction for those without correction during baseline measurement, and no correction for those who were tested with correction at baseline), if they were tested at baseline. Additionally, a subset of the emmetropic participants were made artificially hyperopic with minus lenses (-3.00D to -0.50D) and a repeat WRR measurement was undertaken while they wore this correction. Repeat measurements were undertaken after approximately a week of the baseline measurement.

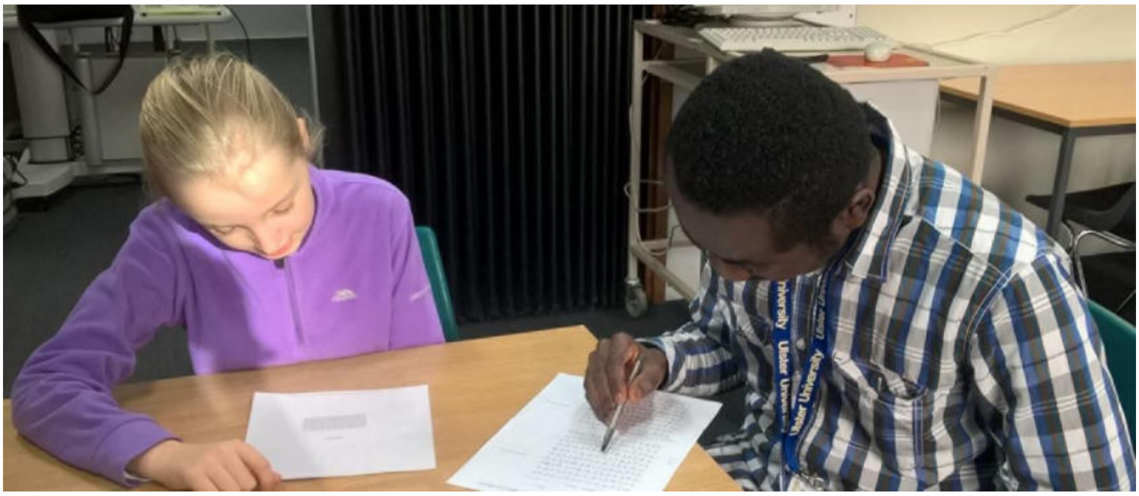


Figure 3.4.5 Image demonstrating assessment of rate of reading in a participant without correction.

3.4.10 Cycloplegic Refraction

Cycloplegic refraction, also referred to as wet refraction, involves the use of pharmacologic agents to paralyse accommodation, by the action of the agents on parasympathetic receptors of the ciliary muscles. Consistent with previous epidemiological studies of refractive error and those evaluating visual functions in young hyperopia patients (Kleinstein *et al.* 2003; Ip *et al.* 2008a; O'Donoghue *et al.* 2010; Kulp *et al.* 2014; Ciner *et al.* 2016), cycloplegic refraction was employed in the present study to define refractive error.

In the present study, one drop of 1% Cyclopentolate hydrochloride eye drop was used to achieve cycloplegia in each eye. In Caucasian eyes, a lower dosage of cycloplegic agents has been established as safe and effective for achieving cycloplegia (Manny *et al.* 1991; Bagheri *et al.* 2007). Prior to instillation of the Cyclopentolate eye drop, 0.5% Proxymetacaine hydrochloride eye drop was instilled to anaesthetise the ocular surface, to provide comfort (less stinging) during the instillation of the Cyclopentolate eye drop. Thirty minutes after the instillation of the Cyclopentolate eye drop, the eyes were assessed for maximum cycloplegia. This was achieved by asking the child to read print at near. Failure to see and read the print, and an examination of the pupil size was used ascertain maximum cycloplegia (He *et al.* 2004; Ip *et al.* 2008a; Ip *et al.* 2008b). Once this was determined, both eyes were refracted by an experienced optometrist using retinoscopy. After testing, in addition to feedback about the vision assessment, participants were given a College of Optometrists information leaflet on cycloplegic eye drops to bring home to parents and given disposable sunglasses to reduce discomfort when playing outside. Cycloplegic refraction was undertaken after the participant performed the sustained accommodative tasks during the first visit.

3.5 Assessment of Sustained Accommodative Function

Sustained accommodative accuracy was investigated using eccentric, infrared photorefraction while participants engaged in a reading and movie-watching tasks at 25cm. This technique occurred binocularly, enabling simultaneous assessment of vergence and pupil size. These tasks were performed under two experimental conditions.

3.5.1 Experimental Conditions

3.5.1.1 Experimental Condition I

In the first experimental condition, participants wore their habitual refractive correction while they engaged in reading and watching a movie. Hyperopic participants who wore glasses and presented with their glasses at the time of assessment performed the tasks wearing their correction. Those who were uncorrected, as well as emmetropic participants, performed the two tasks without correction.

3.5.1.2 Experimental Condition II

Experimental condition II was undertaken approximately a week after the first assessment visit. In this condition hyperopic participants who did not wear a correction during experimental condition I were given temporary correction (full correction based on the cycloplegic refraction), while those in the hyperopic group who wore spectacle correction for experimental condition I, forwent their correction during condition II. Minus lenses ranging from -3.00D to -0.50D were used to simulate hyperopia in a subset of the emmetropic participants while they performed the assessment tasks in experimental condition II. The remaining emmetropic participants were not tested after participation in Experimental Condition I.

3.5.2 Tasks for Sustained Accommodation Assessment

There were two tasks in each Experimental condition, both of which were performed for a period of 15 minutes: reading and watching a movie. While studies have reported a 15-minute window to be a typical length of time that school children aged 8 years and above spend performing work at school (Ritty *et al.* 1993), it was recognised that the youngest participants could find it difficult to sustain attention for this length of time, so the examiner endeavoured to engage their attention for as long as possible, up to a maximum of 15 minutes. A 25cm target distance was chosen for assessment based on a previous publication which reported this distance as the typical near working distance for children in school (Rosenfield *et al.* 2001). Before commencement of data collection, it was envisaged that there could be high attrition or low completion rates with the reading task if participants engaged in the movie task first. Therefore, the protocol commenced with the reading task. However, to assess the possible influence of "order effect" on the outcome of the two tasks, the *counterbalancing technique* of implementing intervention in an experimental study was introduced in a subgroup of the participants (Harvey *et al.* 2014). This involved reversing the order of assessing the two tasks and getting the participants to perform the movie task before reading.

Prior to starting the reading or movie task at 25cm, participants briefly looked at a Maltese cross target at 1m to provide baseline refraction data from which the change in refraction (denoting accommodation) was computed.

3.5.3 Literacy Activity (Mirroring a Visually Demanding and Stimulating Activity Comparable with Reading Tasks Conducted in School)

Participants engaged in a reading aloud activity, which was designed to simulate a visually demanding activity undertaken in school. The task was not meant to assess reading ability, but as a means to measure accommodation. Participants read from an

Amazon Kindle presented at a near distance of 25cm while simultaneous measurement of accommodation, gaze position, and pupil sizes were recorded by the PowerRef 3™ camera. Participants made appropriate saccadic eye movements associated with reading a text on a Kindle. The Kindle was housed in a wooden box with a forehead rest. Two Velcro straps were attached to the wooden box and wrapped around the participants' head to restrict and minimise head movements during the task (Figure 3.5.1). Depending on the age and ability of the participant at the time of assessment, one of the following books on the Kindle was selected for them to read: The Pony-Mad Princess (by Diana Kimpton, 2014 edition, Amazon standard identification number (ASIN) – B00KTDOKK4), Frankie's Magic Football (by Frank Lampard, 2013 edition, ASIN – B00JMK3DE), and Horrid Henry (by Francesca Simon, 2010 edition, ASIN – B004BDOJW2). The font type, size, and background illumination on the Kindle were equal for all the books used. A Futura font type, an 8-point font (the second smallest font size option on the Kindle), measuring a height of 1.1mm, with an average background illumination of approximately 40 cd/m^2 across the screen was chosen. At a reading distance of 25cm or 250mm, this corresponded to a visual angle of 0.25 degrees. Custom-made reading material was carefully designed for the youngest children who could not read any of the books on the Kindle. The content of the custom-made reading material consisted of high-frequency reception words (year 0, 4-5 years), and year 1 (5-6 years) words with pictures to match. This was designed on a series of PowerPoint slides, with a Futura font type, having the same letter height of 1.1mm as that of the Kindle books, and subtending the same visual angle (0.25 degrees). This was presented on a portable monitor which was also used for the movie task. The monitor subtended 16.70^o by 10.20^o at 25cm while the viewing window of the kindle subtended 14^o by 10.20^o at 25cm. The monitor was dimmed to an average background illumination of 50 cd/m^2. The background illumination selected on both the Kindle and monitor provided sufficient contrast while allowing pupil sizes to be maintained within the operational range of the PowerRef 3™. Background illumination of the two screens was measured with the ColorCal MK II™ Colorimeter. The vertical gaze angle (angle of tilt) while viewing the Kindle and LCD monitor was 20.4^{o} which falls within the ergonomic range for comfortable reading (Hill *et al.* 2006; Shieh and Lee 2007).

3.5.4 Task 2: Passive Free-Viewing Activity (Recreational Visual Activity)

In the passive free-viewing activity, which was meant to simulate a recreational type of activity undertaken by children, participants watched an animated movie while simultaneous measurement of accommodation, vergence and pupil sizes were recorded by the PowerRef 3™ at 25cm. The movie target was a popular, commercially available stop-motion animated movie (Wallace and Gromit, Aardman animations), containing broadband spatial frequency content. There was varying background illumination of the target corresponding to the changing scenes during the movie task, with an average background illumination of 30cdm^2 (range: 10–50cd/m^2). This target was chosen to engage and sustain interest and attention of participants, especially the younger participants. The target has been previously used to assess the accommodative response in children with and without Down's syndrome (Doyle *et al.* 2016). Participants' attention to detail contained in the movie was assessed during the task by asking questions about aspects of the movie. Speakers allowed relay of the movie soundtrack to further attract and maintain participants' attention.

Figure 3.5.1 Image of the PowerRef 3™ set-up, showing a participant engaged in the movie task. The PowerRef 3™ was positioned 1m from the participant and connected to a computer (desktop) monitor. The participant's head was stabilised using two Velcro straps.

3.5.5 Set-Up of PowerRef 3™ for Measurement of the Two Sustained Tasks

The photorefraction system has been previously used to assess accommodation and vergence in different age groups, under different task conditions, and under different recording times: mostly for brief testing times (Seidemann and Schaeffel 2003; Harb *et al.* 2006; Tondel and Candy 2008; Bharadwaj and Candy 2008). However, in the present study, the PowerRef 3™ was deployed to measure accommodation and gaze position at a sustained testing time of 15 minutes. The PowerRef 3™ camera was mounted on a custom-designed bench (Figure 3.5.1) at 1m±0.05m. The traditional method of reflecting infrared light from the instrument's camera aperture into the eye as described in Chapter 2, where a combination of "cold" mirror to direct infrared light towards the "hot" mirror at 45^{o}, and from the "hot" mirror into the eye at 45^{o} was adopted in the present study.

This periscopic set-up ensured the camera was on-axis for data collection, yet out of participants' field of vision. The box which housed the Kindle and monitor subtended 6.8^{o} at 25cm, while the whole set-up from the bench to the black box was designed to subtend a tilt angle of 16.7^{o}, which is less than the 30 degrees, beyond which tilt angle affects reading (Firth *et al.* 2007). To ensure that the angle between the two mirrors remained unchanged for any adjustment made to the set-up, a custom-made protractor was used to measure the angle between the two mirrors frequently during the data collection. The tilt angle of the set-up, together with a lab stool with an adjustable height and backrest ensured optimal comfort for the participants during sustained reading. This also mimicked the traditional posture for reading and viewing near targets, which are typically in downgaze. Varying pupil size/shape does not affect estimates of refraction when using the photorefraction technique (Choi *et al.* 2000; Harb *et al.* 2006), consequently, scanning the passage while reading on the kindle would not have affected the PowerRef 3™ estimates of accommodation so far as participants eyes were in the field of the camera. Furthermore, the horizontal dimension (extent of horizontal gaze) of the Kindle used in the present study is comparable to previously published dimensions (Harb *et al.* 2006; Roberts *et al.* 2018a)

3.6 Individual Defocus and Gaze Position Calibration

The case for individual calibration of the conversion factors for obtaining accommodation and gaze position from the PowerRef 3™ has been previously discussed in Chapter 2. Against this backdrop, lens and prism-based calibration routines were attempted on all participants.

In the present study, the calibration routine was performed prior to the second set of sustained accommodative tasks measurement. The range of lenses and prisms used (+4D to -4D, and 4ΔD to 16ΔD respectively) were the same as the protocol described in Chapter 2. Similarly, the target used consisted of the Maltese cross target. However, unlike the protocol that was adopted in Chapter 2, and previously reported in some published works (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Jagini *et al.* 2014), the target distance was 25cm and not the traditional 1m adopted for calibration. This target distance was selected for calibration in the present study, to reflect/match the "dynamic" measurement of accommodation and gaze position at near distance and be specific to our protocol of measuring accommodation and gaze position at this distance. Moreover, previous studies in which accommodation and vergence were measured using a version of the PowerRef 2™ have adapted the calibration routine to near testing distances such as 33cm and 50cm (Horwood and Riddell 2008; Bharadwaj and Candy 2009). Each calibration lens was held for an average of four seconds of data, with the duration being less for uncooperative participants or more when there were many reflections from participant's eyes interrupting data collection. The custom-designed algorithm in MATLAB™ used for the analysis of data in Chapter 2, was employed for data extraction and analysis in the present study.

3.7 Data Management

3.7.1 Data Storage

A data recording form was designed for the entry of subjects' demographic and clinical information (See Appendix 5). These were kept in a string-tie closure A4 file bags and stored in a secured office locker. The information contained in the data recording form was also entered into Stata $^{(R)}$ (version 14, StataCorp LLC, Texas, USA) on a password-protected computer for statistical analyses.

3.7.2 Data Extraction of PowerRef 3™ Output

The PowerRef 3™ records outputs of accommodation, gaze position and pupil size in an Excel spreadsheet in a comma-separated file format and saved on a memory stick. To obtain these data, a custom-written algorithm in MATLAB™ was used to import the data from excel. This software incorporated the criteria previously used for data extraction by ours and other research groups (Candy and Bharadwaj 2007; Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Doyle *et al.* 2016).

This included:

1. Exclusion of data points outside of the PowerRef 3™ operating range (+ 5D to - 7D)
2. Exclusion of data points outside the horizontal range of the PowerRef 3™ (±15°).
3. Exclusion of data points for pupil sizes less <3mm and >8mm.
4. Despite careful consideration and study design, when participants read the text on the Kindle from top to bottom of each page and continued this pattern for the entire period of assessment, reading lower text sometimes resulted in a lowering of the upper eyelids in downgaze which interrupted the PowerRef 3™ readings (Figure 3.7, panel A). To overcome this challenge, data below the 5th percentile

and above the 95th percentile were excluded to eliminate data arising from these sessions of measurement (Figure 3.7, panel B). These were extreme outliers, which could have potentially affected the results and were therefore removed. The use of percentiles to remove outliers in data, also called *winsorisation,* has been reported (Yang and Berdine 2016). Thus, 90% of central data was preserved and used for analysis.

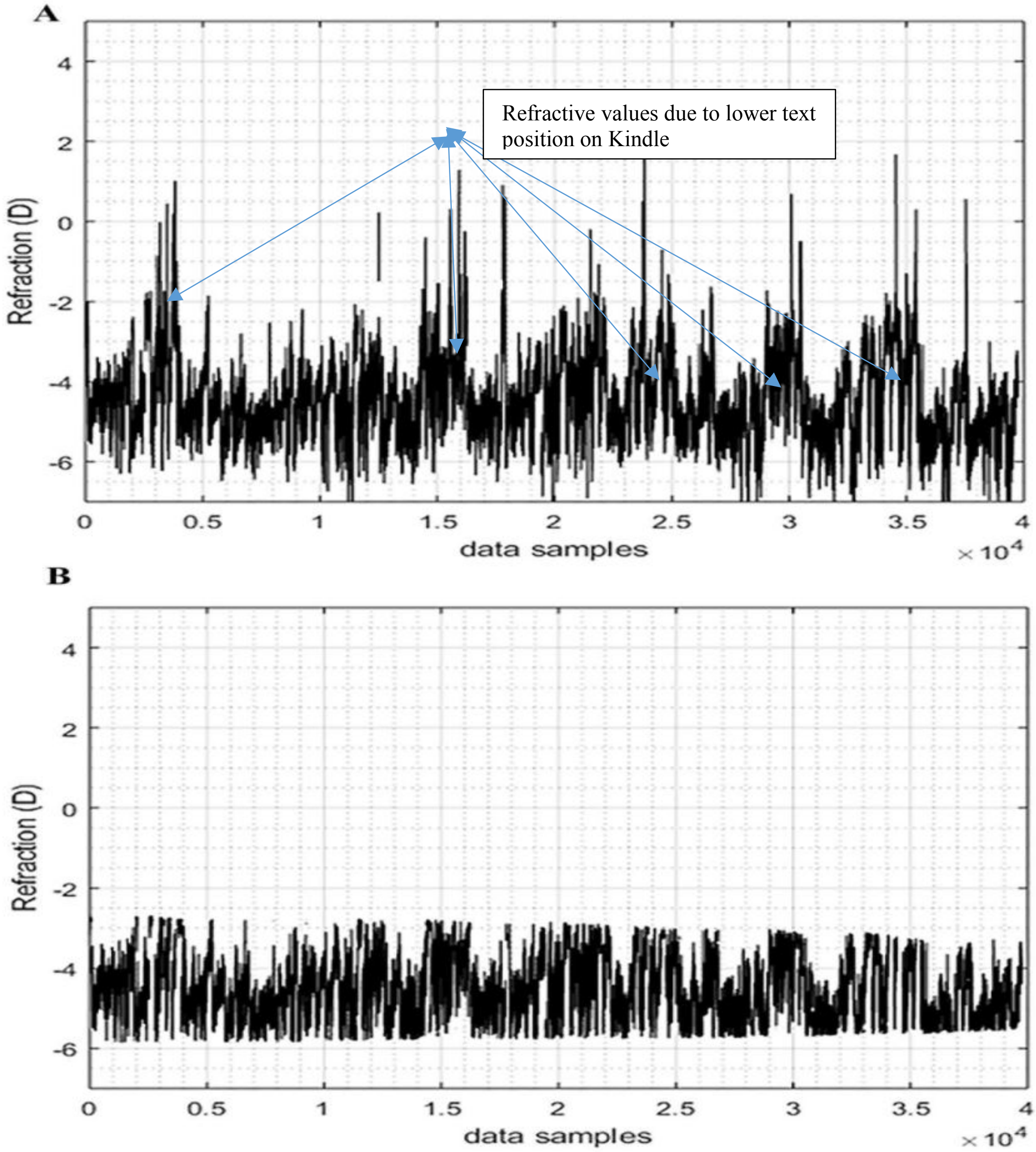


Figure 3.7 Image showing (A) the effect of lower text position on Kindle on PowerRef 3™ reading, (B) exclusion of peripheral refractive values (below 5th percentile and above 95th percentile) due to extreme text position (high or low) on the Kindle.

The PowerRef 3™ has a sampling rate of 50 Hz, therefore, 10 seconds of baseline data at 1m, and 15 minutes of sustained reading or movie task at 25cm amounted to approximately 45000 data points (50Hz * 900 seconds). For the tasks performed at 25cm, the data were indexed into one-minute segments depending on the duration (Harb *et al.* 2006). For example, for a subject who read or watched a movie for 15 minutes, there were 15 segments each containing one-minute worth of data. However, for each one-minute segment, 10 seconds worth of data (~ 500 samples) were indexed and the mean of the indexed data used for analysis of accommodative, eye position, pupil sizes and IPD.

Stability of accommodative response (microfluctuations) was analysed in the time domain using Root Mean Square (RMS) deviation of accommodation, and in the frequency domain using power spectrum analysis. Power spectrum analysis using the Fast Fourier Transform (FFT) was performed for each segment (Harb *et al.* 2006). Prior to running FFT, missing data points were interpolated using cubic spline algorithm (Collins *et al.* 1995; Candy and Bharadwaj 2007). The *direct current* (DC) offset of the signal (mean amplitude displacement from zero), was then removed by subtracting the average response of each segment from the data (Harb *et al.* 2006; Roberts *et al.* 2018a) after which a Gaussian filter (with a window size = 10) was applied to smooth the data. The accommodative microfluctuation in the frequency was characterised as the area under the curve for the LFC (≤0.6Hz) (Roberts *et al.* 2018a). The area under the curve for this frequency range (> 0 to ≤ 0.6 Hz) was calculated for each one-minute segment, and the average of these one-minute segments was generated as the mean power spectrum for each subject (Harb *et al.* 2006).

3.7.3 Statistical Analyses

Statistical analyses were carried out in Stata [(R)] (version 14, StataCorp LLC, Texas, USA). Descriptive statistics including mean (±SD) and percentages were used to summarize parametric data, while median (25^{th} and 75^{th} Interquartile range) were used to summarise non-parametric data. Independent t-test was used to test for difference between groups for parametric data. For non-parametric data, the Mann-Whitney test was used. The one-way Analysis of Variance (ANOVA) was used to test for group differences where there were more than two groups, while the Kruskal Wallis test was used to assess group differences for non-parametric data. Univariate associations between variables were assessed using Pairwise correlation and Spearman's rank correlation for parametric and non-parametric variables respectively. Multiple variables analyses were made using ANOVA, Analysis of Covariance (ANCOVA), and multiple linear regression. Statistical significance was set at $P<0.05$.

3.8 Strengths and Limitations

The present study describes how sustained accommodative and vergence responses were measured in children with and without hyperopia using the photorefraction technique. The use of two everyday tasks – reading and movie, to measure accommodative and vergence response is a strength of this study as the two tasks reflect natural use of accommodation in typically developing children. The differences in the two tasks such as attentional demand and spatial frequency content allowed investigation of the accommodation and vergence responses under two different task conditions. The use of photorefraction also allowed investigation of the effect of spectacle correction on sustained accommodative and vergence response for the first time.

A strength of the present study also relates to the use of a large sample of children with hyperopia to investigate sustained accommodation and vergence. The use of large sample size enhances the statistical power of studies (Chung *et al.* 2002). A recently published study on sustained accommodation in uncorrected hyperopic children used a relatively small sample size (n=54) (Roberts *et al.* 2018a). Recruitment of children from community optometric practices enriched the sample of hyperopes used for investigating sustained accommodative and vergence responses in the present study.

The study protocols described in this chapter, while being generally robust, have some limitations which are discussed below:

There may be concerns about the lack of randomisation of the two tasks and its effect on the study results. The rationale for not randomising the order of tasks has been discussed earlier in this chapter. To explore the possibility of any *order effect*, the counterbalancing technique was introduced in a subgroup of the study participants during data collection, where the task order was reversed. The results are discussed in Chapter 5.

Although head movements were minimised with double Velcro straps around the head of subjects, some micro-movements were likely to be present, particularly in the youngest and least compliant participants, but the impact of these micro-movements on the results would be likely insignificant. There may be also concern regarding the cooperation of the youngest participants given the sustained nature of the tasks. However, every effort was made to engage and sustain the interest and attention of participant during the task, especially in the reading task, where for example, applause and compliments were used to encourage reading. Data regarding completion and success rates with sustained tasks are discussed further in Chapter 5.

In the present study, participants who were non-habitual spectacle wearers were given temporary correction to assess the effect of spectacle correction on sustained accommodative and vergence functions. These prescriptions were glazed using two generic PDs (54 and 58mm). Concern about differential prismatic effect was considered in detail and found to be insignificant. For example, the participant who received the highest temporary correction (+4.50 D with a frame PD of 58) had a PD of 59mm. This would result in a prismatic effect of 0.09 ΔD base-in, too small to affect the results of sustained measures and patient comfort during wear.

Participants who wore habitual refractive correction at the time of testing, were tested with their correction for the baseline visual measures, and the sustained accommodative and vergence measures. There is a limitation associated with using the habitual refractive correction for assessing these measures, as in case of inaccurate prescriptions, results obtained could have been affected. However, cycloplegic refraction was performed on this cohort, which allowed comparison between their habitual correction and the cycloplegic refraction to be made, and in all such participants, their prescriptions were considered appropriate, viz a' viz the cycloplegic refraction.

There may be concerns with lens effectivity affecting the photorefractive estimates of the accommodation during the sustained near tasks. However, in the majority of study participants, a +4.00D lens was the highest prescription given, and a calculated effect of lens effectivity was +0.45D of additional accommodation. This is less likely to have affected the results, as a recent study of the effect of lens magnification/minification on the photorefraction estimates, reported that lenses up to +4.00D, have less effect on magnification/minification, as well as effectivity, especially if the vertex distance is small (Bharadwaj *et al.* 2018). Bharadwaj *et al.* (2018) further reported that the PowerRef 3™ under-estimates the refraction/accommodation where measurement is made through a plus lens. Therefore, the calculated +0.45D due to lens effectivity would not necessarily cause an increase in the photorefractive estimates according to the findings of Bharadwaj *et al.* (2018). Additionally, in the present study, stick-on nose pads were used to maintain a constant vertex distance of 12mm, which would have minimised any effects. In a few participants (n=3) whose prescriptions were greater than +4.00D, the effect of lens effectivity on accommodation is still less than a 1.00D (for example 0.85D for a +7.00D prescription (highest)).

Given the battery of baseline visual functions tested, an additional examiner was employed to assist with data collection. The assistance of supervisors and another experienced optometrist was sought to help administer cycloplegic eye drops to participant, as the author of this thesis was not a GOC licensed optometrist. The use of different examiners to assess these measures could present a risk of measurement bias which could affect the results. However, a standard protocol describing how each test was to be carried out was handed to an examiner to ensure consistency in the way measurements were made, which may have minimised the risk of bias.

In the assessment of reading speed using the WRR test, participants were instructed to read the passage as quickly as they can. The instruction did not include statements which could assess accuracy such as, "I want to you to read the passage as quickly and carefully as you can". Therefore, the WRR test used in the present study could not measure accuracy, and this is acknowledged as a limitation.

There may be concerns with the choice of the prism-based calibration technique for calibrating sustained vergence measures in the present study, given that the results of gaze position calibration techniques, discussed in Chapter 2 demonstrated it was the least accurate and repeatable. This occurred because results from the prism-based technique in Chapter 2 only came to the fore after data collection for the prism-based technique for use with sustained accommodative and vergence measures had commenced.

In the next three chapters, results are presented and discussed for the research questions and methods described in this chapter. Chapter 4 describes results of demographics and baseline visual profile, Chapter 5 presents results of sustained accommodative and vergence functions in children with and without uncorrected hyperopia, and Chapter 6 discusses the effect of spectacle correction on sustained accommodative and vergence functions in children with hyperopia, and the effect of simulated hyperopia in emmetropic controls.

Chapter 4: Demographic characteristics, and visual profile of participants with and without hyperopia

4.1 Introduction

This chapter presents the results and discussion of the baseline demographic and visual measures of participants with and without hyperopia. The purpose of these measures was to characterise participants in terms of their visual status and to further explore relationships between these baseline measures and sustained accommodative and vergence measures (chapter 5). An outline of the chapter is given below:

- Descriptive statistics of demographic and visual measures
- Univariate analysis of demographic and visual measures
- Multivariate analysis of demographic and visual measures
- Discussion
- Chapter summary

4.2 Success rate for baseline measures

Out of the total 137 participants seen, 17(12%) were excluded due to one of the following reasons: myopia (n=3), significant astigmatism > 2DC (n=3), refusal of cycloplegic refraction (n=5), strabismus (n=3), and Non-Caucasian participants (n=3). Of the remaining 120 participants, three were uncooperative during the assessment of baseline visual profile measures and so data from these individuals were also excluded from further analysis. There was thus a 98% success rate for testing of baseline measures.

4.3 Descriptive Statistics of demographic and visual measures

4.3.1 Demographic measures

The mean age of participants was 7.88±1.54 years, range (5-10 years). There was no statistically significant difference between the age of emmetropes and hyperopes (8.08±1.40 vs. 7.79±1.60 years, independent t-test: t=-0.96, p=0.34). Mean spherical equivalent refraction of the least plus eye (mean least plus spherical equivalent refraction) for all participants was 1.67±1.42 D, range (0 to 7.25 D). There were more female participants 68 (58%) than males 49 (42%) in the study. Out of the 117 participants, 19 (16%) were habitual spectacle wearers (Table 4.1).

Table 4.1 Table showing data on habitual correction in participants.

Refractive status at time of visit	**Number (%)**
Uncorrected	98 (84%)
Without correction	7 (6%)
With correction	12 (10%)
Frequency of wear among habitual spectacle wearers	**Number (%)**
Everyday	13(68%)
Once a week	1 (5%)
Twice a week	2 (11%)
3- 6 days	3 (16%)

4.3.2 Results of visual acuity measures

Single letter acuity score of all participants ranged from 0.00 to 0.70 logMAR, [median (IQR:25th – 75th): 0.20 (0.10-0.20 logMAR)]. The difference in median score of single letter acuity across refractive groups was not statistically significant (Kruskal-Wallis test, X^2=3.66, p=0.30). Crowded letter acuity scores ranged from 0.00 to 0.73 [median (IQR:25th – 75th): 0.175(0.13-0.23 logMAR)]. Difference in median score of crowded letter acuity across refractive groups was statistically significant, with hyperopes > 2 D having significantly higher (worse) crowded acuity scores (Kruskal-Wallis test, X^2=10.20, p=0.02) (see also Figure 4.3.1). The median (IQR:25th – 75th) score in the near acuity test was 0.00 (0.00-0.03 logMAR), range (0.00 to 0.83 logMAR). The median difference in near acuity score across groups was not statistically significant (Kruskal-Wallis test, X^2=1.96, p=0.58).

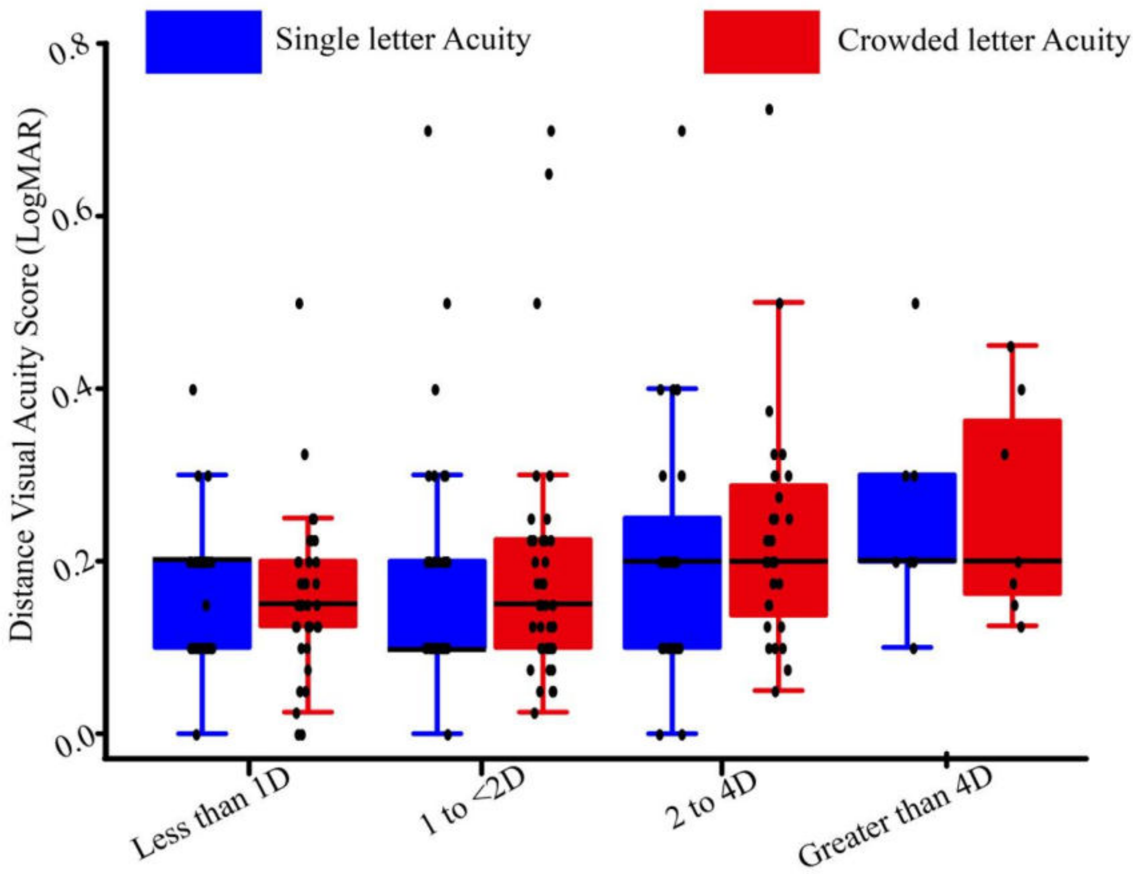


Figure 4.3.1. Box plot showing presenting distance acuity score (single and crowded letter) across refractive groups. Black circles represent individual data points. Please note: due to non-normal distribution of VA scores, median values coincide with 25^{th} and 75^{th} percentiles in some of the groups for the single letter acuity (less than 1D, 1 to <2D, Greater than 4D).

4.3.3 Results of ocular posture and binocular coordination measures

The majority of participants, 115 (98%), were orthophoric at distance. At near, the distribution of the phoria type is shown in Figure 4.3.3.

Stereoacuity scores of participants ranged from 5 to 340 minutes of arc [median (IQR:25^{th}-75^{th}): 30 (20-40 minutes of arc)]. Median difference in stereoacuity score across refractive groups were not statistically significant (Kruskal-Wallis test, X^2=4.36, p=0.23). See Figure 4.3.2

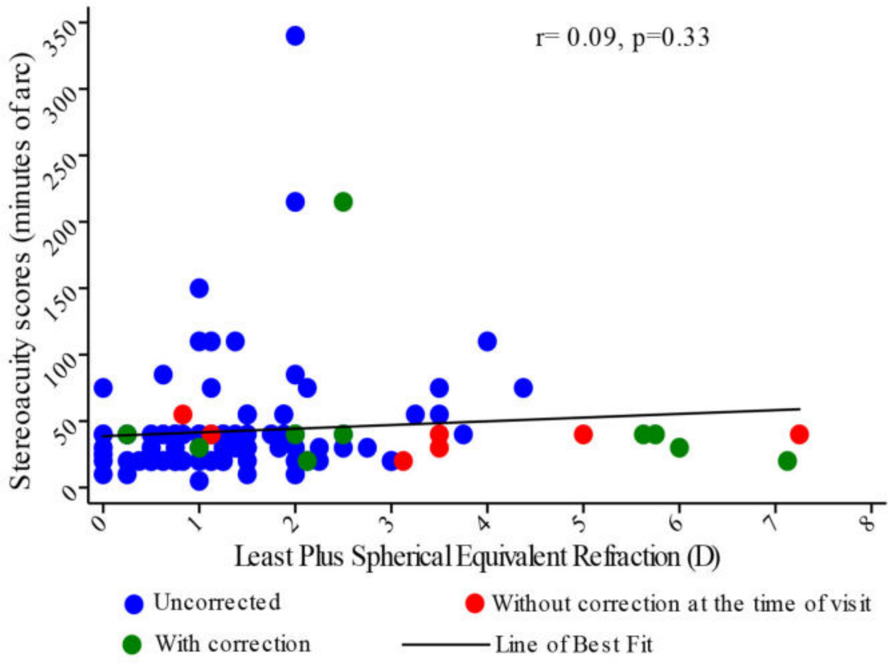


Figure 4.3.2 Scatter plot showing stereoacuity scores with least plus spherical equivalent refraction. "Uncorrected" participants had never worn spectacle correction previously, while "without correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing.

Results of ocular motility test using a swinging pendulum ball revealed that in 76 (66%) of participants, the quality of eye movements were excellent, 31 (26%) demonstrated fair quality of eye movement, and in 10 (8%) of participants, the quality of eye movements were graded poor.

The mean (±SD) near point of convergence of all participants was 6.39±1.75 cm, range (5 to 15cm). Results of the mean (±SD) and range of near point of convergence across refractive group are presented in Table 4.2. There was no statistically significant difference in NPC between refractive groups (One-way ANOVA: $F_{(3,111)}$ =0.42, p=0.74).

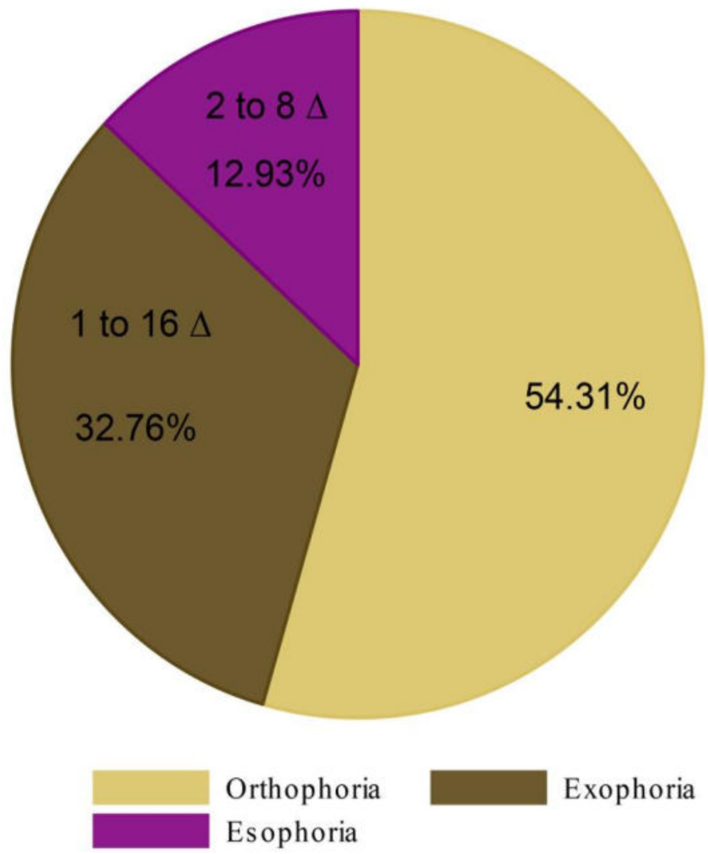


Figure 4.3.3 Pie chart showing distribution and range of near phoria in study participants

4.3.4 Results of accommodative measures

The mean (±SD) binocular amplitude of accommodation of all participants was 13.59±3.62 D, range: 5.00 to 20.00 D. Accommodative response by Nott retinoscopy ranged from 1.81 to 5D (Mean±SD: 3.59±0.54 D), which translates to a lag/lead of accommodation -1 to 2D [median (IQR:25th -75th): 0.4(0 – 0.7D)]. Lower amplitudes of accommodation were observed in the groups with hyperopia greater than 2.00D. Similarly, lower accommodative response (significant lag of accommodation) was observed in participants with increasing levels of hyperopia. Refractive group data for amplitude of accommodation and accommodative response are also presented in Table 4.2. Mean amplitude of accommodation was not statistically significantly different between hyperopes tested with correction, without correction at the time of testing, and those who had never wore correction ($F_{(2, 107)} = 0.27$, p=0.76).

4.3.5 Rate of reading score

The mean (±SD) rate of reading score in all participants was 85.66±2.69 words per minute, range:19 to 147 words per minute. Rate of reading scores for individual refractive groups are presented in Table 4.2. No significant differences in the rate of reading score were observed between any of the refractive groups.

Table 4.2. A summary of mean (SD), and range of baseline visual measures by refractive groups.

Refractive group (n)	**Age (yrs.) Mean±SD (min, max)**	**LSER (D) Mean±SD (min, max)**	**AA(D) Mean±SD (min, max)**	**NPC (cm) Mean±SD (min, max)**	**Nott Ret.(D) Mean±SD (min, max)**	**RR (wpm) Mean±SD (min, max)**
Overall (117)	**7.88±1.54** (5,10)	- (0-7.25)	**13.59±3.62** (5,20)	**6.39±1.75** (5,15)	**3.59±0.54** (1.81,5)	**85.66±2.69** (19,147)
Emmetro (37)	8.08±1.40 (6,10)	0.45±0.25 (0,0.83)	14.71±2.90 (5,20)	6.35±2.19 (5,15)	3.57±0.41 (2.5,4.35)	87.18±24.69 (19,131)
Low Hyp (40)	7.85±1.59 (5,10)	1.32±0.27 (1,1.88)	13.80±3.73 (6,20)	6.21±1.34 (5,11)	3.77±051 (2.2,5)	88.84±21.39 (50,147)
Mod Hyp (32)	7.63±1.62 (5,10)	2.58±0.0.63 (2,4)	12.81±3.98 (5,20)	6.53±1.54 (5,12)	3.52±0.58 (1.81,5)	80.16±25.33 (39,126)
High Hyp (8)	8.13±1.64 (5,10)	5.88±1.05 (4.38,7.25)	10.31± 2.24 (6.5,13)	6.88±2.10 (5,11)	3.09±0.70 (2,4.16)	83.57±24.57 (41,120)
Difference	One-way ANOVA: $F_{(3,113)}$ =0.57, p=0.64	-	One-way ANOVA: $F_{(3,109)}$=4.21, **p=0.007**	One-way ANOVA: $F_{(3,111)}$=0.42, p=0.74	One-way ANOVA: $F_{(3,110)}$=4.23, **p=0.007**	One-way ANOVA: $F_{(3,93)}$=0.70, p=0.56

SD- Standard deviation; LSER – Least plus spherical equivalent refraction; AA – Amplitude of Accommodation (BE); NPC – Near Point of Convergence; Nott Ret – Accommodative Response by Nott retinoscopy; RR – rate of reading score; wpm – words per minute; Emmetro – Emmetropia; Mod. – Moderate; Hyp- Hyperopia.

4.4 Univariate analysis of demographic and baseline visual measures

There was no association between age and refractive error (least plus spherical equivalent refraction), (Pearson correlation: r = -0.04, p=0.68).

4.4.1 Relationship between visual acuity measures and refractive error

There was a positive correlation between crowded letter acuity at distance and least plus spherical equivalent refraction (Spearman correlation: rho=0.25, p=0.008). Worse VA was associated with increasing hyperopia. There was no effect of habitual refractive status at the time of visit on the relationship between crowded letter acuity and least plus spherical equivalent refraction ($F_{(2,110)} = 0.52$, p= 0.59). See also Figure 4.4.1 (panel A). However, there was no statistically significant association between refractive error and single letter acuity at distance (rho=0.10, p=0.31) or between refractive error and near acuity (rho=0.09, p=0.34). Participants with worse visual acuity score at distance also exhibited poorer scores at near (rho = 0.60, p<0.001). See also Figure 4.4.1 (panel B).

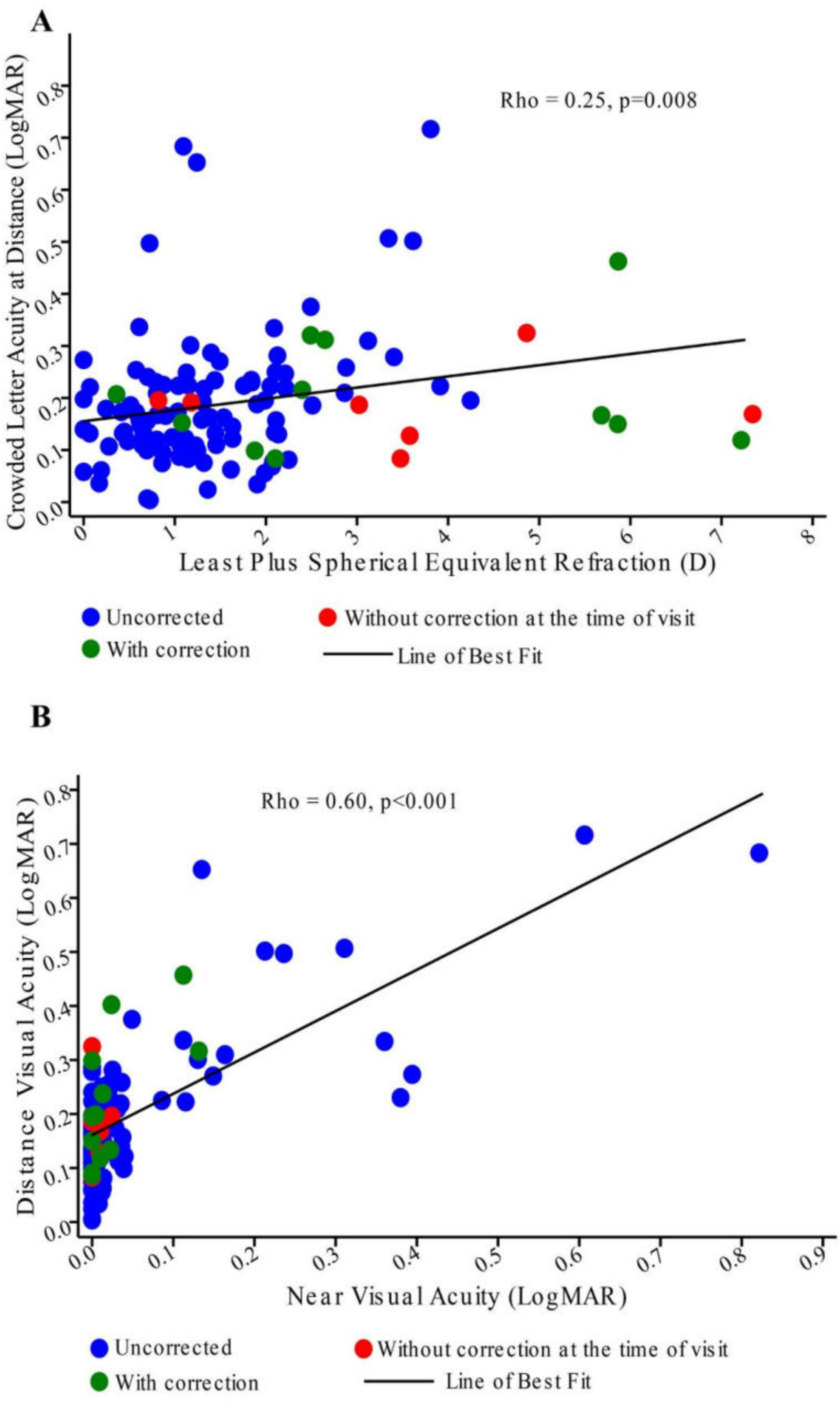


Figure 4.4.1 Scatter plots showing (A) crowded letter acuity at distance with least plus spherical equivalent refraction (B) distance visual acuity (crowded letter) with near visual acuity. "Uncorrected" participants had never worn spectacle correction previously, while "without

correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing.

4.4.2 Relationship between binocular coordination measures and refractive error

The association between stereoacuity and least plus spherical equivalent refraction approached statistical significance (Spearman's correlation: rho=0.18, p=0.06). However, the association between NPC and least plus spherical equivalent refraction was not statistically significant (Spearman's correlation: rho=0.10, p=0.28). Also, there were no statistically significant associations between ocular posture determined by prism cover test at distance and near, and refractive error: (Fisher's exact test: X^2=4.11, p=0.89, and X^2=13.65, p=0.08 for distance and near respectively). Similarly, the association between refractive error and ocular motility was not statistically significant (Fisher's exact test: X^2=9.80, p=0.12). These associations reported are in all hyperopes, whether corrected or uncorrected as there was no difference observed whether a participant was corrected or not (p>0.05).

4.4.3 Relationship between accommodative measures and refractive error

There was no statistically significant association between age and amplitude of accommodation (r = -0.13, p=0.16). A negative association was observed between the amplitude of accommodation, and the least plus spherical equivalent refraction (Pearson's correlation: r = -0.30, p=0.001) See Figure 4.4.2 (panel A). Similarly, there was a statistically significant association between the accommodative response by Nott retinoscopy and least plus spherical equivalent refraction (Pearson's correlation: r = -0.21, p=0.02). See also Figure 4.4.2 (panel B).

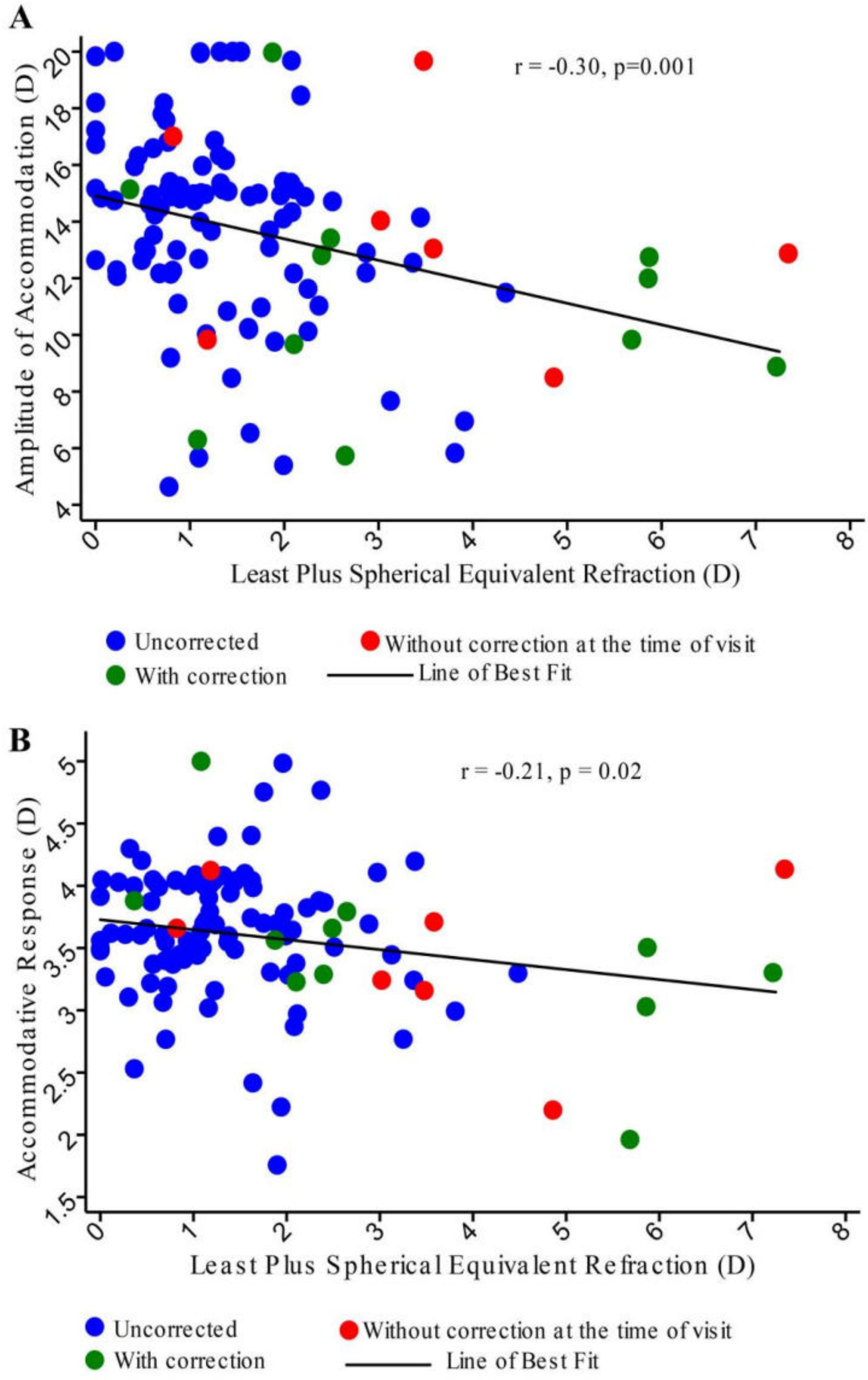


Figure 4.4.2 Scatter plots showing (A) amplitude of accommodation with least plus spherical equivalent refraction (B) accommodative response with least plus spherical equivalent refraction. "Uncorrected" participants had never worn spectacle correction previously, while "without correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing.

4.4.4 Relationship between rate of reading score and refractive error

Although the rate of reading score tended to decrease with increasing refractive error, this relationship was not statistically significant (Pearson's correlation: r= -0.12, p=0.25). See also Figure 4.4.3.

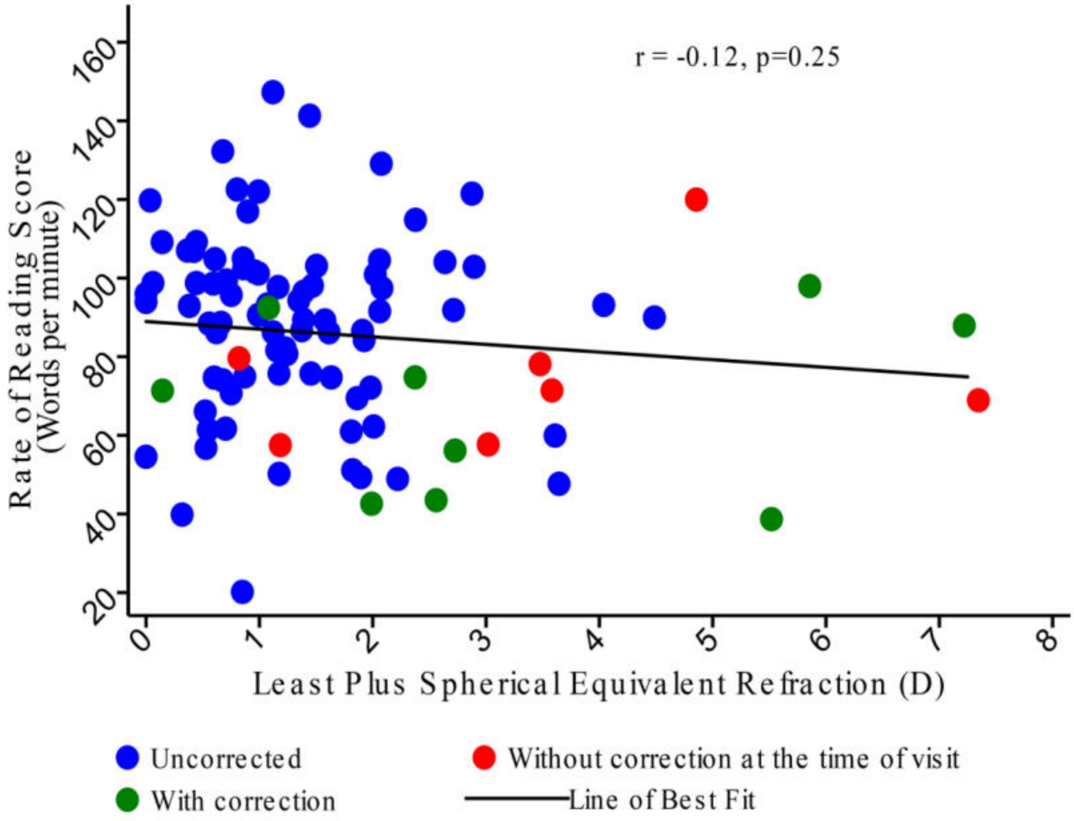


Figure 4.4.3. Figure showing the rate of reading score with the least plus spherical equivalent refraction. "Uncorrected" participants had never worn spectacle correction previously, while "without correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing.

4.5 Relationships between baseline visual measures

4.5.1 Relationship between accommodative measures and visual acuity

There were negative associations between the binocular amplitude of accommodation and all visual acuity measures (Spearman's correlation: rho = -0.25, p=0.008; rho = -0.34, p=0.0003; and rho = -0.37, p=0.0001) for single, crowded letter acuity at distance, and near acuity scores respectively. See also Figure 4.5.1. However, the associations between accommodative response by Nott retinoscopy and visual acuity measures, were weak and not statistically significant (p> 0.05 for all).

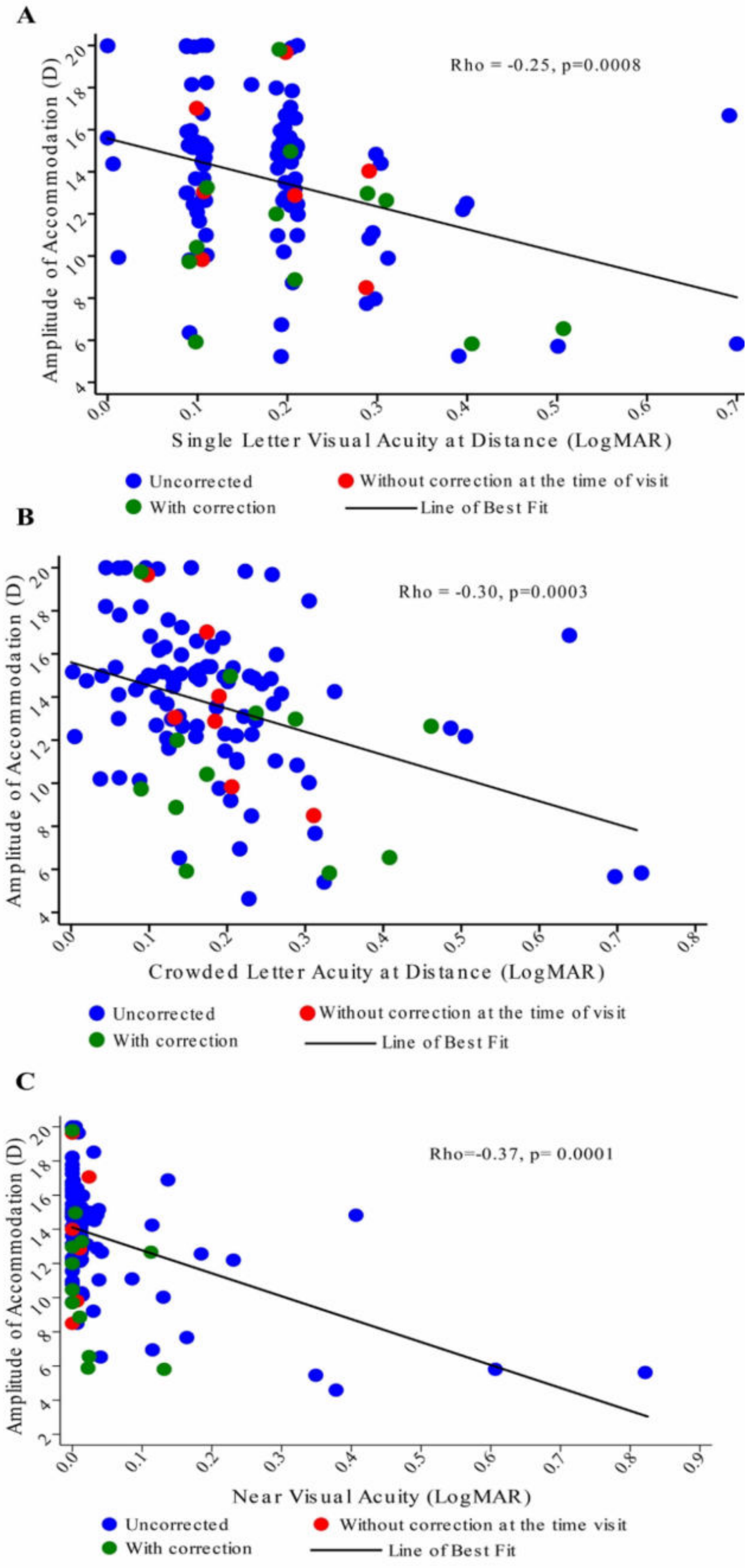


Figure 4.5.1 Scatter plots showing (A) Amplitude of accommodation with single letter acuity at distance, (B) Amplitude of accommodation with crowded letter acuity at distance, (C) Amplitude

of accommodation with near visual acuity. "Uncorrected" participants had never worn spectacle correction previously, while "without correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing. These plots have been modelled after the analyses presented by Mutti (2007).

4.5.2 Relationship between visual Acuity score and binocular vision measures

There was statistically significant relationship between stereoacuity and visual acuity measures (Spearman's correlation: rho = 0.30, p = 0.0012; rho = 0.43, p<0.0001; rho = 0.31, p=0.001) for distance single, crowded and near acuity respectively.

4.5.3 Relationship between rate of reading score and other baseline measures

There was a statistically significant association between the rate of reading score and age of participant (Pearson's correlation: r=0.43, p<0.0001). The rate of reading score was negatively associated with stereoacuity (Spearman's correlation: rho=-0.40, p=0.0001), and near visual acuity (rho=-0.21, p=0.04). See also, Figure 4.5.2. However, there were no statistically significant associations between rate of reading score and NPC (Spearman's rho=0.02, p=0.89), amplitude of accommodation (Pearson's correlation: r=0.14, p=0.17), and accommodative response by Nott retinoscopy (r=0.05, p=0.58). The association between rate of reading score and ocular motility was not statistically significant (Fisher's exact test (X^2) = 88.82, p=0.74).

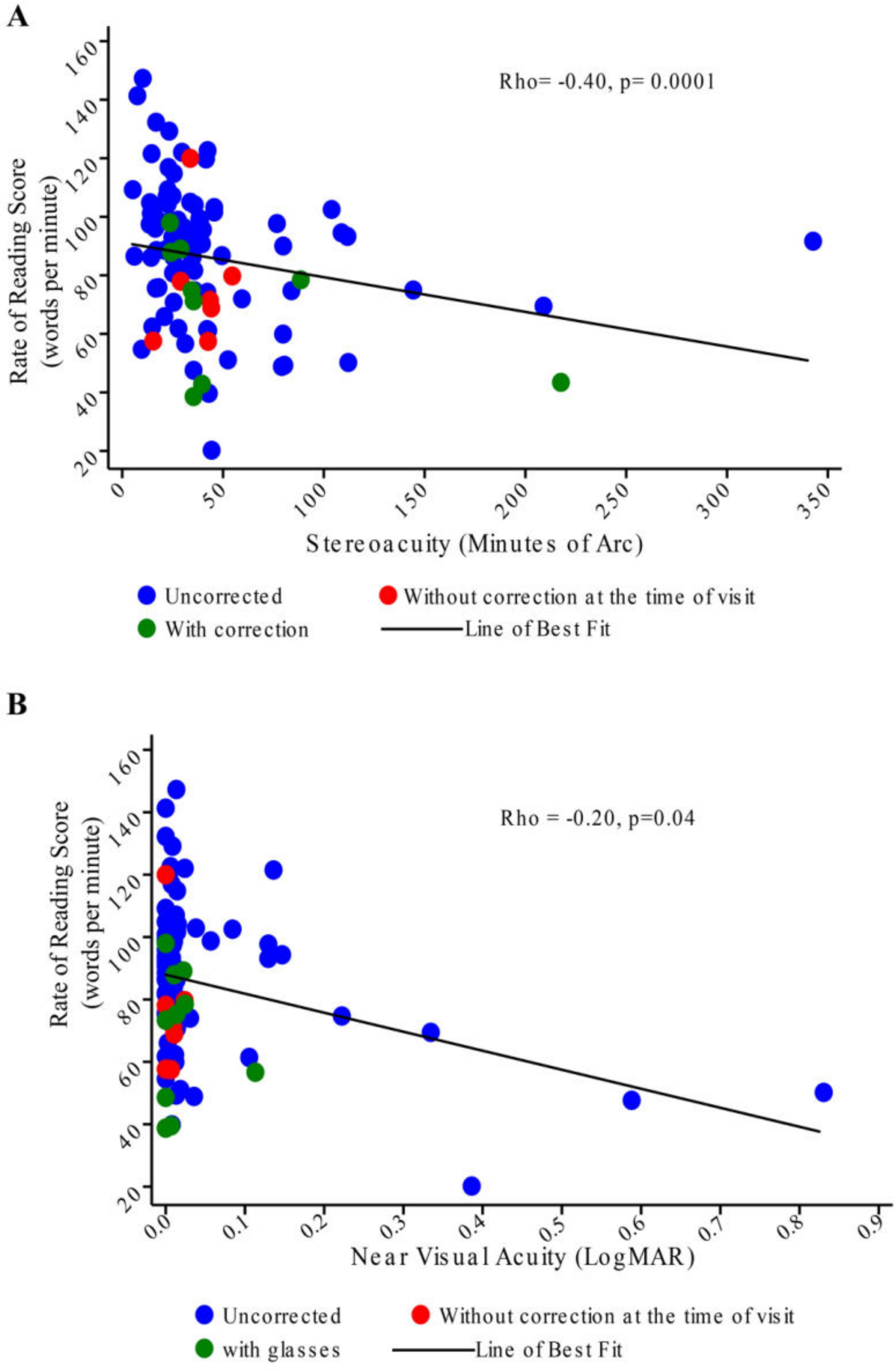


Figure 4.5.2 Scatter plots showing (A) rate of reading score with stereoacuity score (B) rate of reading score with near visual acuity. "Uncorrected" participants had never worn spectacle correction previously, while "without correction" were habitual spectacle wearers who did not present them at the time of visit. "with correction" were habitual wearers who had their correction at the time of testing.

4.6 Results of multivariate analyses of demographic and baseline visual measures

Univariate analyses which were statistically significant were examined further using multivariate linear regression. The association between crowded letter acuity at distance and refractive error (least plus spherical equivalent refraction) was statistically significant after controlling for age and amplitude of accommodation (p=0.002). Results of multivariate regression analyses of other baseline measures are presented in Table 4.3.

Table 4.3. Results of multivariate regression of baseline visual measures.

Dependent	**Independent**	**Beta coefficient**	**95% CI**	**P-value**
Crowded letter acuity	Intercept	19.31	12.67 to 25.94	**0.000**
	Age	-.38	-.83 to 0.06	0.09
	†Acc. response	-.37	-1.63 to 0.90	0.57
	††Refractive error	-.74	-1.20 to -0.27	**0.002**
Amplitude of Acc.	Intercept	17.63	14.10 to 21.17	**0.000**
	Age	-.34	-0.77 to 0.09	0.12
	Refractive error	-.77	-1.21 to -0.32	**0.001**
Stereoacuity	Intercept	75.45	8.40 to 142.5	**0.03**
	Age	-1.40	-6.65 to 3.86	0.60
	Near visual acuity	89.05	22.31 to 155.78	**0.009**
	Acc. response	-12.32	-27.93 to 3.29	0.12
	Refractive error	0.79	-4.93 to 6.51	0.78
Rate of reading	Intercept	-9.37	-57.49 to 38.75	0.70
	Age	8.54	5.2 to 11.86	**0.000**
	Near visual acuity	-63.39	-99.52 to -27.25	**0.001**
	NPC	0.75	-1.59 to 3.08	0.53
	Acc. response	7.53	-1.00 to 16.05	0.08
	Stereoacuity	-0.06	-0.15 to 0.04	0.22
	Refractive error	-1.39	-4.35 to 1.56	0.35

† Acc. response - accommodative response by Nott retinoscopy; ††refractive error – Least plus spherical equivalent refraction (uncorrected)

4.7 Discussion

Assessment of baseline demographic and visual factors was carried out to characterise participants with and without hyperopia in terms of their visual status and how these might influence sustained accommodative and vergence measures presented later in chapter 5. Results of these measures would also contribute to the scholarship on performance of uncorrected hyperopic children on measures of visual function, particularly at near. There was a high success rate of testing for these baseline visual measures in participants, despite many participants' relatively young age. This high success rate is impressive, considering the battery of tests which were applied.

The present chapter's findings demonstrate that participants with hyperopia greater than 4D, had the lowest amplitude of accommodation and the poorest accommodative response by Nott retinoscopy (Table 4.2). This is consistent with previous studies reporting reduced amplitude of accommodation in hyperopes compared with other refractive groups (McBrien and Millodot 1986); and a reduced accommodative response/significant lag in uncorrected hyperopia (Horwood and Riddell 2011; Candy *et al.* 2012). The amplitude of accommodation is the maximum amount of accommodation the eye is capable of producing when an object is progressively moved closer to the eye (McClelland and Saunders 2003; Win-Hall and Glasser 2008). In the case of the uncorrected hyperope, who has to use accommodation to overcome blur during distance fixation, this results in less accommodative capacity being available for use at near. As demonstrated in this study, this is increasingly problematic as the magnitude of hyperopia increases. Whilst the amplitude of accommodation is generally higher in younger children, the observed association between the amplitude of accommodation and refractive error remained statistically significant, after controlling for the age of participants. However, the results of the amplitude of accommodation in study participants could be affected by the test instruction "tell me when the words become fuzzy", as younger children could be confused as to what real fuzziness mean.

The present study also shows that habitual refractive correction may have effect on the amplitude of accommodation, particularly in those with increased levels of hyperopia. This can be observed qualitatively in Figure 4.4.2 (panel A), although not statistically significant. Participants who wore optical correction at the time of testing, or without correction at the time of testing but who do normally wear habitual correction, appear to have some visual benefit by way of their improved amplitude of accommodation.

Normative data in children suggests that children tend to hypoaccommodate to targets at near (McClelland and Saunders 2004). Particularly in uncorrected hyperopes, a significant lag of accommodation has been observed (Horwood and Riddell 2011; Candy *et al.* 2012). Results of the accommodative response to a target at 25cm using Nott retinoscopy in this study also revealed increased lag of accommodation (hypoaccommodation) with increasing hyperopia; with hypoaccommodation being particularly evident when hyperopia is greater than 4 D. The accommodative response in this group was also more variable (as evident in the standard deviation of the mean accommodative response) compared to the other refractive groups.

The mechanism underlying hypoaccommodation in significant uncorrected hyperopia is unclear, as several possible factors have been put forward, including a defect in blur sensitivity (Ingram *et al.* 1994). Another possible hypothesis is an adaptive mechanism, whereby some hyperopic subjects with inflexible accommodation-vergence interaction may sacrifice clarity for single vision (Horwood and Riddell 2011; Candy *et al.* 2012; Suh *et al.* 2016), and therefore choose to accommodate less to achieve binocular single vision. It is also possible that these subjects do not have enough physical capacity to produce more crystalline lens change.

The visuosensory implications of hypoaccommodation in uncorrected hyperopic children, particularly for those with increased and variable lags, have been discussed by previous authors. These include a role for hypoaccommodation as a risk factor for abnormal visual experience and for the development of conditions such as strabismus and amblyopia (Candy *et al.* 2012; Babinsky and Candy 2013).

Consensus from clinical practice guidelines by some professional groups such as the America Academy of Ophthalmology, suggest paediatric hyperopia greater than or equal to +4–4.5D to be the threshold for optical management or monitoring because of the potential for abnormal visual development (*American Academy of Ophthalmology, Preferred Practice Patterns. Amblyopia PPP, 2007)*. Results of baseline accommodative measures in this study support such guidelines. Qualitatively, there appears to be some benefit of habitual refractive correction on the accommodative response at near, particularly in participants with high hyperopia (Figure 4.4.2, panel B). This is consistent with the work of Mutti (2007), who showed that participants of the CLERRE Study who wore optical correction (n=28), demonstrated reduced lag of accommodation compared to those without correction (n=711).

The finding of hypoaccommodation in participants with significant uncorrected hyperopia, however, is inconsistent with a recent study by Roberts *et al.* (2018a), who found no significant difference in the accommodative response of emmetropes and uncorrected hyperopes during sustained (10 minutes) performance of an “active” and “passive” reading tasks using photorefraction. As raised by Candy *et al.* (2012), it is possible for the accommodative response in uncorrected hyperopia to be reduced initially, but then improve during a sustained task. Results of sustained accommodative response during a reading and movie tasks in participants will be presented in chapter 5.

Poorer visual acuity scores at distance were significantly associated with increasing uncorrected hyperopia, after adjusting for the age and accommodative response of participants. This finding is consistent with a previous study by Ciner *et al.* (2016), whose emmetropic participants recorded better distance logMAR acuity compared to their hyperopic peers. However, for participants who wore habitual refractive correction (either at the time of testing, or even without correction at the time of visit), there appears to be some benefit of refractive correction on their distance visual acuity (Figure 4.4.1). This agrees with the data previously reported by Mutti (2007). It is possible that some participants with uncorrected hyperopia failed to accommodate accurately for distance at the time of testing, or do so habitually, which may have resulted in their inability to clearly resolve the optotypes at distance, although multivariate regression analysis did not suggest an explanatory role from accommodation. A closer look at the data (Figures 4.3.1 and 4.4.1 (both panels)) show that outliers, which represent extremely poor VA score were recorded in participants whose uncorrected hyperopia could be considered moderate. This is consistent with the recent data of the VIP-HIP study in children aged 4-5 years with hyperopia ranging from >= +3.00 DS (Ciner *et al.* 2016). Such uncorrected hyperopes may benefit from optical correction for improved vision.

This study also found that near VA scores were not statistically significantly associated with the amount of uncorrected hyperopia, contrary to what was reported by Ciner *et al*. (2016). Differences in study methods, including differences in age of participants, and the use of different near VA charts, could account for the apparent differences in our findings. The study of Ciner *et al.* (2016) conducted in children aged 4-5 years, which is different from the age range of participants included within the present study (5 -10 years). They also used the crowded HOTV letters for testing which is different from the Sonksen near test. However, the results of the present study agree with that of Suh *et al.* (2016) who examined children (n=117) aged 3 – 5 years, using ATS4 Near Acuity test.

The present study is the first study to have used the Sonksen LogMAR test for a predominantly hyperopic cohort. It was surprising to find similar near VA scores for subjects with low and high levels of hyperopia. Perhaps the near VA, tested with the Sonksen logMAR test, was not sensitive enough in this cohort. Nonetheless, there was a trend toward poorer near VA for those who had poor distance VA. A similar finding was reported by Suh *et al*. (2016) in their study of moderate uncorrected hyperopic children aged 3 – 5 years.

Distance VA has been used as a screening criterion (6/9 or 20/30) to refer children with hyperopia for refractive examination and treatment (Ciner *et al.* 2016; Bruce *et al.* 2018), or for inclusion in some research studies (Williams *et al.* 2005; van Rijn *et al.* 2014; Suh *et al.* 2016). Given that near VA was a significant predictor of stereoacuity in participants of this study, and in other studies (Ciner *et al.* 2016; Suh *et al.* 2016), perhaps, it may be important to consider its inclusion as part of the criteria for referral during visual screening. Stereoacuity is an important visual function which can be used to predict hyperopic children at risk of strabismus or amblyopia (Robaei *et al.* 2007; Kulp *et al.* 2019). Needless to say, adequate near VA may be a factor which influences the outcome of other near visual function measures (Ciner *et al.* 2016).

Results of the present study show that older participants had a significantly higher reading speed (rate of reading score), although, the lowest rate of reading score (19 words per minute) was recorded in an older participant (aged 10). However, when effect size (r^2=0.19) was considered, only 19% of the variability in the rate of reading score is explained by age. The association between age and reading speed have been previously reported (Vlachos and Papadimitriou 2015). Differences in reading speed between younger and older children have been attributed to factors such as ongoing maturation of the brain/cognitive and visual systems (Dawes and Bishop 2008) and differences in visual attention span between older and younger children, which could influence the relationship between visual processing speed and reading speed (Lobier *et al.* 2013). After controlling for baseline visual measures, including NPC, stereoacuity and accommodative response, near VA was statistically significantly associated with the rate of reading score. This finding may reflect the importance of good near VA for resolving the words on the Wilkin's rate of reading test cards. It is also possible that a synergistic effect of other baseline measures could contribute to the variability in the rate of reading score, as the effect size due to age and near VA alone could not account for the variability in rate of reading. The rate of reading score was also not related to the amount of refractive error of participants. For example, the participant with the lowest rate of reading score (19 words per minute) had a refractive error of 0.75D. This finding is in contrast to the findings of a previous study by van Rijn *et al.* (2014) which reported a higher rate of reading score in myopes compared to hyperopes. The present study did not include myopes. Differences in subjects' characteristics, including age, range of refractive errors sampled, as well as differences in reading test kit, could account for the difference in results. It has been suggested previously that the impact of blur on reading speed may be minimal if the font size of the reading material is large enough (Chung *et al.* 2007). The letters in the Wilkins rate of reading kit may be comparable to the N8 of the N-notation near VA cards, which could have been easily resolved by participants, even those with significant uncorrected hyperopia (O'Leary *et al.* 2014). It is possible that beyond optical factors, the range of reading speed scores obtained in this study may be influenced by behavioural factors, particularly because participants were instructed to read as quickly as possible.

In terms of ocular posture and other measures of binocular coordination, the results of the present study did not indicate any statistically significant refractive group differences. The majority of participants were orthophoric at distance, and at near low levels of phoria were observed independent of refractive error.

4.8 Chapter summary

- **The amplitude of accommodation was significantly reduced in participants with uncorrected hyperopia, particularly in those greater than 4D.**
- **Mean accommodative response by Nott retinoscopy at 25cm, was lower in hyperopes (of all magnitudes) compared to emmetropes.**
- **A trend of poorer crowded distance letter acuity was observed with increasing hyperopia.**
- **Poorer near VA was associated with a reduced rate of reading.**

Chapter 5: Sustained Accommodative and Vergence Functions in Children with and without Uncorrected Hyperopia

5.1 Introduction

This chapter presents results and discussions of accommodative and vergence functions in children with hyperopia and emmetropic controls during performance of sustained reading and movie tasks. Children with hyperopia were uncorrected during testing. The chapter presents results and discussion for the following questions:

- Are the characteristics of the accommodative response different in hyperopic children compared to emmetropic controls?
- Where inaccurate accommodative response exists in parallel with hyperopia, does correction of hyperopia restore accurate accommodation responses?
- Do children with poorer accommodative function also have deficits in vergence (eye coordination) performance?
- Is reading speed influenced by uncorrected hyperopia and/or poorly sustained accommodation?

The chapter is organised in the following outline:

- Success rates and results of calibration protocol for sustained near tasks
- A brief recap of data analysis protocol
- The Accommodative Response Results
- The Vergence Response Results
- Relationships between sustained accommodative and vergence functions, and baseline visual profile of participants without correction.
- Chapter discussion and summary

5.2 Results

5.2.1 Success rate for sustained measures of accommodation and vergence functions

Out of the total 137 participants seen, 17(12%) were excluded due to one of the following reasons: myopia (n=3), significant astigmatism >2DC (n=3), refusal of cycloplegic refraction (n=5), strabismus (n=3), and Non-Caucasian participants (n=3). Of the remaining 120 participants, three were uncooperative during the assessment of the baseline measures/visual profile, or during the performance of the sustained near tasks, whose data were excluded from further analysis. There was thus a 98% success rate for testing of sustained near tasks.

5.2.2 Results of Lens and Prism Calibration

Although the lens calibration protocol was attempted on all participants, usable data of sufficient quality for analysis were available for 96 (80%) participants. Poor quality data arising from small pupil sizes less than 3mm, and significant reflections from lenses introduced during calibration were excluded. Individual calibration slopes ranged from 0.61 to 1.10, with a mean calibration slope of 0.81±0.12. There was no difference in the lens calibration slope between hyperopes and emmetropes (t=-0.09, p=0.93). Table 5.1 provides a summary of mean, range, and R^2 of the regression for the two refractive groups. Each participant's calibration slope was applied to the raw refractive error measure (from which accommodative response was computed) during analysis where available. Where lens calibration slope was not available for a participant, the pooled mean of 0.81 was applied to the participant's raw refractive data. This was applied in 27 (23%) of participants.

In the prism calibration, usable data was only available for 48 (40%) participants with a mean calibration slope of 0.63±0.1, range (0.49–0.93), translating into a mean HR of 18.2°/mm. With the majority of participants having poor quality data in the prism calibration, and lower calibration slopes (higher HRs) recorded, the default calibration factor (11.82 °/mm) of the PowerRef 3™ was used for all participants.

Table 5.2.1. A summary of the mean (±SD), range and R^2 of lens calibration data across the two refractive groups.

Group (N)	**Lens Calibration Slope**	**R^2**
	Mean±SD (Min, Max)	**Mean±SD (Min, Max)**
Emmetropes (28)	0.814±0.12 (0.66, 1.10)	0.96±0.040 (0.82,0.99)
Hyperopes (68)	0.809±0.12 (0.61, 1.08)	0.96±0.041 (0.81,0.99)
Difference	t=0.16, p=0.87	t=0.47, p=0.64.

5.3 Discussion

5.3.1 Success Rates

There was a high success rate in the present study (98%) for the two sustained near tasks. Given the age range of participants (5-10years) and the sustained nature of the reading and movie tasks, this finding is significant. This result is higher than the 86% success rate reported by Roberts *et al.* 2018a, the only study to have also measured sustained accommodative response in children with and without uncorrected hyperopia, aged 3-10 years using the photorefraction technique for 10 minutes. Differences in the nature of the task targets may account for the difference in success rates. In the present study, the choice of popular children's Kindle books or custom-designed picture stories, coupled with a popular animation-clay movie for children (Wallace and Gromit) might have contributed to the higher success rate observed as these tended to stimulate the interest of participants. In the study of Roberts *et al.* (2018a), tasks consisted of an "active task" where participants read story passages or answered questions about displayed shapes and a "passive task" where subjects looked at letters or shapes placed at 33cm. Additionally, assessment of these sustained tasks on the school premises for the majority of the participants (95%), where encouragement from teachers and peers were observed, may contribute to the high success rate.

5.3.2 Lens and Prism Calibration

There was a good success rate with the lens calibration protocol for estimates of refractive error in the present study compared with other studies; 68% in the study by Bharadwaj and Candy (2009) and 61% in the work of Doyle *et al.* (2016). The result of the mean lens calibration slope in the present study, 0.81, is less than the 0.99 previously reported by Doyle *et al.* (2016) in their healthy controls aged 6-16years, and the 1.06 reported by Blade and Candy (2006) in their infant participants aged 2 to 24 weeks. In the present study, the target for lens and prism calibration was placed at a near distance of 25cm; a shorter distance than the traditional target distance of 1m previously reported (Blade and Candy 2006; Bharadwaj *et al.* 2013; Doyle *et al.* 2016). The 25cm distance was chosen to generate a "dynamic" scaling factor for measurement of accommodation and gaze position at near distance and make it specific to our protocol of measuring accommodation and gaze position at this distance. This might explain, in part, the difference in calibration slopes reported in the present and previous studies. There was no difference in the mean lens calibration slopes between uncorrected hyperopes and emmetropic controls in the present study, therefore, results of the pooled mean were used where calibration slopes were unavailable for a participant. This method has been previously applied in published studies using the PowerRef 3™ and similar test protocols (Doyle *et al.* 2016).

The majority of participants (60%) in the present study did not have useable frames of sufficient quality for analysis in the prism-based calibration of gaze position due to significant reflections from the prisms introduced during calibration, as well as small pupil sizes. The prism calibration slopes in the present study were low, translating into higher HRs. The mean prism calibration slope in the present study was lower compared to the mean slope of 0.88 by Doyle *et al.* (2016). Differences in target distances could account for this observed difference in mean calibration slopes. The positioning of the calibration target at 25cm in the present study increases the visual angle, and it is possible that prism-induced eye movements were reduced in these conditions, resulting in the present finding. Results presented in Study 1 (in Chapter 2) show that the prism-based technique tended to exhibit higher and more variable HRs compared to the eccentric and theoretical techniques. On account of these factors, a pragmatic approach was adopted to use the default calibration factor (of 11.82°/mm) of the PowerRef 3™ for all participants. The use of the PowerRef 3™ default calibration function in cases where the individual calibration is unavailable or unreliable, as was the case in the present study, has previously been documented (Bharadwaj and Candy 2009).

5.4 A Brief Recap of Data Analysis Procedures for Sustained Accommodative and Vergence Measures

The mean accommodative responses for the reading and movie targets were derived for each participant in one-minute segments for the duration of the task. For example, if the participant read for 15 minutes, this resulted in 15 mean values (one per one-minute segment). For each one-minute segment, however, 10 seconds of data (approximately 500 samples) were indexed for analysis. The result of repeated measure ANOVA analysis of accommodative response (reading task) over time, for all participants, revealed no statistically significant difference across mean accommodative response over time ($F_{(3.08,357.28)}=1.80$, $p=0.15$, Greenhouse-Geisser correction applied). Consequently, an average of the one-minute segment means was computed and used for all statistical analyses, similar to the approach utilised by Harb *et al.* (2006). The same procedure was used to analyse the stability of accommodative response (RMS and LFC), vergence response and pupil sizes.

5.5 The Accommodative Response

5.5.1 What happens to the accommodative response during sustained reading and movie tasks in children with and without uncorrected hyperopic refractive error?

This question was considered in terms of the accuracy of the response.

5.5.1.1 Accuracy of the mean accommodative response measured while participants were uncorrected.

There was large inter-subject variability in mean accommodative response for both tasks (Table 5.5.1). The mean accommodative response differed by task, with a higher response observed in the reading task compared to the movie task ($F_{(1,98)}=24.62$, $p<0.0001$), four-way ANCOVA (mean response in the movie task as covariate, habitual refractive correction/status, order of introduction of task, and refractive group as factors). There were no significant interactions observed between these factors: $F_{(12, 98)}= 1.29$, $p=0.24$), See also Figure 5.5.1.

Table 5.5.1 Descriptive statistics of accommodative response and pupil size across the two tasks by refractive group. NB Task distance/demand was 25cm/4D.

	Type of Task Accommodative Response (D)		**Type of Task Pupil Size (mm)**	
Refractive Group (N)	Reading Mean±SD (min, max)	Movie Mean±SD (min, max)	Reading Mean±SD (min, max)	Movie Mean±SD (min, max)
-0.25 to <+1D (32)	2.95±0.62 (1.66-4.41)	2.22±0.81 (-0.01-4.41)	5.04±0.65 (3.66, 6.25)	5.17±0.66 (3.67, 6.43)
+1 to <+2D (40)	2.91±0.74 (1.45-4.65)	2.27±0.77 (0.15-4.09)	5.08±0.82 (3.26, 6.64)	5.49±0.62 (4.1, 6.77)
+2 to +4D (32)	3.21±1.04 (0.95-5.78)	2.49±0.98 (0.35-4.68)	4.88±0.56 (3.95, 5.88)	5.36±0.57 (4.34, 6.34)
>+4D (8)	3.34±0.76 (2.15-4.26)	2.18±0.78 (1.10-3.19)	4.65±0.54 (3.92, 5.64)	5.17±0.64 (3,67,5.61)
Difference	One-way Anova ($F_{(3,113)}$ =1.40, p=0.25)	One-way Anova ($F_{(3,113)}$ =0.74, p=0.53)	One-way Anova ($F_{(3,113)}$ =1.21, p=0.31	One-way Anova ($F_{(3,113)}$ =1.95, p=0.13

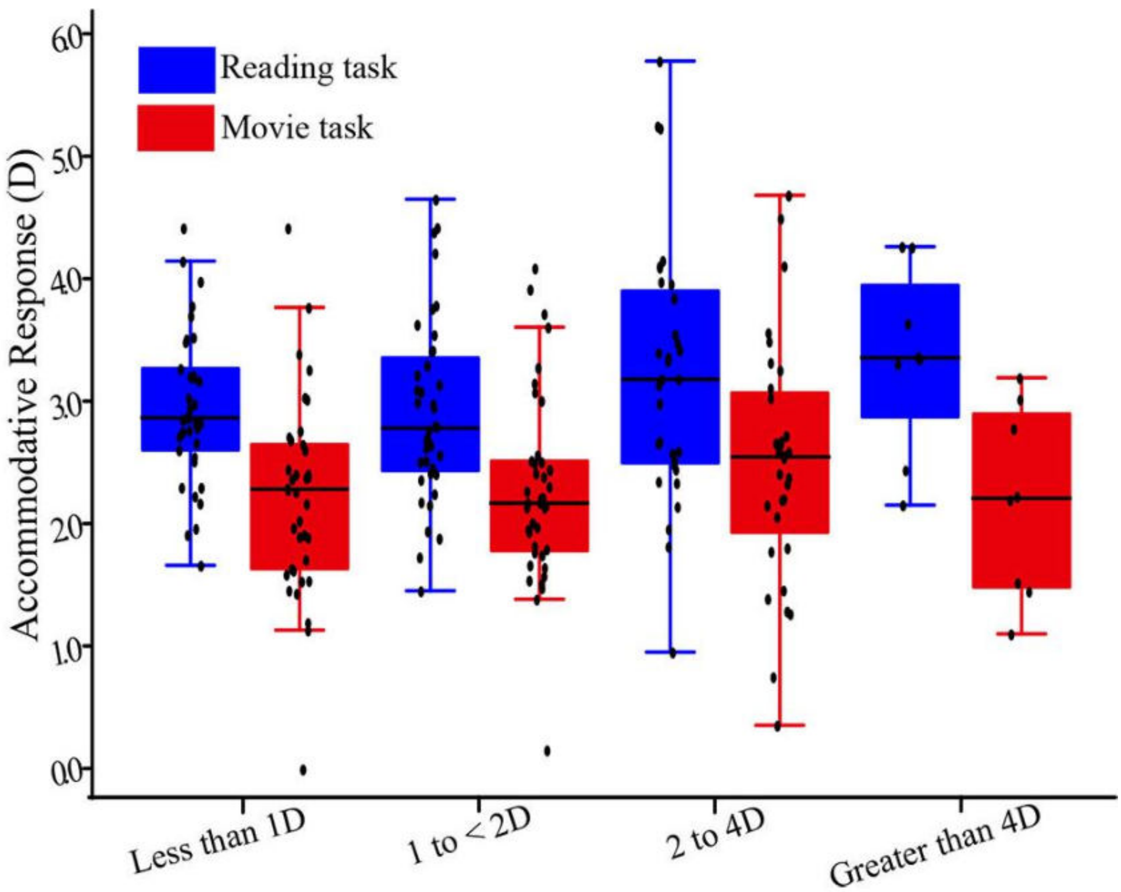


Figure 5.5.1 Box plots of mean accommodative response in reading and movie tasks across refractive group while participants were uncorrected. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

5.5.1.2 Effect of Refractive Error and Habitual Spectacle Correction on Mean Accommodative Response

The relationship between the mean accommodative response and the least spherical equivalent refractive error across the two tasks was weak and did not reach statistical significance (r=0.02, p=0.8 and r=-0.06, p=0.5 for reading and movie tasks respectively, see also Figure 5.5.2). The habitual refractive status of a subject (habitual spectacle wearer vs non-wearer) had no effect on their mean response in the uncorrected reading task (two-way ANCOVA (least plus SE as covariate): $F_{(1,112)}$=1.11, p=0.30 for habitual refractive status and $F_{(1,112)}$ =0.19, p=0.67 for least plus SE with no significant interaction between the two factors ($F_{(1,112)}$=0.16, p=0.69). However, in the uncorrected movie task, habitual spectacle wear had a statistically significant effect on the mean accommodative response ($F_{(1,112)}$=6.60, p=0.01, being more accurate in habitual wearers than non-wearers), and independent of the SE refraction (no interaction ($F_{(1,112)}$=3.45, p=0.07).

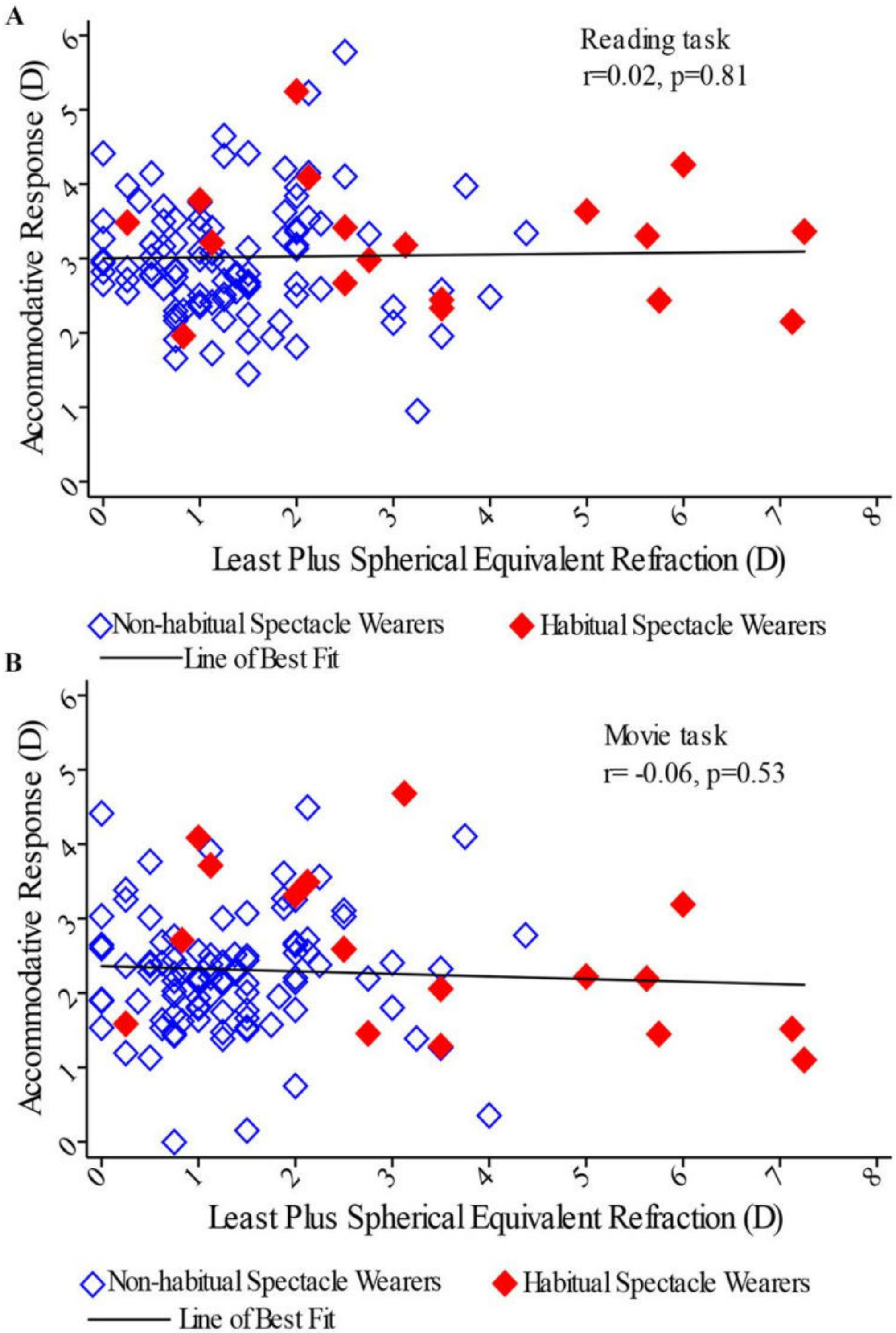


Figure 5.5.2 Scatterplots showing (A) mean accommodative response in reading task with least plus spherical equivalent refraction by habitual refractive status (spectacle wearer vs non-wearer) (B) mean accommodative response in movie task with least plus spherical equivalent refraction by habitual refractive status. All participants were uncorrected during testing.

However, when the mean accommodative response was considered in relation to the total accommodative response (i.e. the sum of the mean response to the 4D target, and the response required to correct subject's underlying spherical equivalent refractive error of the least plus eye), statistically significant associations were observed for both tasks ($r=0.51$, $p<0.0001$, and $r=0.47$, $p<0.0001$ for reading and movie tasks respectively), Figure 5.5.3.

In a two-way ANOVA of reading task measures, total accommodative response was influenced by refractive group ($F_{(3,108)} = 42.19$, $p<0.001$), but not by the habitual refractive status of the participant ($F_{(1,108)}=2.89$, $p=0.09$). No significant interaction was observed between the two factors ($F_{(3,108)} =0.95$p$=0.42$). A post-hoc test on main effect of refractive group using Bonferroni pairwise comparison revealed significant differences between refractive groups ($p<0.01$). In the movie task, total accommodative response was influenced by both participant's refractive group ($F_{(3,108)} =31.24$, $p<0.01$) and habitual refractive status ($F_{(1,108)} =4.71$, $p=0.03$). There was no significant interaction between the two factors ($F_{(3,116)}=1.04$, $p=0.38$). A post-hoc test of significant main effects using Bonferroni pairwise comparison revealed significant differences between groups across the two factors ($p<0.01$).

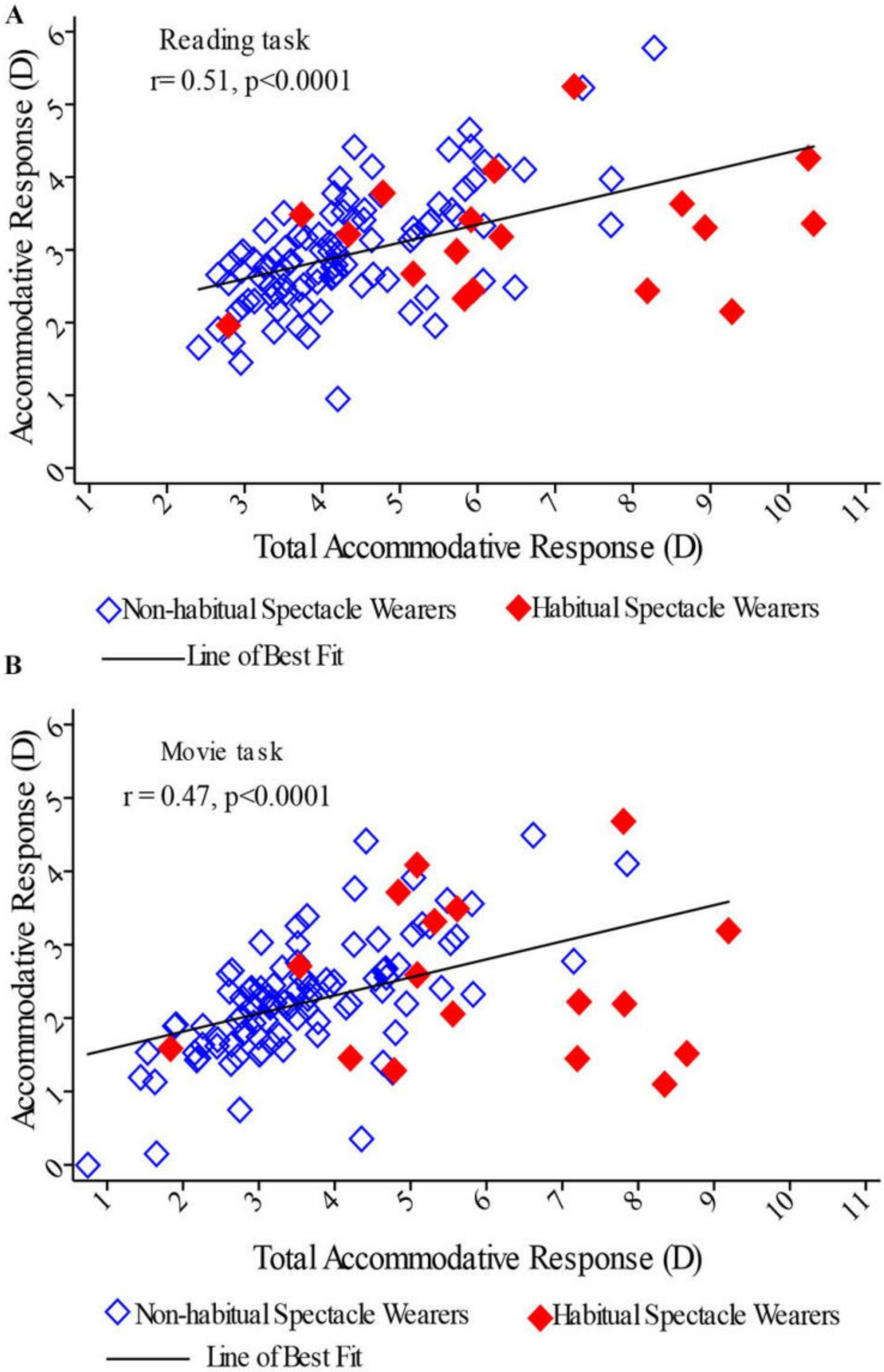


Figure 5.5.3. Scatter plots of (A) mean accommodative response with total accommodative response by habitual refractive status in the reading task (B) mean accommodative response with total accommodative response by habitual refractive status in the movie task. All participants were uncorrected during testing. Total accommodative response = mean accommodative response to 4D target + subject's cycloplegic refractive error (least plus eye).

5.5.1.3 Effect of Age and Pupil Size on Mean Accommodative Response

There were reduced pupil sizes in the reading task compared to the movie task ($F_{(1,109)}$=49.50, p<0.0001) and significant differences in pupil size across refractive group ($F_{(3,109)}$=7.02, p<0.001); with significant interaction between pupil size and refractive group ($F_{(3,109)}$=6.06, p<0.001). Significant differences were observed between emmetropes (-0.25 to <+1 D) and hyperopes in the group (+1 to less than +2 D) in a post-hoc test using Bonferroni pairwise comparison (p<0.01). Results of two-way ANCOVA tests (age and refractive group; pupil size and refractive group) revealed no statistically significant effects of age and pupil size on the mean accommodative response in either reading or movie tasks (p>0.05 in all cases).

5.5.1.4 Within-Subject Characteristics Across Two Tasks

Overall, participants who exhibited good accommodative responses in the reading task also tended to demonstrate good responses in the movie task (Figure 5.5.4). Using the mean accommodative response in the reading task (chosen because it was the more visually demanding task in this study), subjects were characterised as "good accommodators" where mean accommodative response in the reading task was >2.22D (lower limit variation around the mean response, 3.03D±0.81, in the reading task), and as "poor accommodators" where the mean accommodative response in the reading task was ≤ 2.22D. "Poor accommodators" demonstrated reduced accommodative response in the movie task compared with "Good accommodators" (1.95±0.72 D vs 2.37±0.85 D, t=1.87, p=0.06). Being classed as a 'Poor accommodator' in the reading task was not related to the spherical equivalent refraction of the participant (r=0.04, p=0.99) (Figure 5.5.5).

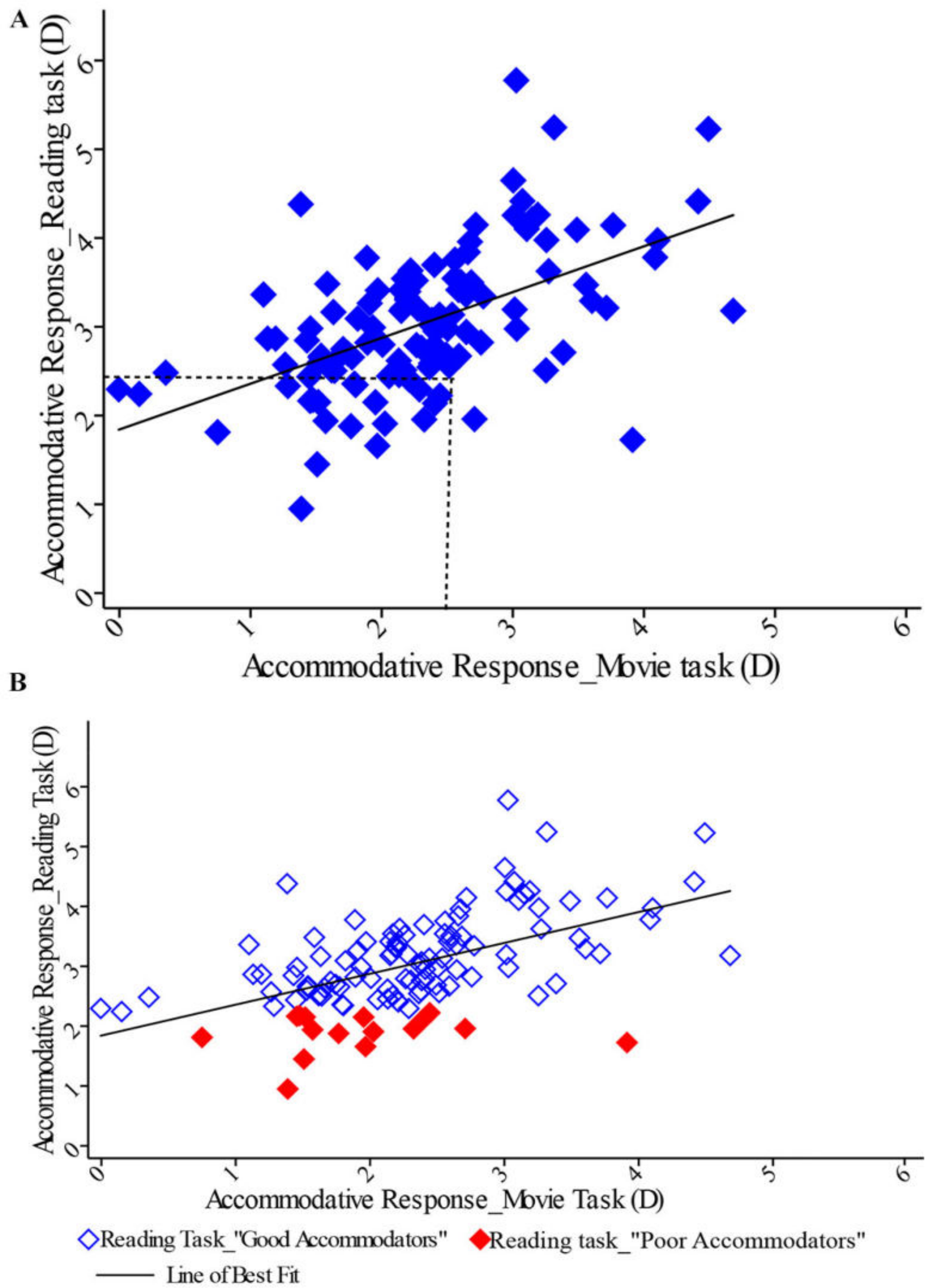


Figure 5.5.4 Scatter plots showing (A) accommodative response during reading task with accommodative response during movie task (B) accommodative response in reading task with accommodative response in movie task colour coded for "good and poor accommodators". Short dashed black lines in panel A encapsulate participants whose data did not show a positive relationship between accommodative response in reading task and movie task.

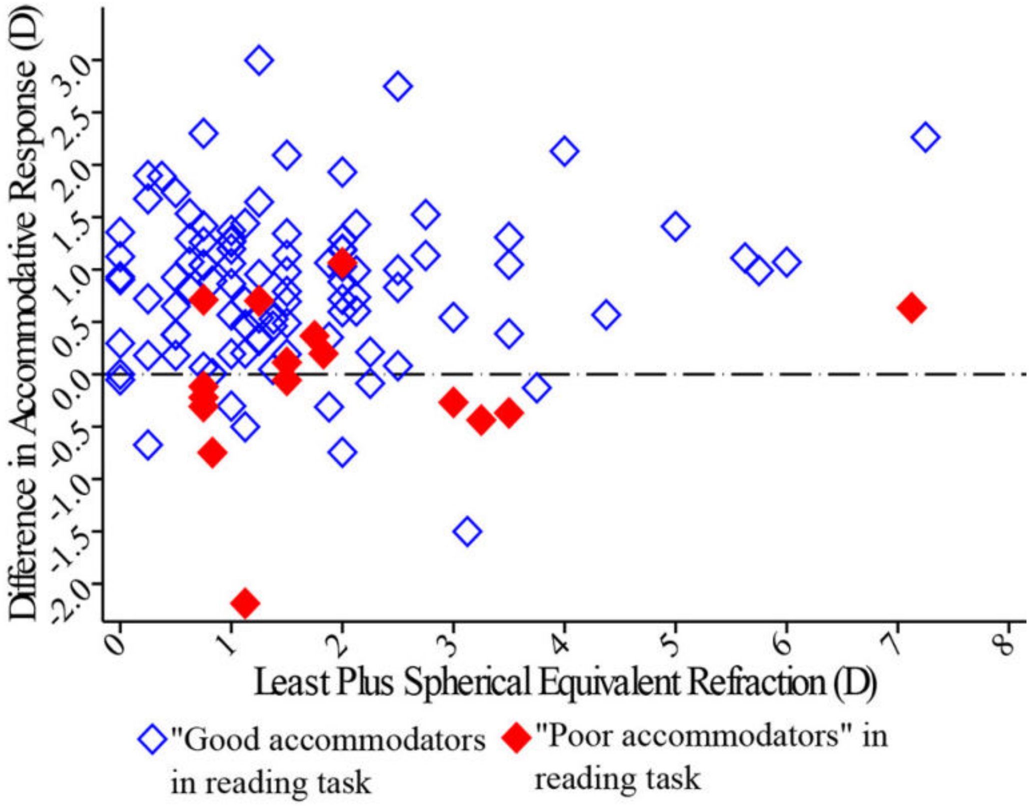


Figure 5.5.5. Scatter plot showing difference in mean accommodative response of reading and movie task with least spherical equivalent refraction.

5.5.1.5 Effect of Anisometropia on Mean Accommodative Response

In a two-way ANOVA to assess the effect of anisometropia on the mean accommodative response across the two tasks, there was no significant interaction between refractive error group and the present/absence of anisometropia ($F_{(2,112)}$=0.38, p=0.68 and $F_{(2,112)}$=1.21, p=0.38 for reading and movie tasks respectively), and there was no effect of presence/absence of anisometropia on mean accommodative performance across the two tasks ($F_{(1,112)}$=0.17, p=0.68, and $F_{(1,112)}$=1.29, p=0.26 for reading and movie tasks respectively).

5.5.2 Accuracy of response in terms of lag/lead of accommodation

The accuracy of the accommodative response differed significantly by task type, with significantly greater lag of accommodation observed in the movie task compared to the reading task ($F_{(1,107)}$=4.67, p=0.03). This was analysed using a four-way ANCOVA with two covariates (least plus SE and lag of accommodation in movie task), and two factors (habitual refractive status and order of introduction of task). There was no significant interaction between the two covariates and the two factors ($F_{(4,116)}$=6.91, p=0.13). The lag/lead of accommodation was not related to the refractive group of participants. See also Table 5.5.2

Table 5.5.2. Median (IQR) of accommodative lag/lead by task type and refractive groups. All participants uncorrected during tasks.

	Accommodative Lag (uncorrected)	
Refractive Group (N)	**Reading Task** **Median (IQR), (min, max)**	**Movie Task** **Median (IQR) (min, max)**
All subjects	1.05(0.52-1.50), (-1.25,2.55)	1.74(1.32-2.23), (-0.49,3.85)
-0.25 to <+1DS (32)	1.13(0.74-1.40), (-0.41,2.34)	1.72(1.36-2.37), (-0.41,4.00)
+1 to <+2DS (40)	1.22 (0.65-1.57), (-0.65,2.55)	1.83(1.49-2.22), (-0.09, 3.85)
+2 to +4DS (32)	0.82(0.10-1.50), (-1.78,3.05)	1.45(0.93,2.07), (-0.68, 3.65)
>+4DS (8)	0.65(0.06-1.13), (-0.26,1.85)	1.79 (1.11-2.52), (0.81,2.90)
Difference	Kruskal-Wallis (X^2 (3)) = 3.38, p=0.34. Same direction when one-way ANOVA was used	Kruskal-Wallis (X^2 (3)) = 2.48, p=0.48. Same direction when one-way ANOVA was used

A plus value represents a lag of accommodation while a minus value represents a lead of accommodation.

The relationship between the mean accommodative lag/lead and the least spherical equivalent refractive error across the two tasks was weak and not statistically significant (Spearman's correlation, r=-0.02, p=0.98 and r=-0.024, p=0.80 for reading and movie tasks respectively, see also Figure 5.5.6). The habitual refractive status of a subject (spectacle wearer vs non-spectacle wearer) had no statistically significant effect on mean lag in the reading task ($F_{(1,112)}=1.11$, p=0.30). This was analysed using a two-way ANCOVA (least plus SE as covariate). However, in the movie task, habitual spectacle wearers had a statistically significantly lower mean accommodative lag ($F_{(1,112)}=6.60$, p=0.01), which did not depend on the of SE refraction (no interaction $F_{(1,112)}=3.45$, p=0.07).

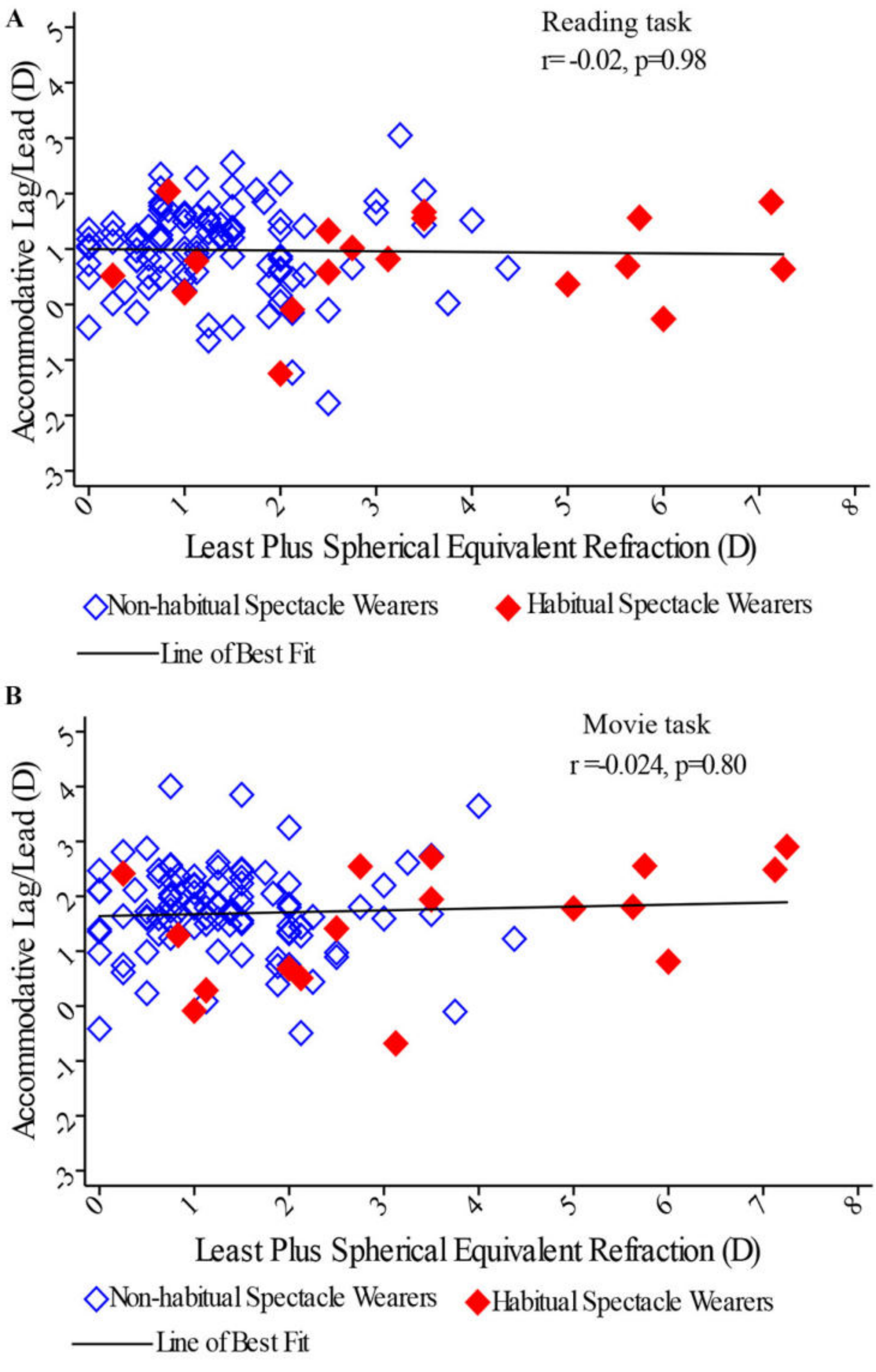


Figure 5.5.6. Scatter plots of (A) mean accommodative lag/lead with least plus SE in the reading task, (B) mean accommodative lag/lead with least plus SE in the movie task. Plus labels represent lag of accommodation while minus labels represent lead of accommodation. Participants were uncorrected in both tasks.

When the mean accommodative lag/lead was considered in relation to the total accommodative response (which is the sum of the mean response and the response needed to correct the subject's spherical equivalent refractive error), statistically significant associations were observed for both tasks (Spearman's correlation r =-0.55, $p<0.0001$, and r = -0.53, $p<0.0001$ for reading and movie tasks respectively), see also Figure 5.5.7. In a two-way ANCOVA to evaluate the effect of habitual refractive status and total accommodative response on the mean lag, there were significant interactions between habitual refractive status and total accommodative response on the mean lag in both tasks ($F_{(1,111)}$=13.87, p=0.0003) and $F_{(1,111)}$=15.80, p=0.0001 for reading and movie tasks respectively). Subjects with higher total accommodative response who were habitual spectacle wearers had significantly reduced lag compared with non-wearers ($F_{(1,111)}$=7.04, p=0.01 $F_{(1,111)}$=8.53, p=0.004), see also Figure 5.5.7.

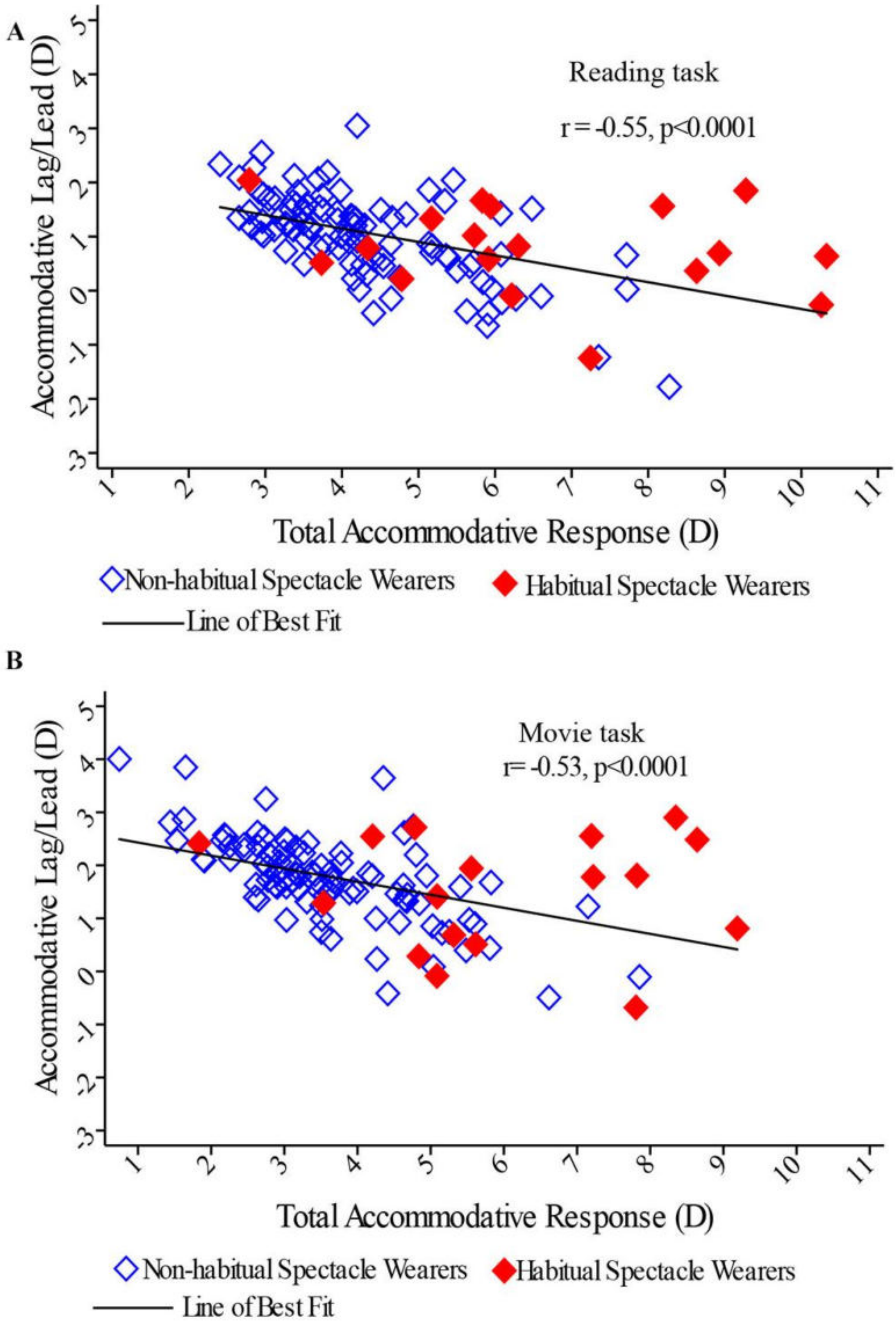


Figure 5.5.7 Scatter plots of (A) mean accommodative lag/lead against total accommodative response in reading task, (B) mean accommodative lag/lead with total accommodative response in movie task. Participants were uncorrected in both tasks. Plus labels represent lag of accommodation while minus labels represent lead of accommodation

5.5.3 Discussion

The results of the present study reveal that the mean accommodative response or accuracy in both uncorrected hyperopes and emmetropic controls differed by task type and was influenced by whether hyperopes were habitual spectacle wearers, or not.
There was a reduced lag of accommodation (higher mean response) in the reading (active) task compared to the movie (passive) task. This is consistent with previous studies which examined accommodative accuracy in subjects under different task conditions (Kruger 1980; Francis *et al.* 2003; Harvey *et al.* 2014; Roberts *et al.* 2018a). The reading task in the present study was specifically designed to be more visually demanding than the movie task. Furthermore, the requirement of higher attentional factors in the reading task and the effect of cognition in interpreting the text have been adduced to explain differences in accommodation accuracy between an "active" task such as reading, and a "passive" task such as observing a movie (Kruger 1980; Francis *et al.* 2003; Roberts *et al.* 2018a).

The present study also demonstrates that uncorrected hyperopes accommodate comparably to emmetropic controls during engagement with two sustained near tasks, regardless of their underlying refractive error. The mean accommodative response tended to increase with increasing hyperopia compared to the emmetropic group, particularly in the reading task. Moreover, when the accommodative response required to correct any underlying refractive error is considered in addition to the mean response generated for the two tasks, it is clear that the uncorrected hyperope responds appropriately, and produces relatively more accommodation. This finding is consistent with the recent work by Roberts *et al*. (2018a) who also examined accommodative performance across a range of uncorrected hyperopic refractive errors (-0.37 to +4.58D) during a 10-minute viewing period in children aged three to less than 10 years. Roberts *et al.* (2018a) reported that uncorrected hyperopes exhibited sufficient accommodation to achieve similarly accurate focus to children with a lesser amount of refractive error. It is unclear which factors drive uncorrected hyperopes to accommodate significantly in levels comparable to emmetropic controls considering their higher accommodative demand. Perhaps, uncorrected hyperopic children have similar blur detection thresholds to emmetropes, given that a recent study did not find any significant effect of uncorrected hyperopia on blur detection (Roberts *et al.* 2018b). However, the finding of comparable accommodative response between uncorrected hyperopes and emmetropes in this study is contrary to previous findings in the literature which report a significant relationship between underaccommodation or hypo-accommodation (significant lag) and magnitude of hyperopia (Horwood and Riddell 2011; Candy *et al.* 2012). The difference in findings between the present study and previous works may be related to a number of factors including the duration of assessing accommodation (few seconds of assessment versus sustained testing), and the target type and distance. Horwood and Riddell (2011) used the photorefraction technique to measure accommodative response over a period of a few seconds at five testing distances (25, 33, 50, 100 and 200cm, target positioned randomly) while their subjects fixated a large, high contrast, looming cartoon target. In Horwood *et al.* (2011) study, hypoaccommodation was independent of whether participant was corrected or not. Candy *et al.* (2012) used Nott retinoscopy to measure accommodation responses in typically developing children whilst they viewed a high contrast cartoon picture positioned at 50cm for a few seconds. In neither study were sustained responses evaluated nor was there any cognitive demand from the subjects other than to look at the target. Accommodative lag recorded using Nott retinoscopy in the present study revealed the same outcomes as Candy *et al.* (2012)'s Nott retinoscopy study, supporting the notion that the difference between the PowerRef 3™ technique and the sustained viewing protocol underpins the different findings discussed above. It has been speculated that outputs of a slow, blur-driven accommodation response, typically present during sustained near viewing, may reduce accommodative error (Rosenfield and Gilmartin 1998), and result in differences between accommodative responses recorded during sustained compared to short periods of accommodation.

There was wide inter-subject variability in the lag of accommodation demonstrated by participants (Table 5.4.2), with some demonstrating lags >2D. Of interest, is how such significant lags did not impede participants' ability to read and conduct the task successfully. Some of these participants with higher lags of accommodation, paradoxically scored higher on the rate of reading test (results presented later in this chapter). Harb *et al.* (2006), speculated that it was possible for some individuals to tolerate significant blur during reading because reading texts typically have high contrast and low spatial frequency content which is visible, even when accommodation is not accurate. In addition, reports that blur adaptation improves spatial sensitivity which reduces the effect of blur on visual performance (Rosenfield and Gilmartin 1998; Harb *et al.* 2006; Le *et al.* 2010) may explain why some of the participants with higher lags of accommodation still managed to do the reading task.

Results from the present study also point to a positive effect of habitual spectacle wear on the mean response measured without correction in the movie task. This finding was independent of the amount of refractive error present – this effect was observed in participants who were classified as "emmetropic" by the study's definition, as well as in hyperopes. It may be that habitual spectacle wear makes wearers less tolerant of blur during the movie task compared to the reading. Also, pupil sizes were, on average, smaller for reading task than movie thus less depth of focus, and more need to produce more accommodation to see the movie. The positive effect of habitual spectacle wear on the movie task – a naturalistic task, suggests spectacle wear helps the visual system to adapt to appreciate clear vision, and this could result in children with correction being able to produce more accurate focusing. In clinical practice, this may be used to encourage compliance.

There was no effect of age on the mean accommodative response, despite previous findings that younger children had larger and more variable lags (Horwood and Riddell 2011; Roberts *et al.* 2018a). The narrow age range of participants in this study might explain the lack of age effect on the accommodative response.

The present study did not find any effect of anisometropia greater than 1.00D on the mean accommodative performance across the two tasks. Previous studies have reported significant effects of anisometropia on near visual function measures such as stereoacuity, near visual acuity and dynamic retinoscopy (Robaei *et al.* 2007; Candy *et al.* 2012; Yang *et al.* 2012; Suh *et al.* 2016; Ciner *et al.* 2016). The lack of agreement between this study and previous findings could be due to the small number of participants with anisometropia (n=3), limiting the statistical power to detect any differences.

Overall, these results demonstrate that uncorrected hyperopes can rise to the occasion to provide significant accommodation for sustained near vision tasks up to 15 minutes. The accommodative response evaluated in the present study was averaged across the duration of the task (approximately 15 mins). However, the question of the stability of this response (being cognisant of the total amount of accommodation exerted), as well as the comfort of the participant while engaged in sustained near task need to be answered. The next section explores the stability of the accommodative response.

5.5.4 Summary

- Mean accommodative response during sustained reading and movie tasks was not significantly related to refractive error; responses from uncorrected hyperopes and emmetropes did not differ significantly.

- However, when the total accommodative effort required to correct underlying refractive errors is considered in addition to the requirement of focusing the target at 25cm, uncorrected hyperopes produced relatively more accommodation.

- There was a positive effect of habitual spectacle wear on the accommodative response achieved without correction. This association reached statistical significance in the movie task, with spectacle wearers demonstrating higher responses compared to hyperopes who were not habitual spectacle wearers.

5.6 What happens to the stability of the accommodative response during sustained reading and movie tasks in children with and without uncorrected hyperopia?

The stability of the accommodative response, also termed microfluctuations or accommodative variability, was analysed in the time domain using the root mean square deviation (RMS) of the 15 one-minute periods (or for the duration of testing, e.g. if only 10 minutes cooperation was achieved, this was 10 one-minute segments), and also characterised in the frequency domain as the area under the curve for the low frequency component (LFC) of 0.1–0.6Hz (Harb *et al.* 2006) using Power Spectrum Analysis (obtained through Fast Fourier Transform). The RMS of the first 10 seconds of each one-minute period was averaged to obtain a mean RMS of microfluctuation for each task. Similarly, the mean microfluctuation for the LFC was obtained by averaging the area under the curve for the one-minute segments of the duration of the test (e.g. 15 one-minute segments for a participant who was tested for 15 minutes).

There was more variability (instability) in the accommodative response in the movie task compared to the reading task ($F_{(1,101)}=4.98$, $p=0.03$), after controlling for age ($F_{(1,101)}=1.70$, $p=0.20$), order effect ($F_{(1,101)}=0.48$, $p=0.49$), and refractive group ($F_{(3,101)}=0.12$, $p=0.95$); with no significant interactions between these factors ($F_{(8,101}=0.96$, $p=0.47$). This was analysed using a four-way ANCOVA with covariates being age and mean RMS of microfluctuation in the reading task. See also Figure 5.6.1.

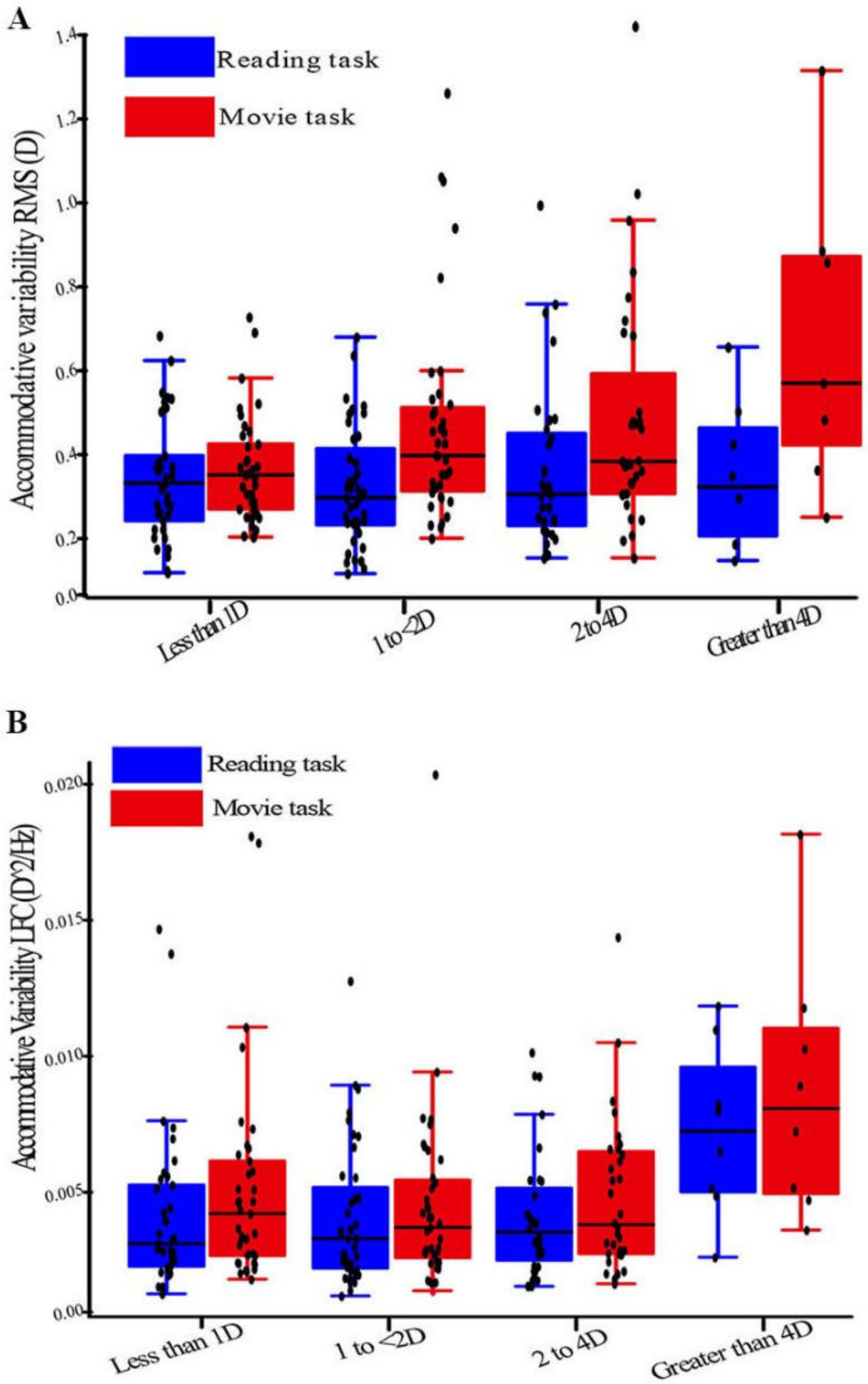


Figure 5.6.1 Box-plot diagrams showing (A) accommodative variability in time domain (RMS) and (B) frequency domain (LFC) by refractive group. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

Univariate analyses using Pearson's correlation revealed weak but statistically significant associations between accommodative variability in the frequency domain (LFC) and least plus spherical equivalent refraction in both reading and movie tasks (r=0.21, p=0.024, and r=0.19, p=0.038 respectively). However, in the time domain (RMS), a statistically significant association was observed only in the movie task (r=0.02, p=0.87, r=0.27, p=0.0042 for the reading and movie task respectively). See also Figure 5.6.2 and 5.6.3.

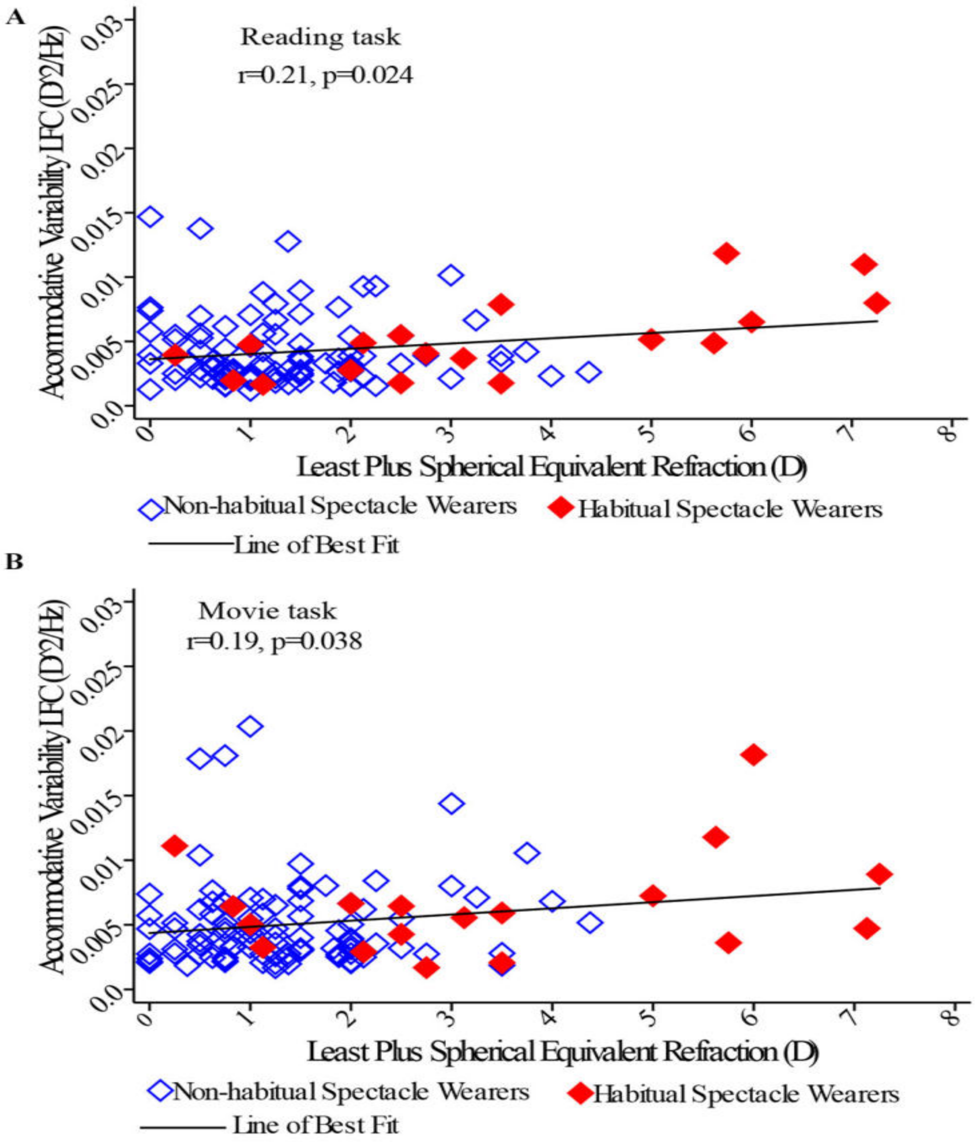
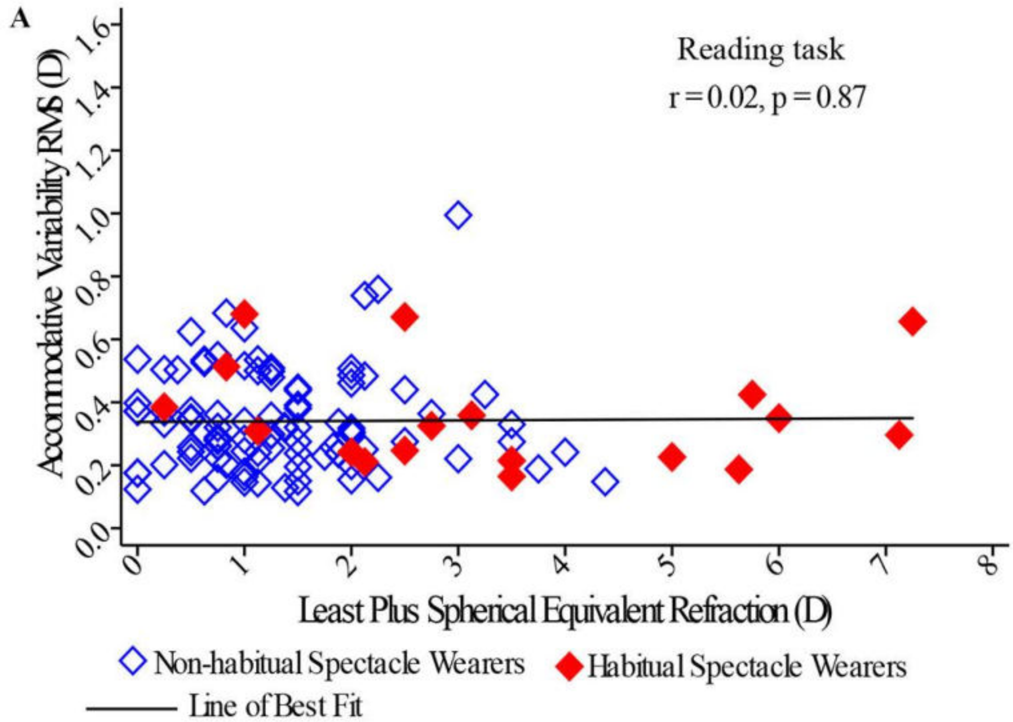


Figure 5.6.2 Scatter plots of (A) Accommodative variability in the frequency domain (LFC) with least plus spherical equivalent refraction in the reading task, (B) Accommodative variability in the frequency domain (LFC) with least plus spherical equivalent refraction in the movie task.



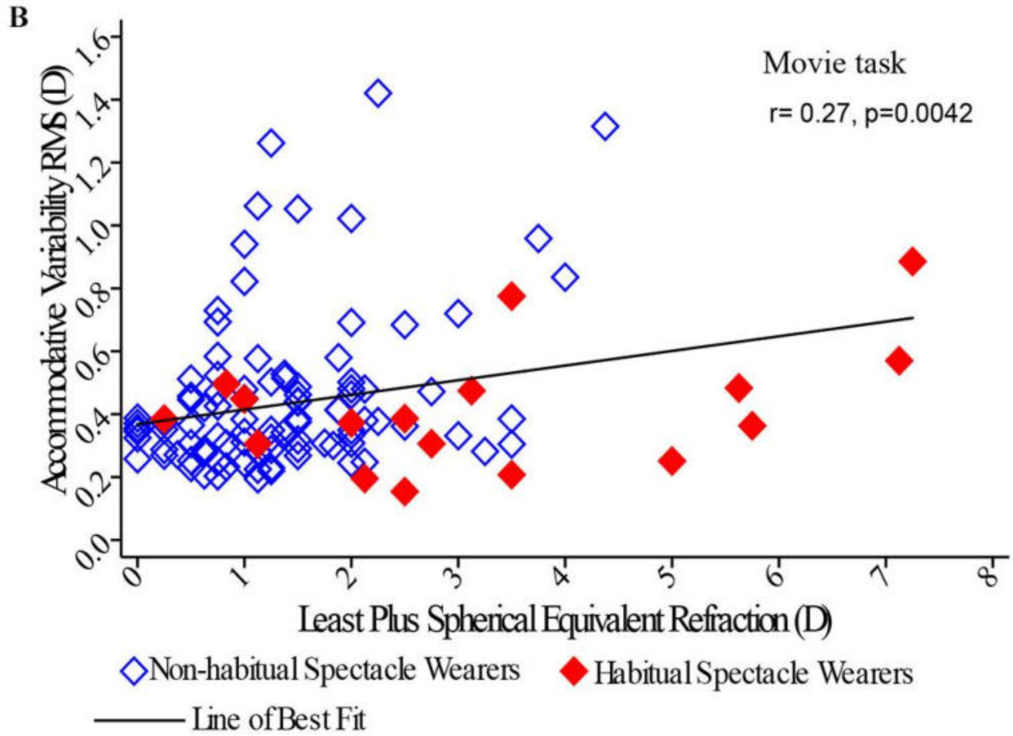


Figure 5.6.3 Scatter plots of (A) accommodative variability in the time domain (RMS) in the reading task with least plus spherical equivalent refraction (B) accommodative variability in the time domain (RMS) in the movie task with least plus spherical equivalent refraction.

When the variability associated with accommodation in both time and frequency domains was assessed against the total accommodative response, the associations observed were weak and not statistically significant in the reading task, but significant in the movie task (RMS): $r=0.08$, $p=0.39$, $r=0.24$, $p=0.0097$ for reading and movie tasks respectively and $r=0.18$, $p=0.05$, $r=0.15$, $p=0.11$ for the reading and movie tasks respectively, (LFC). See also Figures 5.6.4 and 5.6.5.

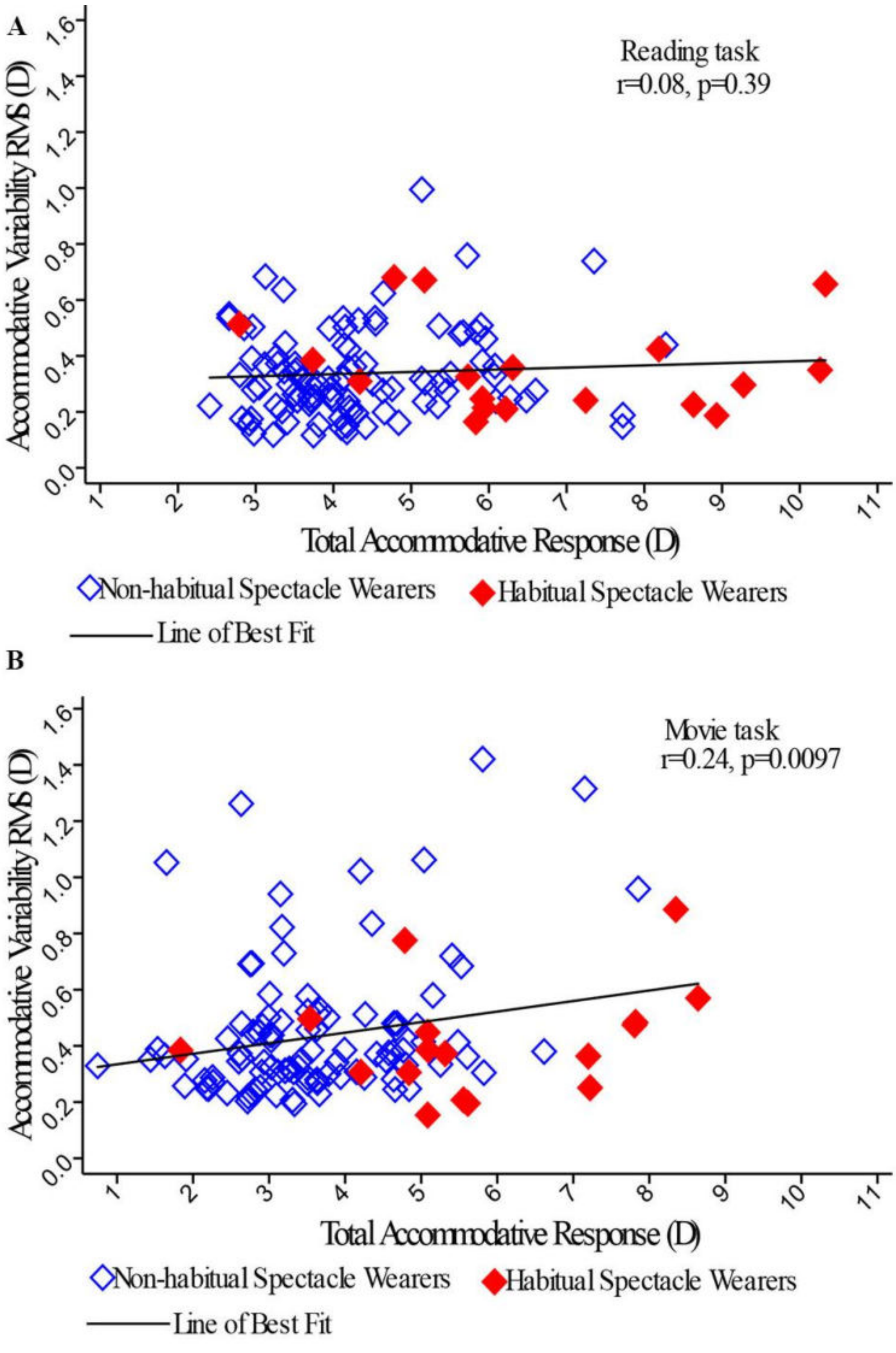
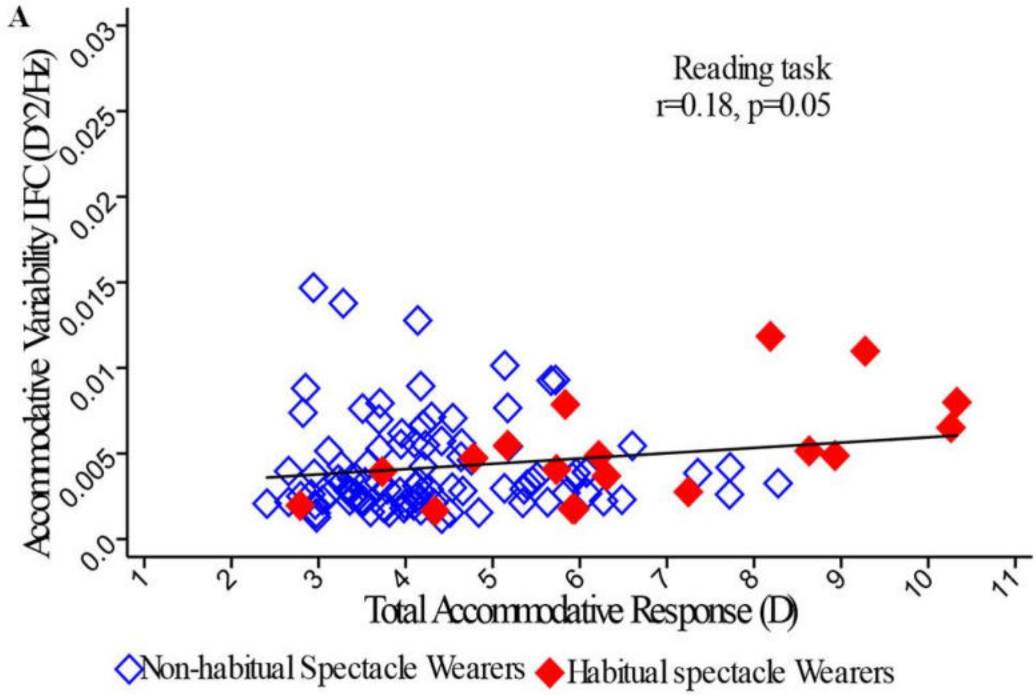


Figure 5.6.4 Scatter plots showing (A) accommodative variability in the time domain (RMS) with total accommodative response in reading task (B) accommodative variability in the time domain (RMS) with total accommodative response in movie task.



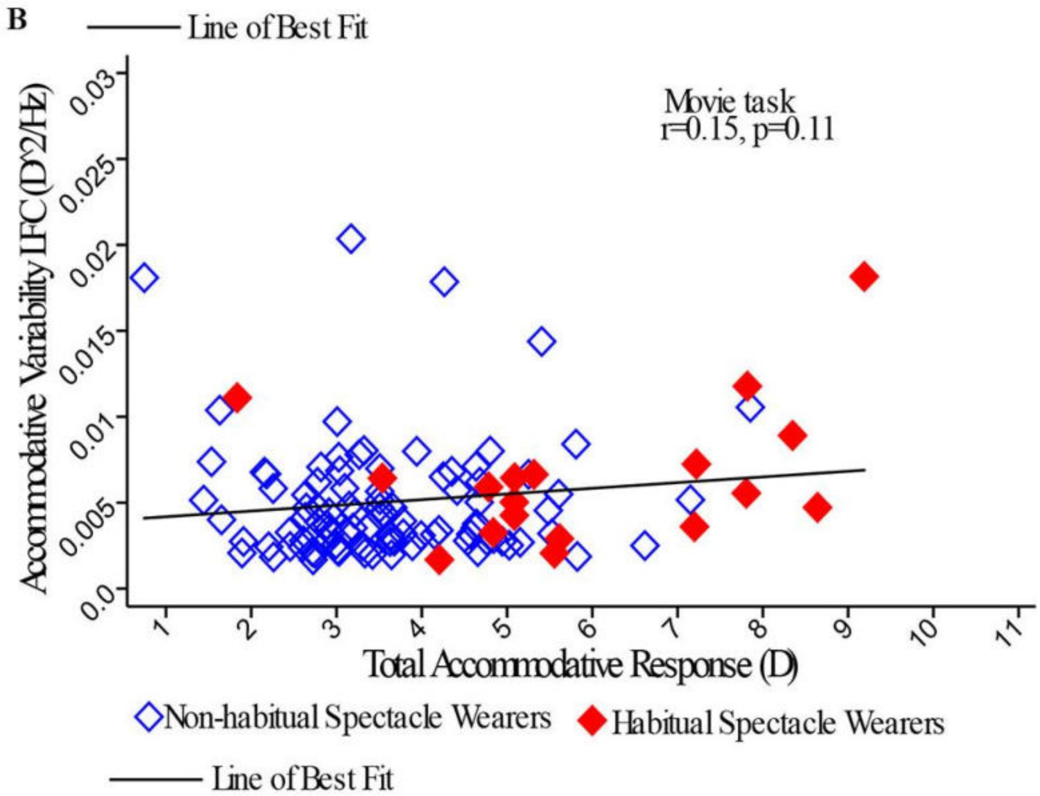


Figure 5.6.5 Scatter plots of (A) Accommodative variability in the frequency domain (LFC) with total accommodative response in reading task, (B) Accommodative variability in the frequency domain (LFC) with total accommodative response in movie task.

Multivariate analyses to investigate the effect of several factors on the accommodative variability in time and frequency domains were carried out using two-way ANOVA and ANCOVA.

5.6.1 Effect of Pupil Size

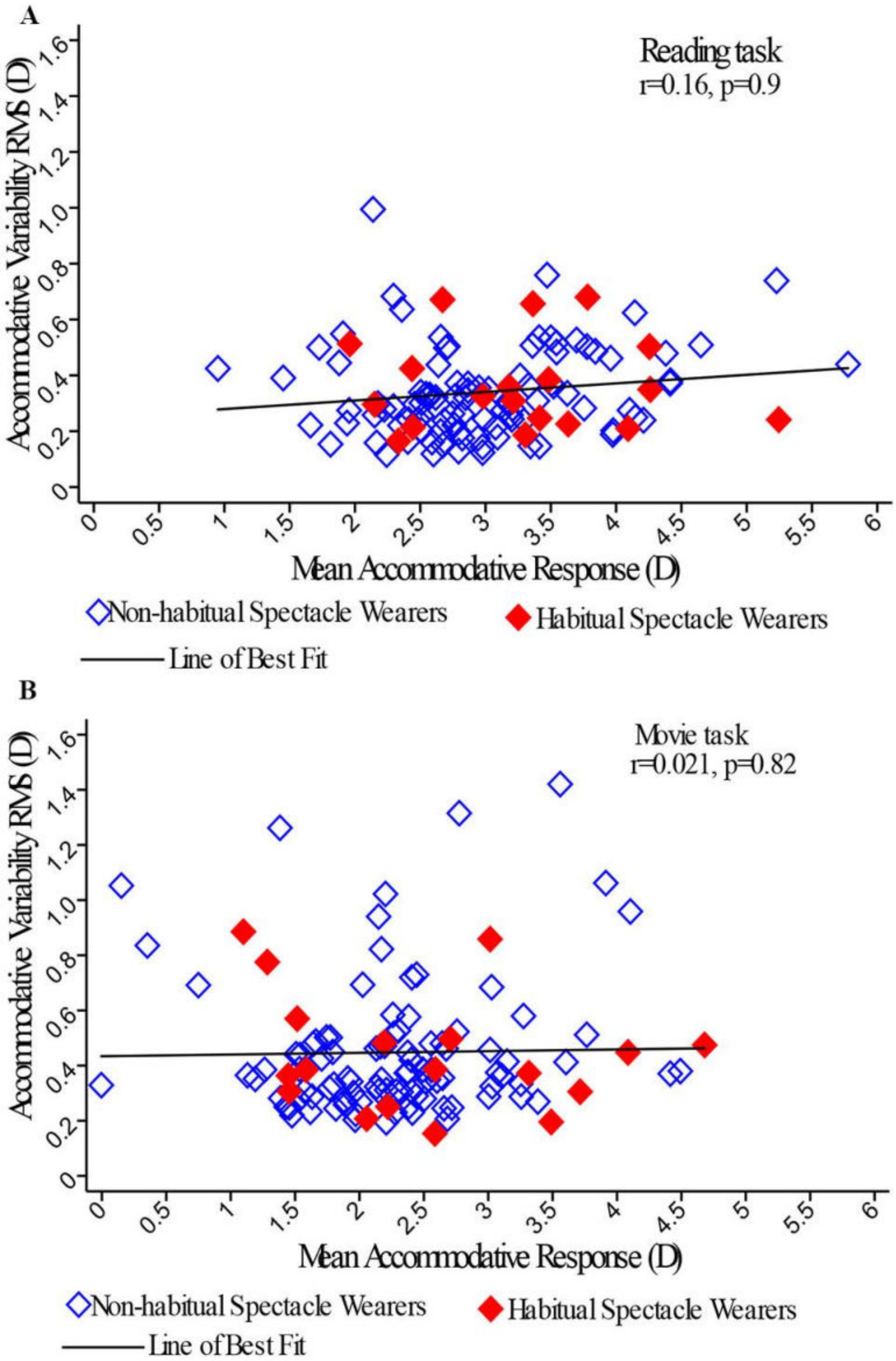
A two-way ANCOVA to examine the effect of pupil size and refractive group on the variability of accommodation in the movie task revealed significant interaction between pupil size and refractive group ($F_{(3,108)}$=3.37, p=0.02), and statistically significant main effects of pupil size ($F_{(1,108)}$=8.81, p=0.004), and refractive group ($F_{(3,108)}$=3.52, p=0.02) in the time domain analysis. However, in the LFC analysis, the interactive effect of pupil size and refractive group was borderline ($F_{(3,108)}$=2.76, p=0.05), with statistically significant main effects of pupil size and refractive group (all p<0.05). Further analysis revealed that subjects with refractive error greater than +4.00D and relatively small pupils had the greatest variability in accommodation (p=0.004 and p=0.005 for RMS and LFC respectively). In the reading task, there was significant interaction between pupil size and refractive group ($F_{(3,109)}$=3.00, P=0.03), with a borderline effect of refractive group ($F_{(3,109)}$=2.74, p=0.05), but no main effect of pupil size ($F_{(1,109)}$=0.74, p=0.39) in the time domain (RMS). Further analysis revealed participants in refractive group (+2.00 to +4.00D) with small pupil sizes had more variability in their accommodative response (p=0.02). Similarly, LFC analyses revealed significant variability in the accommodative response in participants >+4D (p=0.04).

5.6.2 Effect of Age and Habitual Spectacle Wear

There was no effect of age or habitual spectacle wear on the variability of accommodation in the movie task in the frequency domain (LFC, p>0.05, two-way ANOVA, with the other factor being refractive group). However, in the time domain (RMS), there was borderline interaction between habitual spectacle wear and refractive error ($F_{(3,108)}$=2.72, p=0.05), with statistically significant main effects of habitual spectacle wear ($F_{(1,108)}$=6.97, p=0.01), and refractive group ($F_{(3,108)}$=5.51, p=0.002). Significantly more variability in the accommodative responses was observed in the +2.00 to +4.00D and >+4.00D hyperopic groups (p=0.007 and p<0.001 respectively). Moreover, in the >+4.00D group, there was interaction with habitual spectacle wear (p=0.006). In the reading task, habitual spectacle wear ($F_{(1,109)}$=3.33, p=0.07) and refractive group ($F_{(3,109)}$=0.11, p=0.95) did not influence the variability of accommodative response in either time domain or frequency domain ($F_{(1,108)}$=0.54, p=0.47 and $F_{(3,108)}$=0.36, p=0.78 for habitual spectacle wear and refractive group respectively). The effect of age on the variability of accommodation in the reading task was not statistically significant ($F_{(1,109)}$=0.21, p=0.65), and no significant interaction was observed between age and refractive group ($F_{(3, 109)}$=0.12, p=0.95).

5.6.3 Accommodative variability and mean accommodative response

Univariate analyses for associations between accommodative variability and mean accommodative response using Pearson's correlation were not statistically significant in either task for RMS or LFC analyses: (RMS: r=0.16, p=0.9 and r=0.021, p=0.82 for reading and movie tasks respectively; LFC: r=0.03, p=0.78 and r=0.03, p=0.77 for reading and movie tasks respectively. See also Figures 5.6.6 and 5.6.7. However, subjects who exhibited more variability in their accommodative response in the reading task than movie (see Figure 5.6.8, using LFC analysis) tended to have higher accommodative response in the reading task (3.21±0.79D vs 2.92±0.77D t=1.98, p=0.04), although this observed difference becomes statistically insignificant when pupil sizes are accounted for ($F_{(1,111)}$=1.75, p=0.19).



Figures 5.6.6. Scatter plots of (A) Accommodative variability in the time domain (RMS) with mean accommodative response in reading task (B) Accommodative variability in the time domain (RMS) with mean accommodative response in movie task.

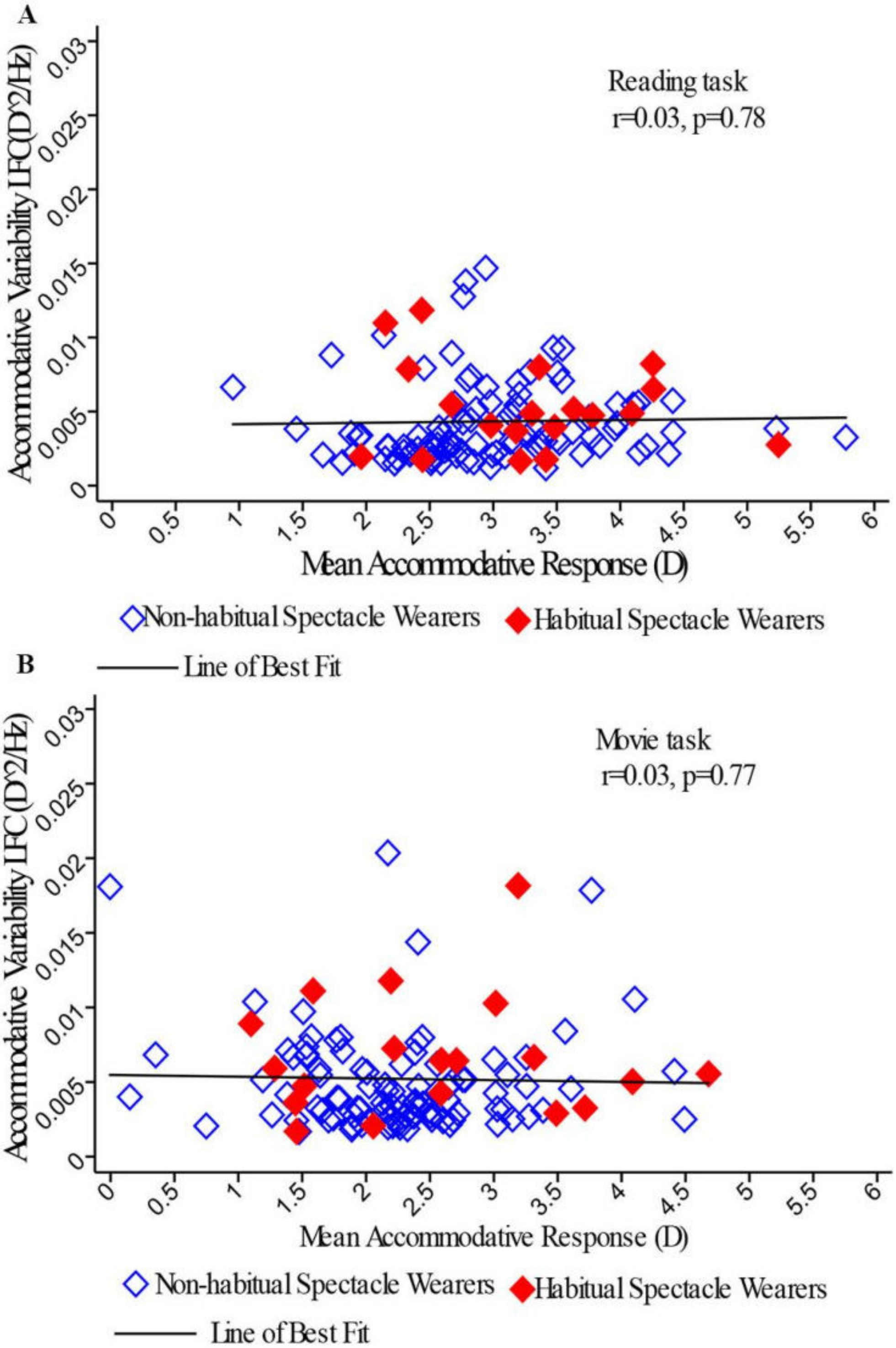


Figure 5.6.7 Scatter plots of (A) Accommodative variability in the frequency domain (LFC) with mean accommodative response in reading task (B) Accommodative variability in the frequency domain (LFC) with mean accommodative response in movie task.

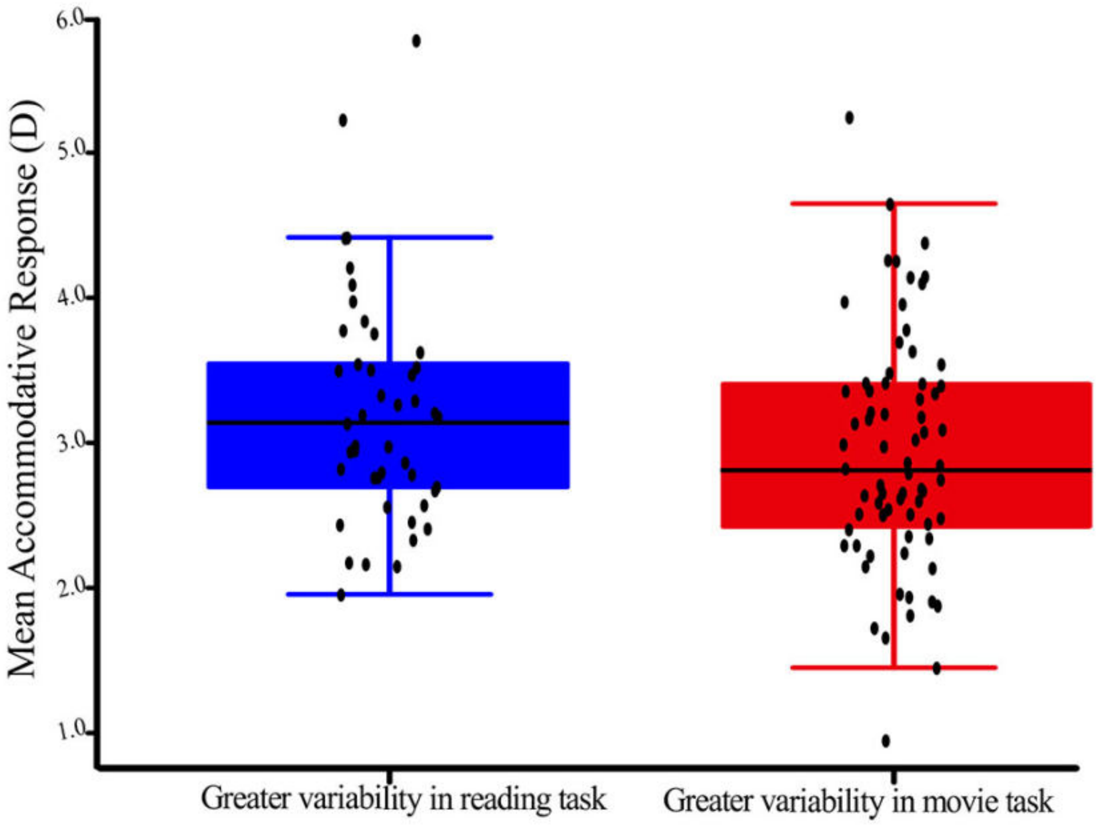


Figure 5.6.8. Boxplot diagram showing mean accommodative response in the reading task by inter-task differences in accommodative variability in the frequency domain (LFC). The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

5.6.4 Stability of Accommodative Response in "Good versus Poor Accommodators"

Although 'poor accommodators' in the reading task had a greater degree of variability in their accommodative response across the two tasks in both time and frequency domains compared to 'good accommodators', these differences were not statistically significant. See Table 5.6.1

Table 5.6.1 Mean (SD) of accommodative variability in time (RMS) and frequency domain (LFC) in "good and poor accommodators". All participants uncorrected during tasks.

	RMS			**LFC**		
Task	**Good**	**Poor**	***p***	**Good**	**Poor**	***p***
Reading	0.37±0.21D	0.34±0.15D	$t=-0.70$, $p=0.49$	$4.2\times10^{-3}\pm3.2\times10^{-3}$ D^2/Hz	$4.4\times10^{-3}\pm2.7\times10^{-3}$ D^2/Hz	$t=0.21$, $p=0.84$
Movie	0.47±0.25D	0.44±0.24D	$t=-0.46$, $p=0.65$	$5.3\times10^{-3}\pm3.6\times10^{-3}$ D^2/Hz	$5.2\times10^{-3}\pm3.5\times10^{-3}$ D^2/Hz	$t=0.13$, $p=0.90$.

5.6.5 Effect of Anisometropia on stability of Accommodation

There was no significant effect of anisometropia on the stability of the accommodative response using two-way ANOVA (factors: refractive group, anisometropia present/absent; RMS: $F_{(1,109)}=1.59$, $p=0.21$, and $F_{(1,108)}=0.67$, $p=0.42$ for reading and movie tasks respectively; LFC: $F_{(1,108)}=1.87$, $p=0.18$, and $F_{(1,108)}=1.41$, $p=0.24$ for reading and movie tasks respectively).

5.6.6 Discussion

When the eye is in focus during steady-state fixation, the accommodative response is thought to oscillate within the range of 0.50D (Charman and Heron 2015). These oscillations have been termed accommodative microfluctuations. The variability in the accommodative response has been characterised in the time domain using the RMS of the mean responses and in the frequency domain by conducting power spectrum analysis on waveform response using Fast Fourier Transform. Two major frequency components have been identified; the low frequency component (LFC; < 0.6 Hz), the high frequency component (HFC; 1 – 2.3 Hz) and a middle range (MFC) of >0.6 and <1.0 Hz (Charman and Heron 1988; Winn and Gilmartin 1992). The LFC is thought to play an active role in the accommodation process, responding to factors which produce a change in depth of focus such as luminance of the target, pupil size, spatial frequency of the target, and accommodative demand (Gray *et al.* 1993a; Gray *et al.* 1993b; Gray *et al.* 2000; Day *et al.* 2006; Day *et al.* 2009a; Day *et al.* 2009b). These characteristics provided the rationale for characterising variability in the accommodative response in the frequency domain using only the LFC in the present study.

All refractive groups in the present study demonstrated more LFC fluctuations during the movie task compared to the reading task. This finding was unaffected by age or the order in which the task was introduced and is consistent with previous work by Harvey *et al.* (2014) who report more variability in a video-viewing task compared to a reading task. It has been reported that accommodative variability increases with increased accommodative demand (Kotulak and Schor 1986; Day *et al.* 2006; Candy and Bharadwaj 2007). Similarly, it would be expected that accommodative variability will increase with a more visually demanding task such as reading, compared to a movie task, particularly in the present study, where small font size was selected for the text. This would occur as the accommodative plant oscillates frequently in an attempt to generate an appropriate response. However, in the present study, we found the opposite result. Possible explanations for this include the difference in the stability of the background luminance of the two targets (a stable background illumination of 40 cd/m^2 in kindle in the reading task vs 10 to 50 cd/m^2 for the LCD screen in the movie task). Moreover, differences in contrast of the movie versus the reading target is likely to have contributed to the observed finding. Varying background luminance and contrast in the movie task could have caused increased accommodative microfluctuations as the accommodative error detector “searches” for consistent feedback information for an appropriate response. These two factors have been reported to affect the magnitude of microfluctuations (Gray *et al.* 1993b; Day *et al.* 2009b). Changes in the level of detail in the movie compared to the more consistent demands of the reading task could also account for differences in attentional factors between the two tasks; promoting a higher level of microfluctuations in the movie task. This is despite the author's efforts to sustain good attention throughout the movie task, including commenting on the action being presented and asking questions about the movie while it was ongoing.

In the present study, higher levels of variability were associated with uncorrected hyperopia >+4D across the two tasks. Moreover, in the reading task, significantly increased levels of variability were observed in conjunction with even moderate amounts of uncorrected hyperopia (+2D and above). While this is consistent with previous studies reporting that subjects with increased accommodative demand have more variable (unstable) accommodative responses (Harvey *et al.* 2014; Roberts *et al.* 2018a; Roberts *et al.* 2018b), our data also demonstrate only weak associations between total accommodative response and accommodative variability in the frequency domain. Other recent studies have found children with uncorrected hyperopia (greater than +4D) perform poorly on some visual function measures (Candy *et al.* 2012; Kulp *et al.* 2014; Ciner *et al.* 2016). It is interesting to note that, the same cohort of uncorrected hyperopes >+4D in the present study also demonstrate increased variability in their accommodative response. While the functional roles of accommodative microfluctuations are yet to be fully understood, it has been proposed that they may be a mechanism to provide feedback error to maintain appropriate response during steady-state accommodation (Gray *et al.* 1993a; Day *et al.* 2009b). Moreover, it has been suggested that where there is increased accommodative effort, such as occurs in high uncorrected hyperopia, there is a decreased zonular tension which causes the lens to move freely resulting in increased microfluctuations (Kotulak and Schor 1986; Day *et al.* 2006). This may aid explanation of the increased variability (LFC result) in the reading task, where there was a borderline association between accommodative variability and total accommodative response.

In spite of any potential functional roles of microfluctuations, they represent temporal instability in the retinal image quality (Candy and Bharadwaj 2007; Langaas *et al.* 2008; Le *et al.* 2010), and have the potential to cause visual discomfort (Simmers *et al.* 2001; O'Hare and Hibbard 2013), which may be evident in uncorrected hyperopia as asthenopia. Additionally, some evidence of an association between uncorrected hyperopia and poorer educational outcomes has been reported (Shankar *et al.* 2007; Kulp *et al.* 2016). Accordingly, the variability of accommodation in the uncorrected hyperopic child could become one of the explanatory factors to this association, at which optical intervention could be targeted.

The effect of small pupil size (typically less than 2mm) on accommodative microfluctuations has been reported (Gray *et al.* 1993a; Day *et al.* 2009b). Increased depth of focus from small pupil size causes a reduced retinal blur circle, which makes the eye less able to detect blur, therefore requiring increased microfluctuations to provide error signals for a response (Day *et al.* 2009b). Although pupil size of less than 3mm was not recorded in participants across the two tasks in the present study, there was significant interactive effect of pupil size on uncorrected hyperopic participants with higher variability in their accommodative response.

It has been previously reported that younger children and infants tend to have increased accommodative microfluctuations compared to adults (Candy and Bharadwaj 2007; Roberts *et al.* 2018b; Roberts *et al.* 2018a). However, the present study did not find any age effect on accommodative microfluctuations, probably due to the narrow age range of study participants.

5.6.7 Summary

- In the present study, there were more accommodative fluctuations observed in the movie task compared to the reading task across all refractive groups. This is likely due to the dynamic range of contrast and spatial content contained in the movie task.
- Increased variability in accommodative response was associated with higher levels of uncorrected hyperopia >+4D, with pupil size interaction.
- There was no effect of age on accommodative variability**.**

5.7 What happens to the accuracy and stability of the vergence response during active and passive sustained near tasks in children with and without uncorrected hyperopic refractive error?

5.7.1 Accuracy of the Vergence Response

In the present study, participants demonstrated higher vergence responses in the reading task (2.91±0.50 MA) compared to the movie task (2.61±0.87 MA), and results of a two-way ANCOVA (covariate - mean vergence response in the movie task, refractive group as factor, and the mean vergence response in the reading task as the dependent variable) revealed no significant interaction between factors ($F_{(3,106)}$=1.11, p=0.35), and a statistically significant difference between the mean vergence response in the reading and movie tasks ($F_{(1,1)}$=5.35, p=0.022), which was independent of the participant's refractive group ($F_{(3,106)}$=1.99, p=0.12). See also Figure 5.7.1.

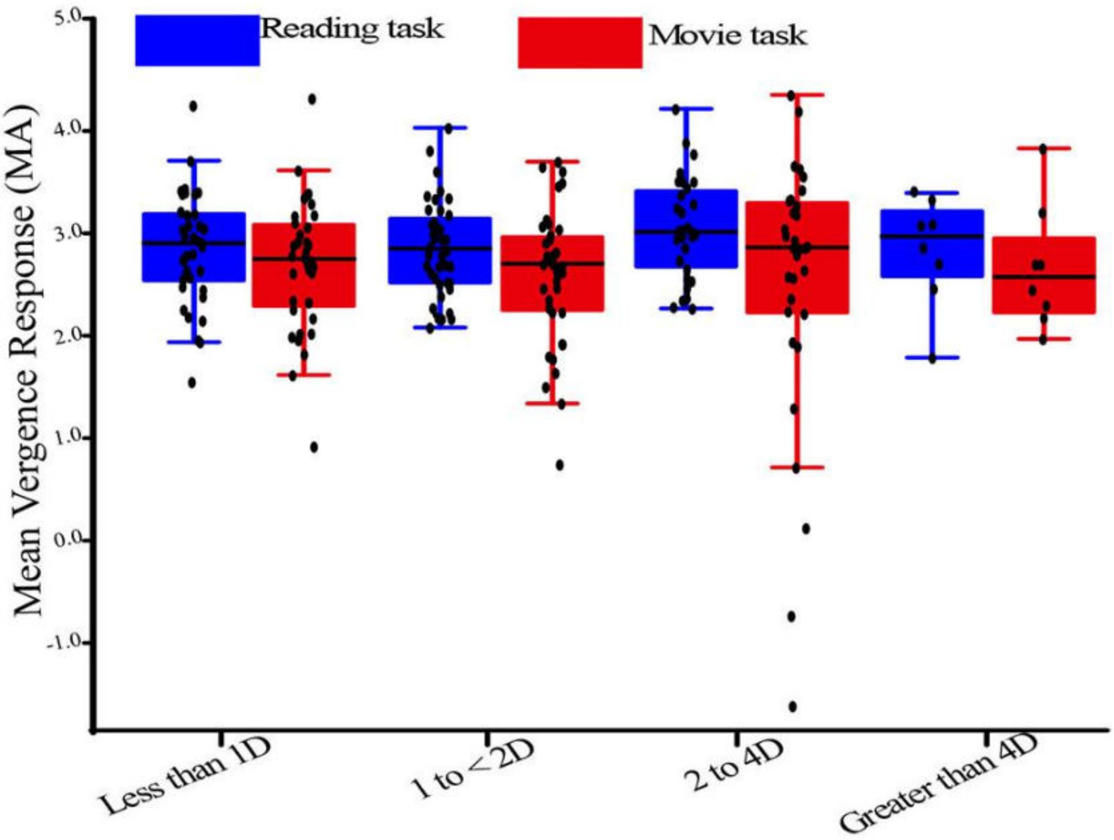


Figure 5.7.1 Boxplots of mean vergence response across the two tasks by refractive group. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

Univariate analysis using Pearson's correlation revealed no statistically significant relationship between refractive error and the mean vergence response across the two tasks (r=0.07, p=0.46, and r=-0.08, p=0.40 for reading and movie tasks respectively). Likewise, there were no refractive group differences in vergence response (One-way ANOVA $F_{(3,113)}$=0.22, p=0.88 and $F_{(3,111)}$=0.24, p=0.87 in the reading and movie tasks respectively).

5.7.1.1 Relationship between Vergence and Accommodative Responses

The relationship between mean vergence response and mean accommodative response was assessed using Pearson's correlation. There was a positive correlation between the mean vergence response and mean accommodative response in the movie task ($r=0.24$, $p=0.01$), but not the reading task ($r=0.02$, $p=0.86$). See also Figure 5.7.2. The mean vergence response (2.61±0.87MA) was also higher than the accommodative response (2.29±0.83D) in the movie task (paired t-test: $t=-3.21$, $p=0.002$). In the reading task, the mean difference between the vergence response (2.91±0.50MA) and the accommodative response (3.03±0.81D) was not statistically significant ($t=1.42$, $p=0.16$).

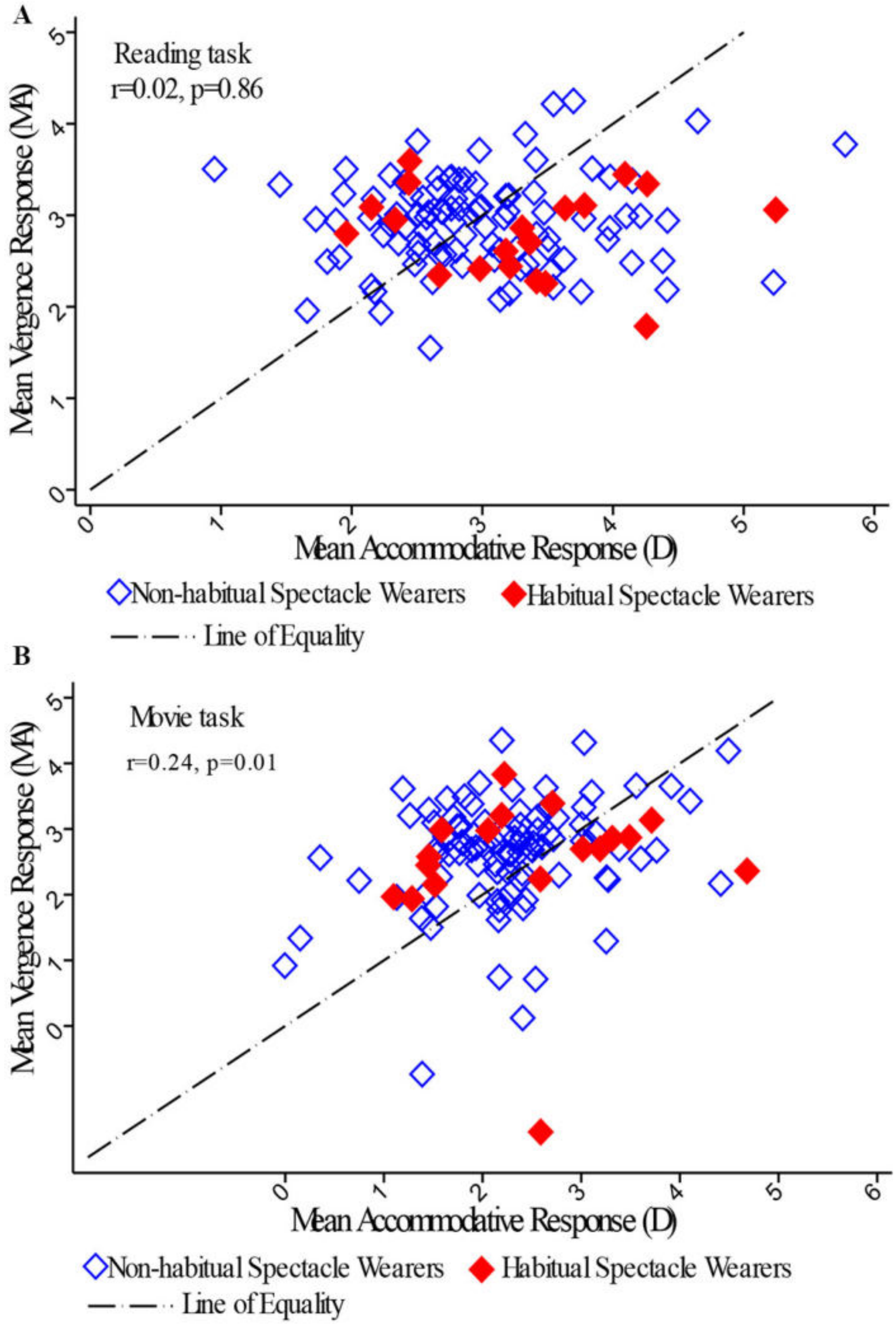


Figure 5.7.2 Scatterplots showing (A) mean vergence response with mean accommodative response in reading task (B) mean vergence response with mean accommodative response in movie task.

Moreover, there was no difference in the mean vergence response between "good" and "poor" accommodators (classification based on reading task performance) across the two tasks (reading: 2.93±0.50 vs 2.81±0.52, t=0.91, p=0.37 and movie: 2.66±0.81 vs 2.30±1.17, t=1.52, p=0.13). See also Figure 5.7.3.

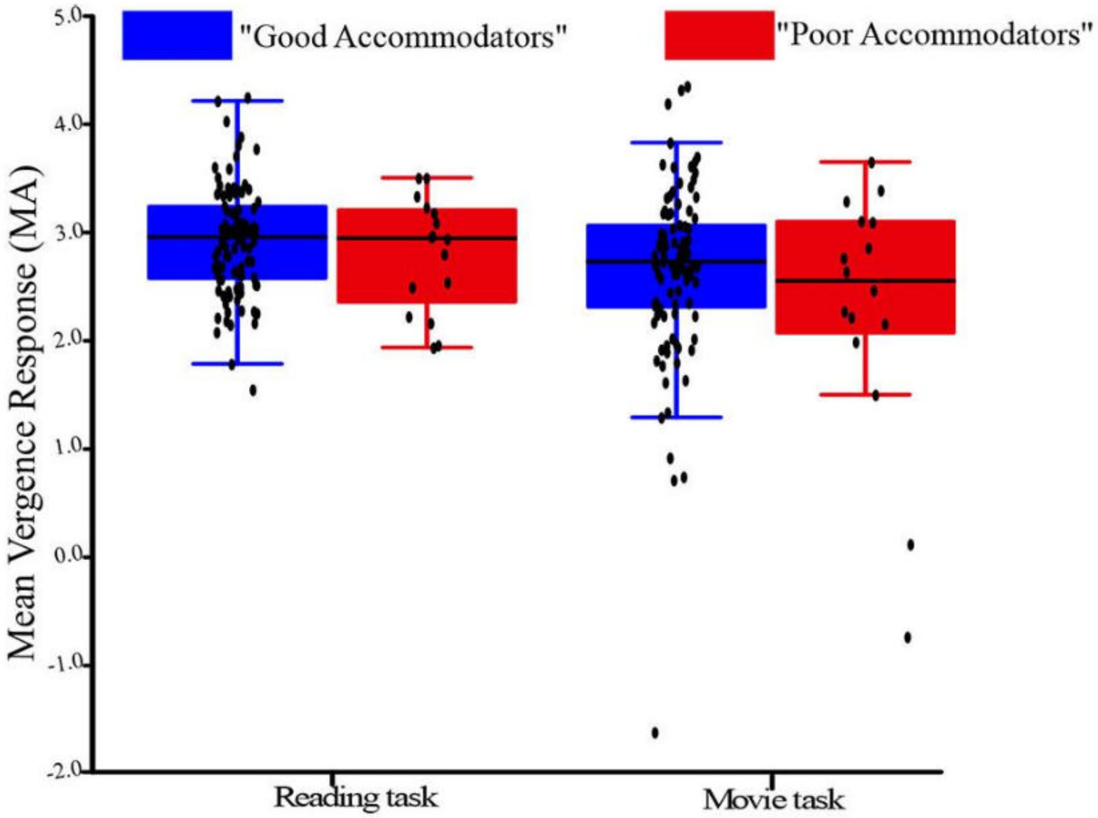


Figure 5.7.3. Boxplot of mean vergence response across the two tasks by accommodative accuracy (in the reading task). The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

5.7.1.2 Relationship between Accommodative-Vergence Responses and Total Accommodative Response

The accommodative and vergence responses (under closed-loop condition) were analysed as the ratio of the accommodative response (D) to the vergence response (MA) and termed AV fraction. There was a statistically significant relationship between the AV fraction and the total accommodative response in the reading task (r=0.35, p=0.0001), and a relationship which approached significance in the movie task (r=0.20, p=0.07). See Figures 5.7.4.

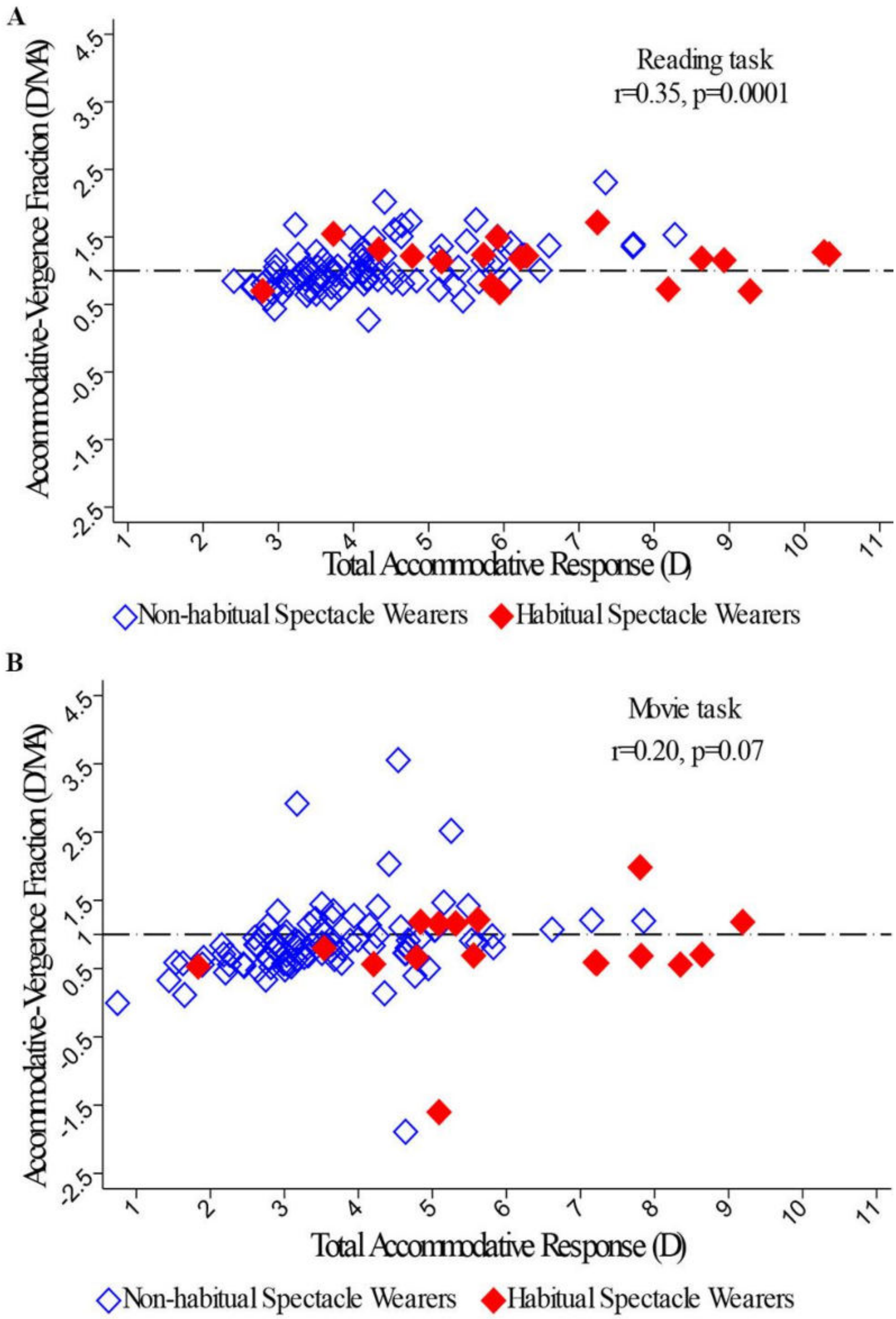


Figure 5.7.4 Scatterplots showing (A) Accommodative-vergence fraction with total accommodative response in the reading task, (B) Accommodative-vergence fraction with total accommodative response in movie task. Long dashed black lines in both panels represent equal

accommodative and vergence responses. In panel (A), effect of axis scaling reduced the trend of association.

In a two-way ANCOVA analysis (total accommodative response in each task as covariate, and refractive group and habitual refractive status as the other factors, with the AV fraction as the dependent variable), the following were observed: there was significant interaction between the total accommodative response and refractive group ($F_{(3,107)}$=2.93, p=0.04). Participants with uncorrected hyperopia greater than +4D who demonstrated higher accommodative response (total) also demonstrated better AV fractions (p=0.005) in the reading task (AV fraction was closer to 1). Similarly, participants who were habitual spectacle wearers had better AV fractions (p=0.002). However, in the movie task, there was no effect of refractive group or habitual spectacle wear on the AV fraction (p> 0.05) and no significant interaction between factors.

5.7.1.3 Effect of Anisometropia on Vergence Response

Across the two tasks, there was no effect of anisometropia on mean vergence response (Simple linear regression analysis: $F_{(1,113)}$=0.12, p=0.72, and $F_{(1,112)}$=0.30, p=0.58 for reading and movie tasks respectively).

5.7.2 Stability of the Vergence of Response

The stability of the vergence response was considered using the sample standard deviation of the average one-minute segments for the duration of the tasks. There was more instability in the vergence response during the movie task compared to the reading task (movie: 0.31±0.20; reading: 0.23±0.1; paired t-test: t=-3.81, p<0.001; Figure 5.7.5). This difference in stability between tasks was independent of the participant's refractive group ($F_{(3,105)}$=0.24, p=0.87), and habitual spectacle wear ($F_{(1,109)}$=1.62, p=0.21).

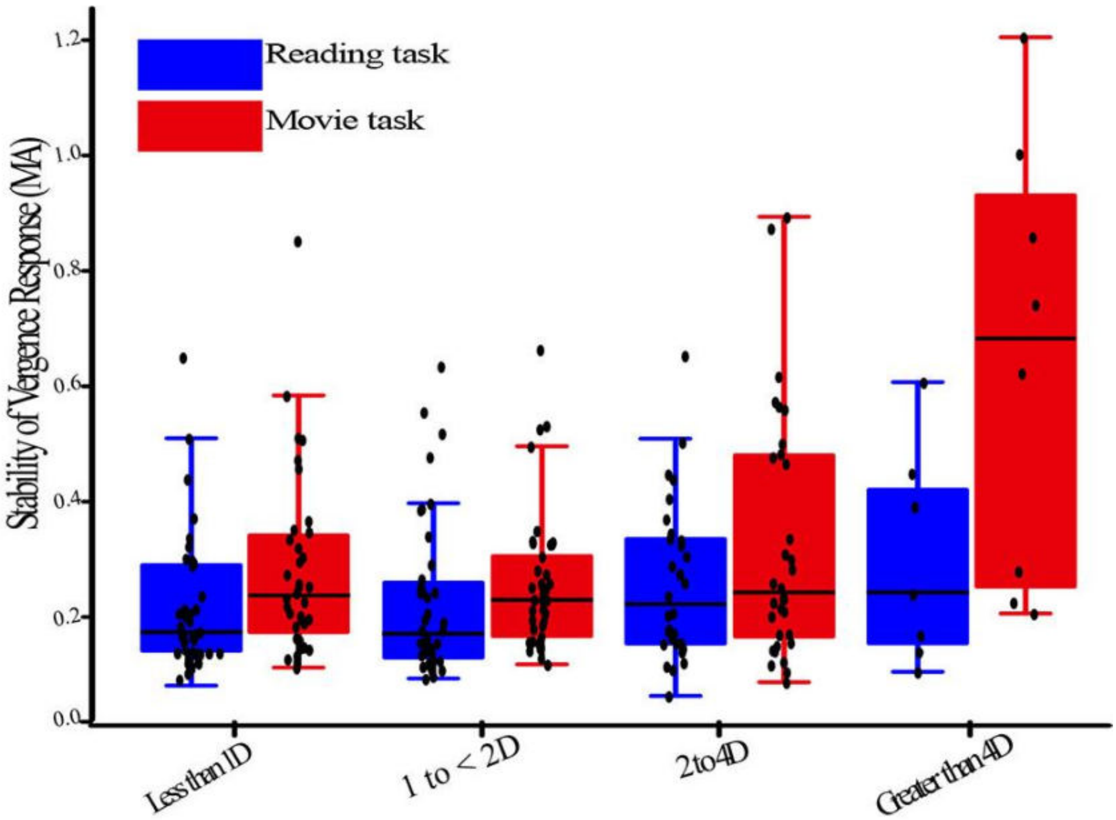


Figure 5.7.5 Box plot showing stability of response across the two tasks by refractive group. The solid horizontal line within the box indicates median value, lower and upper edges of the box indicate the 25th and 75th interquartile range (IQR) and lower and upper whiskers show the 1st and 99th quartiles. The black circles represent individual data points.

5.7.2.1 Relationship between Stability of Vergence Response and Refractive Error

In a univariate analysis using Pearson's correlation, there was a significant association between the stability of vergence response and refractive error (least plus spherical equivalent refraction) in the movie task (r=0.24, p=0.01), but the association failed to reach statistical significance at the 5% level in the reading task (r=0.17, p=0.07). (Figure 5.7.6).

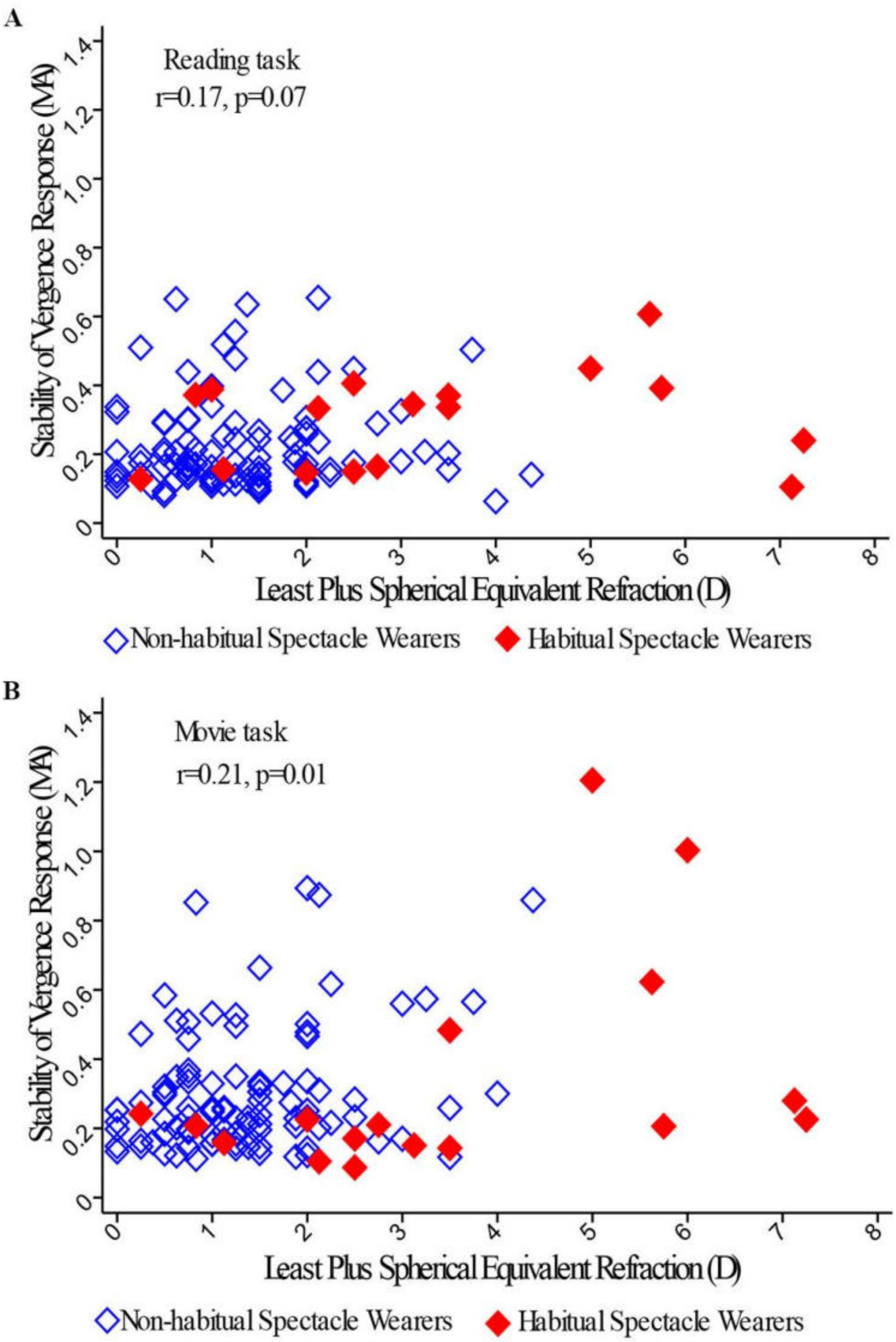


Figure 5.7.6. Scatterplots showing (A) Stability of vergence response with least plus spherical equivalent refraction in reading task (B) Stability of vergence response with least plus spherical equivalent refraction in movie task.

There was a positive correlation between the stability of vergence response and total accommodative response in both reading (r=0.19, p=0.04), and movie tasks (r=0.24, p=0.01) (Figure 5.7.7). There was no difference in vergence stability between “good” and “poor” accommodators in the two tasks (t=-0.60, p=0.55 and t=-0.39, p=0.70 for reading and movie tasks respectively).

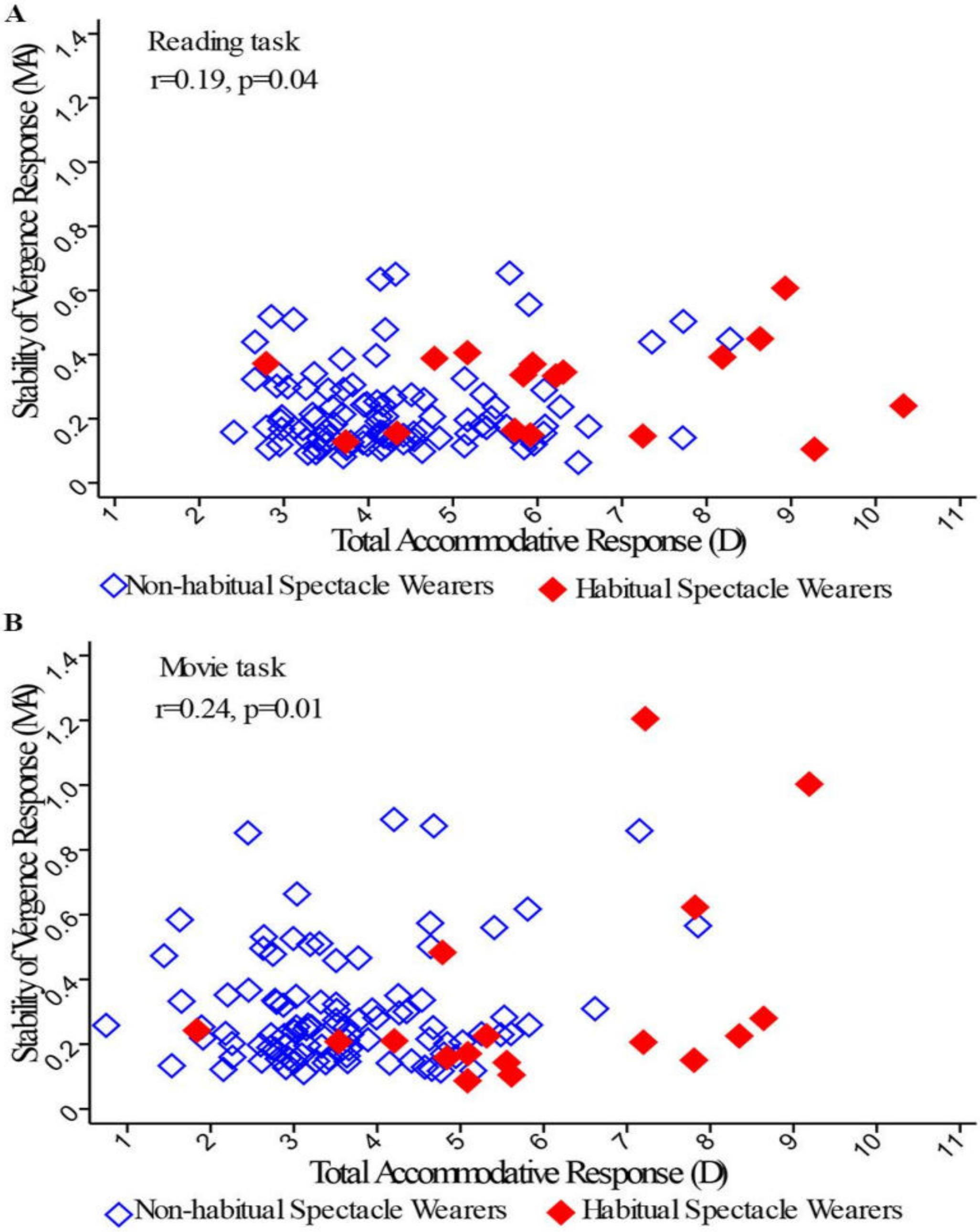


Figure 5.7.7 Scatter plots of (A) stability of vergence response and total accommodative response in the reading task, (B) stability of vergence response total accommodative response in movie task.

5.7.2.2 Relationship between Stability and Mean Vergence Response

Variability in the vergence response increased with increasing vergence response in the reading task (r=0.36, p=0.0001), but not in the movie task (r=0.07, p=0.44). See Figure 5.7.8.

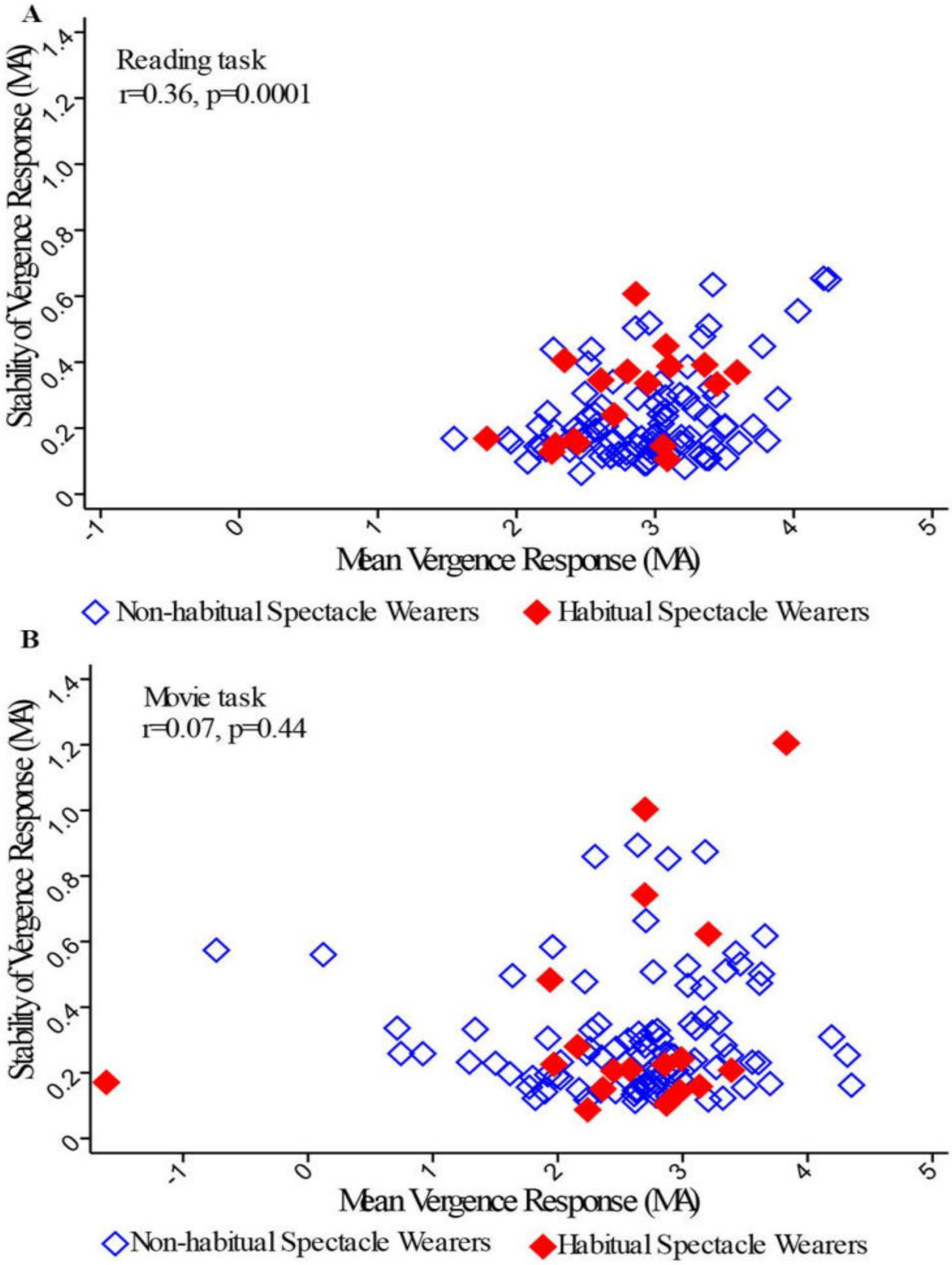


Figure 5.7.8 Scatter plots showing (A) stability of vergence response with mean vergence response in the reading task, (B) stability of vergence response with mean vergence response in movie task.

5.7.3 Discussion

There is a paucity of information regarding the characteristics of vergence responses of children with uncorrected hyperopia in the literature, and little or no data on sustained vergence responses at near. Results of the present study revealed that participants generally converged appropriately at 25 cm in the reading task compared to the movie task (Figure 5.7.2). The reading task, a more visually demanding task compared to the movie task, evoked higher vergence response, similar to the accommodative response demonstrated during this task, although the relationship between vergence response and accommodative response was weak and not significant in the reading the task. This weak and insignificant relationship between mean vergence response and mean accommodative response in the reading task was surprising, given the well-known synkinetic relationship between the two motor systems, whereby an increase in accommodation correspondingly results in increased vergence. Conversely, in the movie task, a positive association between the mean vergence response and the mean accommodative response was apparent. The mean vergence response in the movie task increased with increasing accommodation, and participants tended to converge more appropriately to the target at 25cm, despite underaccommodating in response to this target. Furthermore, the vergence response of participants classified as "good" and "poor" accommodators in the reading task did not differ significantly from each other. Horwood and Riddell (2011) have reported a similar finding; results of their study showed uncorrected hyperopic participants demonstrating better vergence response than accommodation, despite differences in their test target, testing distance, as well as test duration. Our data supports the theory that most individuals are more tolerant of blur than diplopia (Edgar 2007; Babinsky and Candy 2013), and that the vergence response is probably the more dominant of the two systems (Horwood and Riddell 2008). The findings in the present study also demonstrate that the two motor systems may have more flexible interactions than been previously thought. The superior vergence response in the movie task, compared with accommodation, also provides further assurance of the quality of the participants' engagement with the movie target, and suggests that the increased variability in the accommodative response found during the movie task is unlikely to be attributed to poor attention despite the relatively passive nature of the task.

Results of the present study also show that vergence responses were unaffected by refractive error in either the movie or reading tasks. Participants with uncorrected hyperopia demonstrated similar vergence responses compared with emmetropic controls in both tasks. Moreover, when the relationship between the vergence and accommodative response (under closed loop conditions) was considered (referred to as AV fraction in this study), the results show that participants with uncorrected hyperopia >+4D demonstrated the most appropriate relationship (ratio/fraction) in both task conditions. In theory, a 4D target demand should produce 4D of accommodation and 4MA of vergence response, such that a ratio of the two motor responses (under closed loop conditions) equates to unity. While greater accommodative efforts in higher amounts of uncorrected hyperopia, particularly in infants have been associated with excessive convergence leading to accommodative esotropia as a sequela (von Noorden and Avilla 1990; Mohney 2001; Somer *et al.* 2006; Rutstein 2008; Babinsky and Candy 2013), participants in the present study demonstrated flexible interaction between the two motor systems, particularly notable in those with high levels of uncorrected hyperopia who exerted the greatest amounts of accommodation in combination with appropriate vergence. The majority of these individuals demonstrating the most flexible accommodation/vergence relations were habitual spectacle wearers. Without undertaking a prospective evaluation of the accommodation and vergence responses of individual participants it is not possible to determine what role age, maturation of the visual system and spectacle correction has played in achieving this observed flexibility.

An aspect of the vergence response, which has received little or no attention in published studies, but which could be of research and clinical importance is the question of stability of the vergence response in children with and without uncorrected hyperopia. In the present study, there were more unstable responses in the vergence response in the movie task compared to the reading task. It is not clear what might account for this observed difference. Differences in target characteristics could perhaps account for the observation, as fixation target characteristics are reported to affect vergence eye movements (Thaler *et al.* 2013). Results of this study also revealed that instability in the vergence responsible was associated with increasing hyperopia across the two tasks and was significantly related to the magnitude of the total accommodative response, particularly in the reading task. Although no functional role or clinical significance has previously been reported for such instabilities in the vergence response, it is possible that they could have a role in the asthenopic symptoms associated with sustained reading in some uncorrected hyperopic individuals. This speculation is in light of the finding that when there is increased vergence response (which was associated with increased instability from results of the reading task), there is a tendency towards increased symptomatic experience of asthenopia (Collier and Rosenfield 2011).

5.7.4 Summary

The present study found the following:

- There was a higher vergence response in the reading task compared to the movie task.

- The accommodation-vergence interaction under a binocular viewing condition appears to be flexible, as participants converged well even where they demonstrated hypoaccommodation.
- No statistically significant associations were found between accuracy of vergence response and magnitude of uncorrected refractive error in either movie or reading tasks.
- The movie task elicited more unstable vergences responses than the reading task.
- Moreover, instability in the vergence response was associated with increasing hyperopia across both tasks, and significantly related to the magnitude of the total accommodative response.

5.8 Relationship between Sustained Near Task Measures and Baseline Visual Profile of Participants without Correction

5.8.1 Relationship between Sustained Accommodative Performance (uncorrected) and Participants' Visual Profile

Univariate analyses were undertaken to determine any association between sustained accommodative responses (using the reading task response) and the following baseline measures: amplitude of accommodation (both eyes), accommodative response by Nott retinoscopy at 25cm (4D), single and crowded letter acuity at 3m, near acuity at 40cm, and rate of reading score.

There was no significant association observed between binocular amplitude of accommodation and mean accommodative response in the reading task (r=-0.004, p=0.96, Figure 5.8.1). Moreover, there was no difference between the amplitude of accommodation of participants who were "good accommodators" and "poor accommodators" in the sustained reading task ('good': 13.61±3.41D 'poor': 13.46±4.91D; t=0.15, p=0.88).

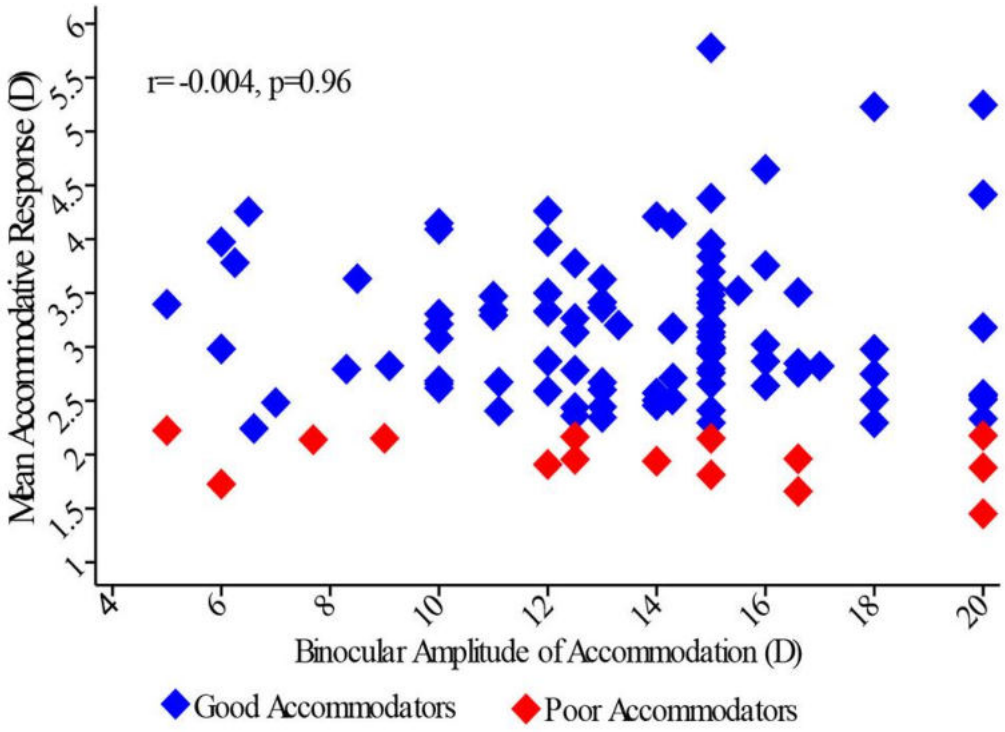


Figure 5.8.1 Scatter plot of mean sustained accommodative response in reading task with binocular amplitude of accommodation.

There was no statistically significant association between mean accommodative response during the reading task and accommodative response by Nott retinoscopy (Spearman's rho=0.10, p=0.28, Figure 5.8.2). 'Good' and 'poor accommodators' in the sustained reading task did not differ significantly in their accommodative response measure by Nott retinoscopy (Mann-Whitney test: z=2.46, p=0.69).

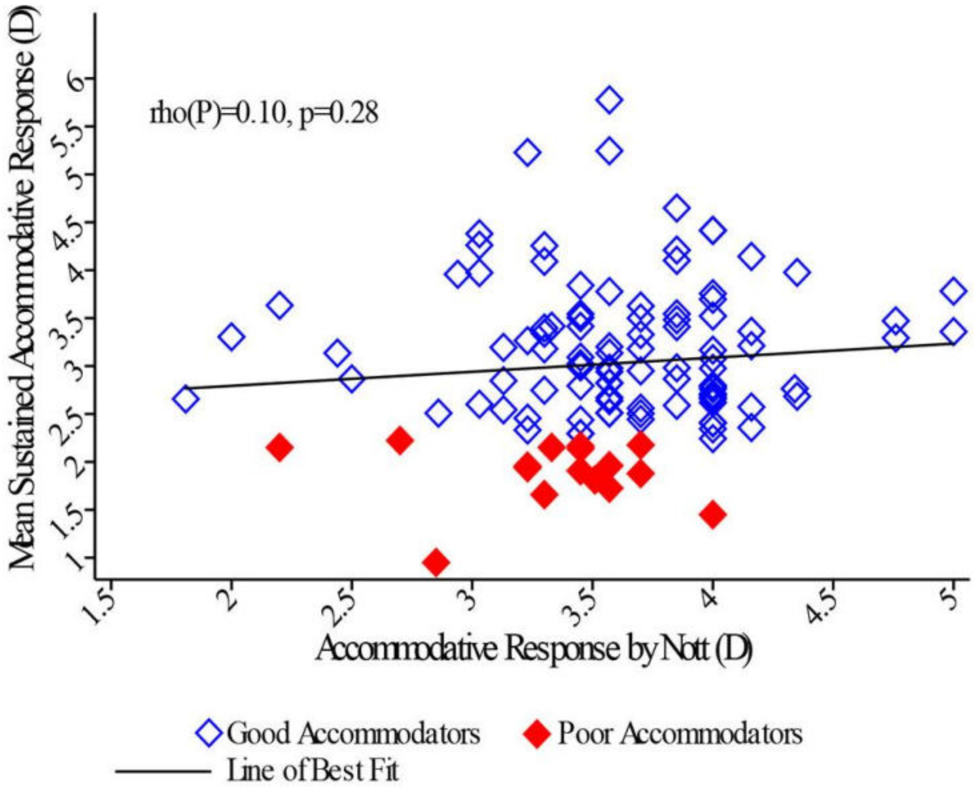


Figure 5.8.2 Scatter plot of mean sustained accommodative response in reading task with accommodative response by Nott retinoscopy.

There were no statistically significant associations between mean accommodative response during the reading task and the following baseline visual measures: single letter acuity (Spearman's rho=0.05, p=0.59), crowded letter acuity (Spearman's rho=0.17, p=0.07), and near acuity (Spearman's rho=-0.01, p=0.91). However, there was a negative relationship between mean accommodative response during the sustained reading task and rate of reading score (r=-0.21, p=0.04, Figure 5.8.3). When the total amount of accommodation exerted during the sustained reading task was compared with the rate of reading score, failed to reach statistical significance (r=-0.20, p=0.06). Similarly, there was no statistically significant difference found between ‘good’ and ‘poor accommodators’ in the sustained reading task and rate of reading score (‘good’: 85.81±23 words/minute ‘poor’ 84.79±28.20 words/minute; t=0.15, p=0.88).

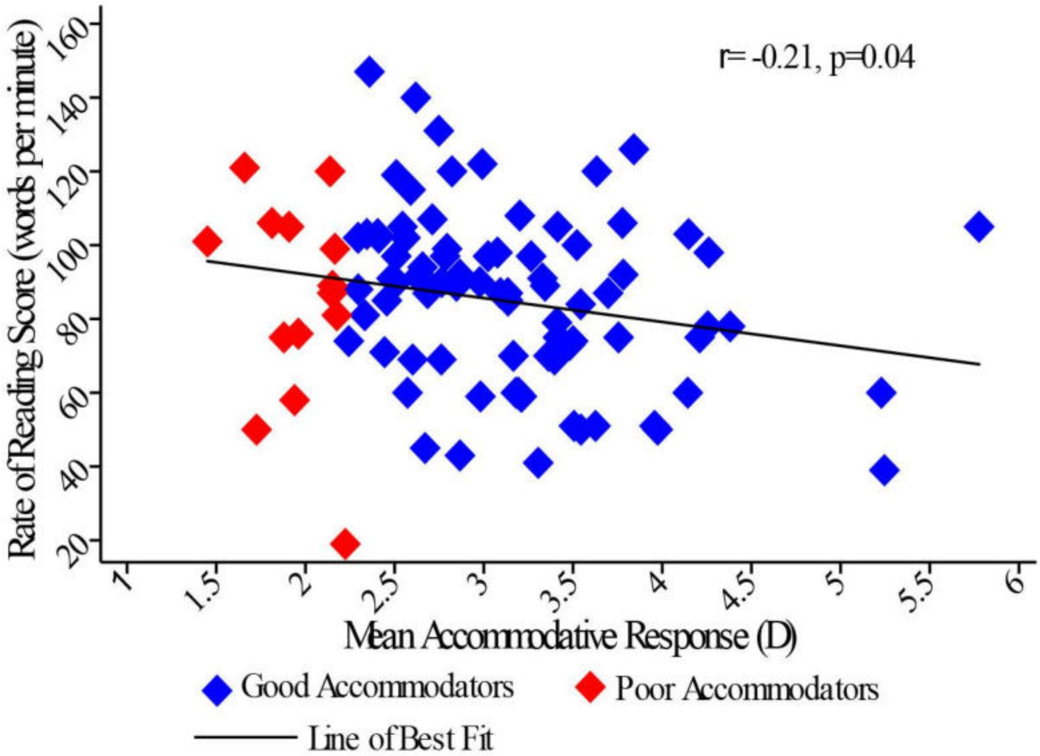


Figure 5.8.3 Scatterplot of rate of reading score with mean accommodative response during the sustained reading task.

There was no statistically significant association between accommodative variability (in both time and frequency domains) and rate of reading score (r=-0.02, p=0.83, and r=-0.17, p=0.10 for time (RMS) and frequency domains (LFC) respectively).

5.8.2 Relationship between Sustained Vergence Performance (uncorrected) and Participants' Visual Profile

Univariate analyses to determine any association between sustained vergence responses (using the reading task response) and the following baseline measures: NPC and rate of reading score were examined.

There was a statistically significant positive association between the mean vergence response in the sustained reading task and the rate of reading score (Spearman's rho=0.21, p=0.04, Figure 5.8.4). Moreover, a negative association (borderline significance) was observed between the stability of the vergence response in the sustained reading task and the rate of reading score (Spearman's rho=-0.19, p=0.05). These relationships lost significance once refractive error was adjusted for, (accuracy: $F_{(1,89)}$=2.29, p=0.14; stability: $F_{(1,88)}$=3.26, p=0.07).

There was no statistically significant relationship between the NPC and participants' mean vergence performance during the sustained reading (Spearman's rho=0.02, p=0.81) and movie tasks (Spearman's rho=0.08, p=0.38).

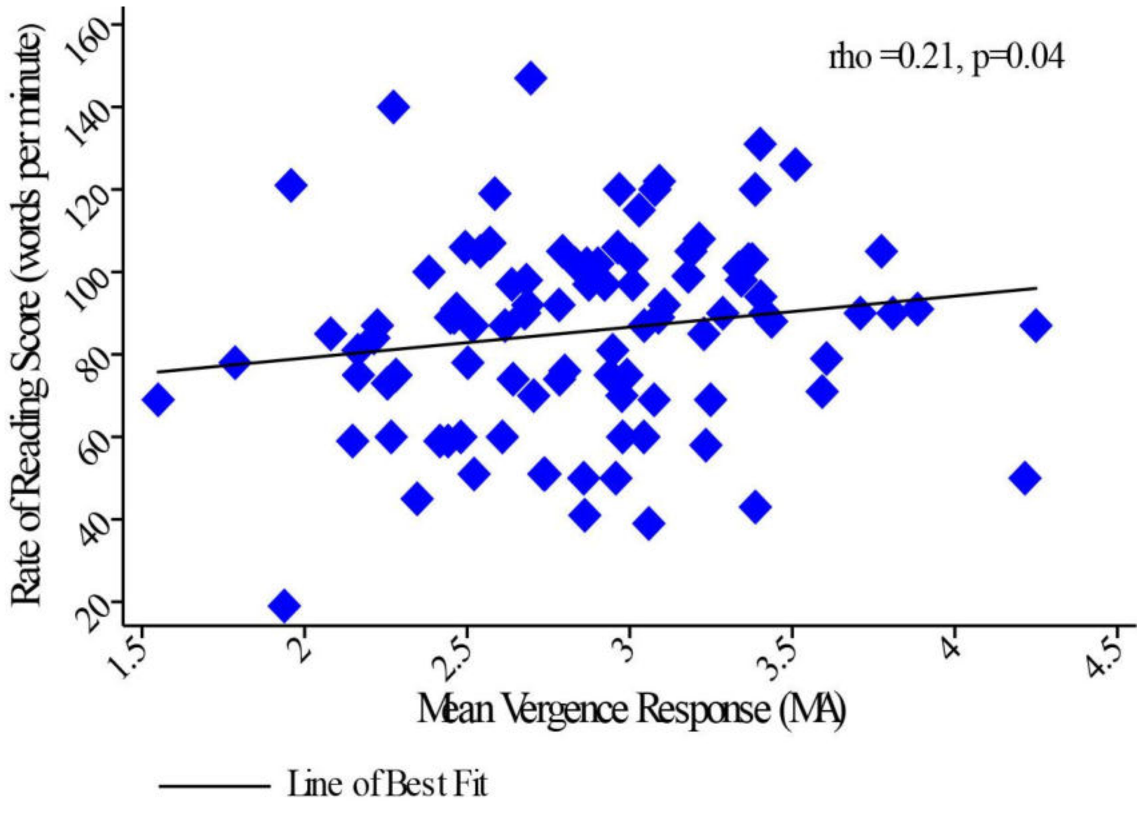


Figure 5.8.4 Scatter plot of the rate of reading score with mean vergence response during the sustained reading task.

5.8.3 Discussion

The present study explored potential relationships between the visual profile characteristics of participants and how they relate to participants' performance during the sustained near tasks. Generally, there were no statistically significant associations between most of the baseline visual profile measures and the sustained near task measures, except in relation to the rate of reading score. A previous study reported that spectacles may improve reading speed in hyperopia (van Rijn *et al.* 2014). However, it is not clear which visual factors spectacle correction may impact on, and how these might also influence the rate of reading. In the present study, the mean accommodative response during sustained reading was negatively associated with the rate of reading score. This result seems counterintuitive, as it would be expected that individuals with poorer accommodative responses would have a lower rate of reading performance, as they are likely to experience more blur during the rate of reading task (Jainta *et al.* 2011). However, rather than a negative association between accommodative response and rate of reading, perhaps the results of the present study more correctly support the notion that accuracy of accommodation has little influence on reading speed/fluency. Our data demonstrate no significant relationship between the total accommodative response produced during the sustained reading task and the rate of reading and no difference between the rate of reading score of "good accommodators versus "poor accommodators" as defined by the sustained reading task. A previous study reported that reading speed was constant (unaffected) in the presence of blur up to 3D when the print size of the reading material is large enough (Chung *et al.* 2007). The letters in the Wilkins rate of reading test compares well with the "N8" Near acuity chart, which is relatively large and may limit the impact of blur in our young participants. On the other hand, the vergence response during sustained reading, in terms of both accuracy and stability, was shown to positively correlate with the rate of reading score. The design of passages in the Wilkins rate of reading test, which can cause “apparent movement of words and letters” would seem to require more accurate vergence response than accommodation based on the results of this study. Similarly, those with unstable vergence responses during the sustained reading task tended to record lower rate of reading score, although this association became statistically insignificant when refractive error was considered.

5.8.4 Summary

- There were no statistically significant associations between the sustained accommodative response and several baseline visual measures of participants including the amplitude of accommodation, the accommodative response by Nott retinoscopy, distance and near VA.
- A negative association was observed between sustained accommodative response and rate of reading score, but this association was not present when total accommodative response was considered.
- More accurate and stable vergence responses during sustained reading were associated with better rate of reading scores.

5.8.5 Chapter Discussion

In the present study, sustained accommodative and vergence responses were tested while children engaged in two tasks – reading on a kindle and watching a movie for approximately 15 minutes. Children frequently engage in these tasks at school and in the home. Therefore, investigating the accommodative and vergence responses while children undertook these tasks during a prolonged period reflects "real-life" use of the vergence and accommodation systems. This is the second study to measure sustained accommodative and vergence functions in children with hyperopia using the eccentric, infrared photorefraction technique, the other study being the recent work of Roberts *et al.* (2018a). However, the present study has several strengths in comparison to the work of Roberts *et al.* (2018a), having a larger sample size (n=137 in this study versus n=54 in Roberts *et al.* (2018a)), and capturing and comparing performance during both "active" and "passive" tasks. Nonetheless, the results of this study are largely in agreement with Roberts *et al*. (2018a); both studies agreeing that mean accommodative responses from uncorrected hyperopes and emmetropes do not differ significantly. The present study provides further insight into the vergence response of uncorrected hyperopes, revealing that participants' vergence responses were generally appropriate even where accommodative response was "poor" and that instability in vergence response was associated with increased uncorrected hyperopia. Investigating the relationships which exist between a participant's baseline visual data and their sustained accommodative and vergence performance also served to enhance understanding of how these visual function measures, routinely measured in the clinic, affect the two oculomotor functions in uncorrected hyperopia.

A few inherent limitations present in this study have been discussed previously in chapter 3, including possible *order effect* due to lack of randomisation of tasks, and unstable fixation due to head movement of, particularly young participants. However, results of the present study show that there were no *order effects* on how tasks were introduced, which should allay concerns about lack of randomisation. Moreover, results of vergence responses reveal that children generally attended well to the targets, so that effects of micro head movements on the results, particularly in younger children, are likely to be negligible.

There may be concern about the lack of cycloplegic calibration of hyperopic subjects at near distance of 25cm. This presents a limitation to the lens calibration results. However, if the assumption of consensuality in accommodation is considered, then the effect of lack of cycloplegia would be minimal as any induced accommodation at the 25cm distance would have similar effect in both eyes. Also, the use of the pooled mean in participants without lens calibration slopes also presents a limitation to the study results, given the inter-subject variability in slope values previously reported.

5.8.6 Chapter Summary

- **Results of this study show that mean accommodative responses from uncorrected hyperopes and emmetropes did not differ significantly during sustained near vision tasks.**
- **There was a positive effect of habitual spectacle wear on the accommodative response achieved without correction.**
- **More variability in accommodative response (microfluctuations) was associated with higher levels of uncorrected hyperopia >+4D.**
- **The accommodation-vergence interaction under a binocular viewing condition appears to be flexible, as participants converged appropriately whilst producing a variety of total accommodative responses.**

- **Unstable vergence responses were associated with increasing hyperopia across both tasks.**

Chapter 6: Effect of Spectacle Correction on Sustained Accommodative and Vergence Functions in Children with Hyperopia

6.1 Introduction

In the previous chapter (chapter 5), results and discussion of sustained accommodative and vergence response in children with and without hyperopia were addressed. The present chapter presents results and discussions of the effect of spectacle correction on accommodative and vergence functions when hyperopic participants were corrected with spectacles while engaged in sustained reading and movie tasks. Habitual spectacle wearers wore their habitual prescription while uncorrected participants were given temporary correction (full correction). Results of the effect of spectacle correction on rate of reading score, as well as the effect of simulated hyperopia on accommodative and vergence responses in emmetropic controls are also presented and discussed. This chapter is thus organised in the following framework:

- Brief synopsis of data analysis procedures
- Presentation and discussion of results in terms of:
    - Effect of spectacle correction on sustained accommodative functions
    - Effect of spectacle correction on sustained vergence functions
    - Effect of spectacle correction on rate of reading score
    - Effect of simulated hyperopia on sustained accommodative and vergence functions in emmetropic controls
- Chapter discussion

6.2 Brief synopsis of data analysis procedures

Measures of sustained accommodative and vergence responses without correction were obtained in 80 hyperopic participants aged 5-10 years (chapter 5). Repeated measurement of these functions with spectacle correction was obtained in 78 of these participants in the reading task, and 75 in the movie task. Refractive group in the present analysis consists of hyperopes (1.00D to less than 2.00D- low hyperopes; 2.00D to 4.00D- moderate hyperopes, and greater than 4D- high hyperopes). In the reading task, two participants were uncooperative during testing, while five participants were uncooperative in the movie task. Three participants did not return for repeated testing in the movie task. There was thus 98% and 94% success rates of testing with spectacle correction for the reading and movie tasks respectively.

Several statistical approaches to analyse the effect of an intervention in a pre-and post-treatment design were reviewed. These include the use of the paired t-test for the pre- and post-treatment measures (Day *et al.* 2008); one-way analysis of variance (ANOVA) of the difference between the pre-and post-treatments across the groups (where there are more than two groups) (Cregg *et al.* 2001); repeated measures ANOVA (Roch-Levecq *et al.* 2008; Vedamurthy *et al.* 2009; Berntsen *et al.* 2010); and analysis of covariance (ANCOVA) with the post-treatment measure as the dependent variable and the pre-treatment measure as a covariate (van Rijn *et al.* 2014; Harvey *et al.* 2016). In the present study, ANCOVA was used to examine the effect of spectacle correction on various measures because it does not only compute the difference between pre-and post-treatment measures but also allows for several confounding variables to this difference (or change) to be accounted for (Dimitrov and Rumrill 2003).

6.2.1 Descriptive Statistics of Accommodative, Vergence and Rate of Reading Measures with Spectacle Correction

Table 6.1 provides a comparison of the means of the various measures with and without spectacle correction.

Table 6.1 A summary of mean (±SD) of accommodative, vergence and rate of reading measures by refractive group.

Variable	Mean±SD, (min, max) Without correction	Mean±SD, (min, max) With correction
Mean Accommodative Response		
Reading task		
Overall (n=78)	3.07±0.88 D (0.95, 5.78)	2.78±0.99 D (1.46, 6.33)
Low Hyperopes (n=39)	2.91±0.74 D (1.45, 4.65)	2.63±0.84 D (1.56, 5.04)
Moderate Hyperopes (n=31)	3.21±1.04 D (0.95, 5.78)	2.92±1.18 D (0.85, 4.63)
High Hyperopes (n=8)	3.34±0.76 D (2.15, 4.26)	3.02±0.83 D (1.91, 4.40)
Movie task		
Overall (n=75)	2.35±0.86 D (0.15, 4.68)	2.40±0.99 D (0.83, 5.62)
Low Hyperopes (n=38)	2.27±0.77 D (0.15, 4.09)	2.21±0.88 D (0.85, 4.63)
Moderate Hyperopes (n=29)	2.49±0.98 D (0.35, 4.68)	2.63±1.17 D (0.83, 5.62)
High Hyperopes (n=8)	2.18±0.78 D (1.10, 3.19)	2.43±0.62 D (1.64, 3.64)
Stability of Accommodation (RMSE)		
Reading task		
Overall (n=78)	0.34±0.17 D (0.12, 0.99)	0.43±0.21 D (0.11, 1.00)
Low Hyperopes (n=39)	0.32±0.14 D (0.12, 0.68)	0.39±0.19 D (0.11, 0.94)
Moderate Hyperopes (n=31)	0.36±0.20 D (0.15, 0.99)	0.48±0.23 D (0.11, 1.00)
High Hyperopes (n=8)	0.35±0.17 D (0.15, 0.66)	0.44±0.18 D (0.25, 0.81)
Movie task		
Overall (n=75)	0.49±0.27 D (0.15, 1.42)	0.41±0.14 D (0.18, 0.90)
Low Hyperopes (n=38)	0.45±0.25 D (0.19, 1.26)	0.36±0.14 D (0.18, 0.80)
Moderate Hyperopes (n=29)	0.49±0.28 D (0.15, 1.42)	0.46±0.14 D (0.23, 0.90)
High Hyperopes (n=8)	0.68±0.37 D (0.25, 1.31)	0.46±0.14 D (0.26, 0.66)
Mean Vergence Response		
Reading task		
Overall (n=78)	2.93±0.48 MA (1.79, 4.21)	2.81±1.30 MA (-1.41, 6.81)
Low Hyperopes (n=39)	2.86±0.46 MA (2.08, 4.03)	2.60±1.15 MA (-1.41, 6.38)
Moderate Hyperopes (n=31)	3.05±0.49 MA (2.27, 4.22)	3.09±1.46 MA (--0.05, 6.81)
High Hyperopes (n=8)	2.84±0.53 MA (1.79, 3.36)	2.69±1.26 MA (-0.22, 4.05)
Movie task		
Overall (n=75)	2.57±0.67 MA (-1.61, 4.35)	3.06±1.12 MA (-1.60, 5.80)
Low Hyperopes (n=38)	2.59±0.66 MA (0.74, 3.70)	2.86±0.91 MA (0.83, 5.80)
Moderate Hyperopes (n=29)	2.52±1.32 MA (-1.61, 4.35)	3.18±1.38 MA (-1.60, 4.89)
High Hyperopes (n=8)	2.66±0.61 MA (1.97, 3.83)	3.61±0.66 MA (2.63, 4.37)
Stability of Vergence Response		
Reading task		
Overall (n=78)	0.25±0.14 MA (0.06, 0.65)	0.73±0.44 MA (0.15, 1.94)
Low Hyperopes (n=39)	0.23±0.14 MA (0.09, 0.64)	0.73±0.42 MA (0.16, 1.78)
Moderate Hyperopes (n=31)	0.26±0.13 MA (0.06, 0.65)	0.72±0.48 MA (0.15, 1.94)
High Hyperopes (n=8)	0.30±0.19 MA (0.11, 0.61)	0.75±0.40 MA (0.26, 1.19)
Movie task		

Overall (n=75) *Low Hyperopes (n=38)* *Moderate Hyperopes (n=29)* *High Hyperopes (n=8)*	0.33±0.23 MA (0.09, 1.21) 0.26±0.12 MA (0.12, 0.66) 0.33±0.21 MA (0.09, 0.89) 0.64±0.38 MA (0.21, 1.21)	0.58±0.35 MA (0.16, 1.79) 0.56±0.25 MA (0.18, 1.23) 0.60±0.45 MA (0.16, 1.79) 0.66±0.38 MA (0.24, 1.33)
Rate of Reading *Overall (n=65)* *Low Hyperopes (n=32)* *Moderate Hyperopes (n=261)* *High Hyperopes (n=7)*	 84.88±23.30 (39, 147) 88.84±21.39 (50, 147) 80.16±25.33 (39, 126) 83.57±24.57 (41, 120)	 87.74±24.05, (30, 143) 91.84±21.82, (48, 143) 81.85±24.45, (30, 132) 90.86±31.13, (40, 132)

Negative vergence value represents divergence. RMSE (Root mean square error of accommodation – time domain analysis).

6.3 Effect of spectacle correction on sustained accommodative functions

6.3.1 What is the effect of spectacle correction on the accommodative response of hyperopes during sustained reading and movie tasks?

This question was answered in terms of the mean difference in the response of the two measures (with glasses and without glasses) across the two tasks. In the present study, effect of spectacle correction was considered with reference to the accuracy of the response. For example, if the mean accommodative response without correction was a lead/excess (e.g. 1.00D), a reduction in the response with correction was considered positive or beneficial, and where there was a lag in the response, an improvement in response with correction was also considered beneficial. Outlined below is classification of the effect of spectacle correction (mean difference/ gain) on the accommodative response:

(i) "Better" response if it either decreased the amount of lag or lead by >0.25D.

(ii) "worse" response if it either increased the amount of lag or lead by >0.25D

(iii) "No effect" if the mean difference between pre-and with-treatment was less than 0.25D.

A 0.25D cut-off for a significant change was chosen based on its use during subjective clinical refraction to determine the spherical endpoint in techniques such as Duochrome test, Plus/Minus spherical refinement, and binocular balancing. A categorical variable termed treatment effect (better, worse and no effect) was used as one of the factors during ANCOVA (the dependent variable being the mean response with correction), together with other factors such as order effect and refractive group (hyperopia/emmetropia) to examine the effect of spectacle correction on the accommodative response. A binary variable to indicate whether participant wore their habitual correction, or the temporary experimental correction (full correction) was used to assess the influence of these two correction types on the results.

Across the two tasks, there was no effect with order of task performance on the outcome of measures [($F_{(1,74)}$ = 0.21, p =0.65) and $F_{(1,70)}$ =0.01, p=0.65) for reading and movie tasks respectively]. Table 6.1 provides a comparison of the means of the various measures with and without spectacle correction.

In a two-way ANOVA to assess the effect of spectacle correction on accommodation during the reading task (two factors: treatment effect (no effect as reference), and refractive group), there was no significant interaction between the two factors ($F_{(4,68)}$= 0.28, p=0.80). "Better" accommodative response was associated with spectacle correction, *post-hoc* comparison (p=0.02), which was independent of refractive group of participant ($F_{(2,68)}$ =0.55, p=0.58). Similarly, in the movie task, there was no significant interaction between factors, ($F_{(4,65)}$=0.53, p=0.71) and "better" accommodative response was independently associated with spectacle wear in participants, *post-hoc* comparison (p=0.032). See also Figure 6.3.1. This was again independent of the refractive group of participants ($F_{(2,65)}$ =1.54, p=0.22). These results were independent of spectacle correction type worn by participants (whether participant's own correction or temporary experimental correction: $F_{(1,71)}$=1.15, p=0.29).

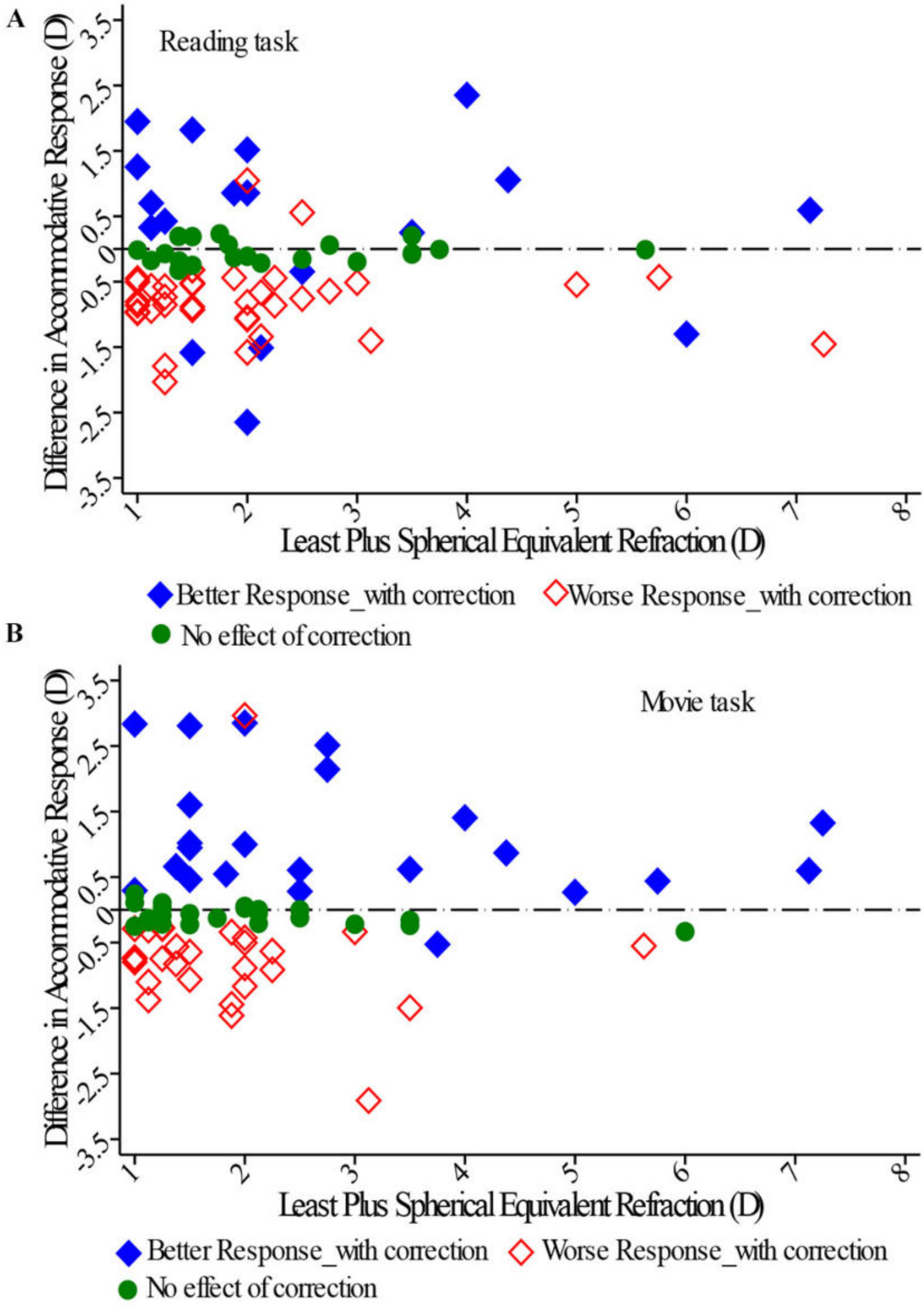


Figure 6.3.1 Scatter plots showing (A) difference in mean accommodative response with least plus spherical equivalent refraction in the reading task, (B) difference in mean accommodative response with least plus spherical equivalent refraction in the movie task. The "Difference in Response" represents (with correction – without correction). Long dashed line represents no difference in mean response with and without correction. "Difference in response" was not statistically significantly related to the amount of spherical equivalent refraction, in the reading task (Linear regression, $F_{(1,75)} = 0.20$, $p=0.66$) and movie task ($F_{(1,72)} = 0.75$, $p=0.39$). It is worth

mentioning that individual points on the graph (which represents the response with and without correction) is quite different from the mean (SD) of group data presented in Table 6.1.

Although spectacle correction improved mean accommodative response in participants who were classified as "poor accommodators" in the reading task when they were tested uncorrected (chapter 5) this was not statistically significant (2.00±0.42D vs 1.85±0.37D; t=1.19, p=0.26). See also Figure 6.3.2. To explore any underlying differences between "positive" responders with correction versus "negative" responders (worse or no effect with spectacle correction), one-way ANOVA was used to assess differences in key visual function measures such as binocular amplitude of accommodation, accommodative response by Nott retinoscopy, crowded letters VA, and stereoacuity. However, there were no statistically significant differences between "positive" responders and "negative" responders in these visual functions: [$F_{(2,71)}$=0.62, p=0.54 for binocular amplitude of accommodation; $F_{(2,72)}$=0.05, p=0.95 for NPC; $F_{(2,72)}$=1.70, p=0.19 for accommodative response by Nott retinoscopy; $F_{(2,74)}$=1.27, p=0.29 for crowded LogMAR letters; $F_{(2,74)}$=1.62, p=0.20, for near VA; and $F_{(2,73)}$=0.21, p=0.82 for stereoacuity].

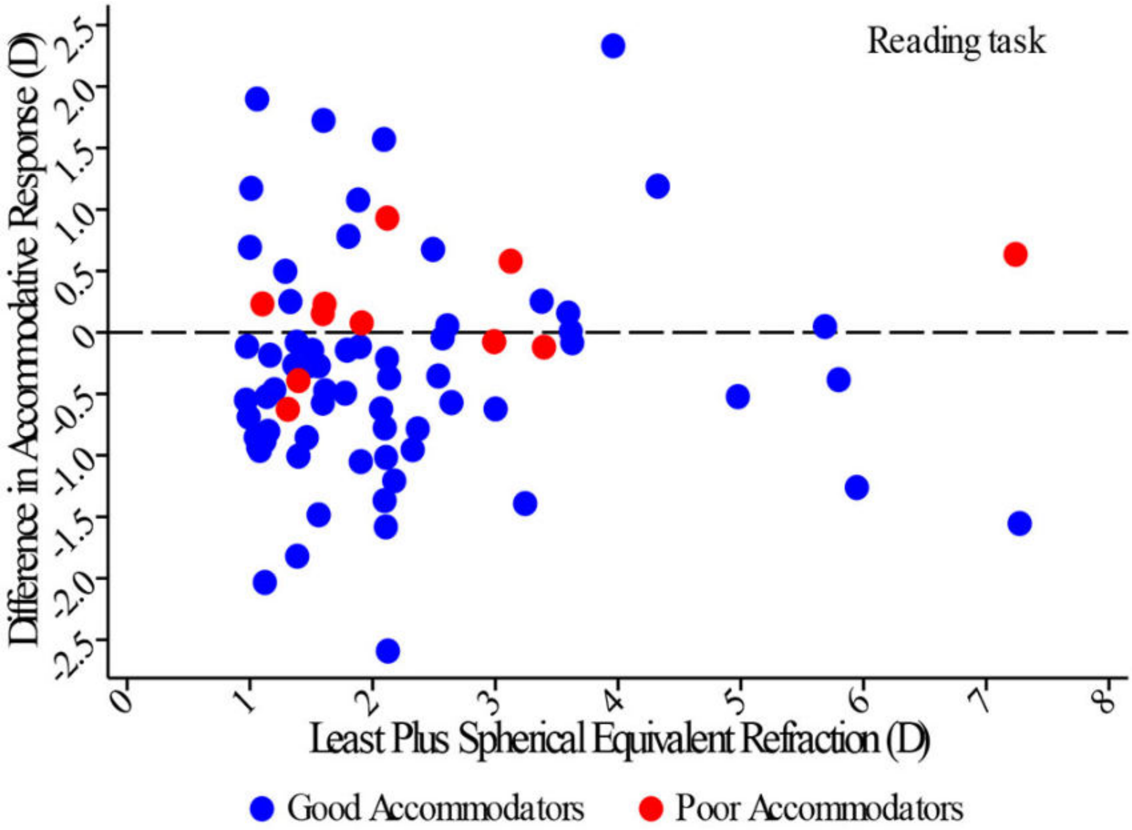


Figure 6.3.2. Scatter plot showing difference in mean accommodative response with least plus spherical equivalent refraction in the reading task, colour coded according to whether participant was a good or poor accommodator in the reading task when tested without correction (Chapter 5). The "Difference in Response" represents (with correction – without correction). Long dashed line represents no difference in mean response with and without correction.

6.3.2 What happens to the stability of accommodative response with spectacle correction during sustained reading and movie tasks?

Variability in the accommodative response with spectacle correction was assessed using time domain analysis (RMS). In a two-way ANCOVA analysis of the effect of correction on accommodation in the reading task (using variability with correction as dependent variable, variability without correction as covariate, and refractive group as the other factor), there was no significant interaction found between the covariate and factor ($F_{(2,72)}$=0.29, p=0.75), but there was more variability with correction, than without correction ($F_{(1,72)}$ = 9.42, p=0.003), which was independent of the refractive group of participant ($F_{(2,72)}$ = 0.25, p=0.78). See also Figure 6.3.3 (panel A). In the movie task, there was no significant interaction between factors, (F (2,68) = 0.09, p=0.92) and there was no effect of spectacle correction on the stability of the accommodative response ($F_{(1,68)}$ = 0.40, p=0.53). See also Figure 6.3.3 (panel B).

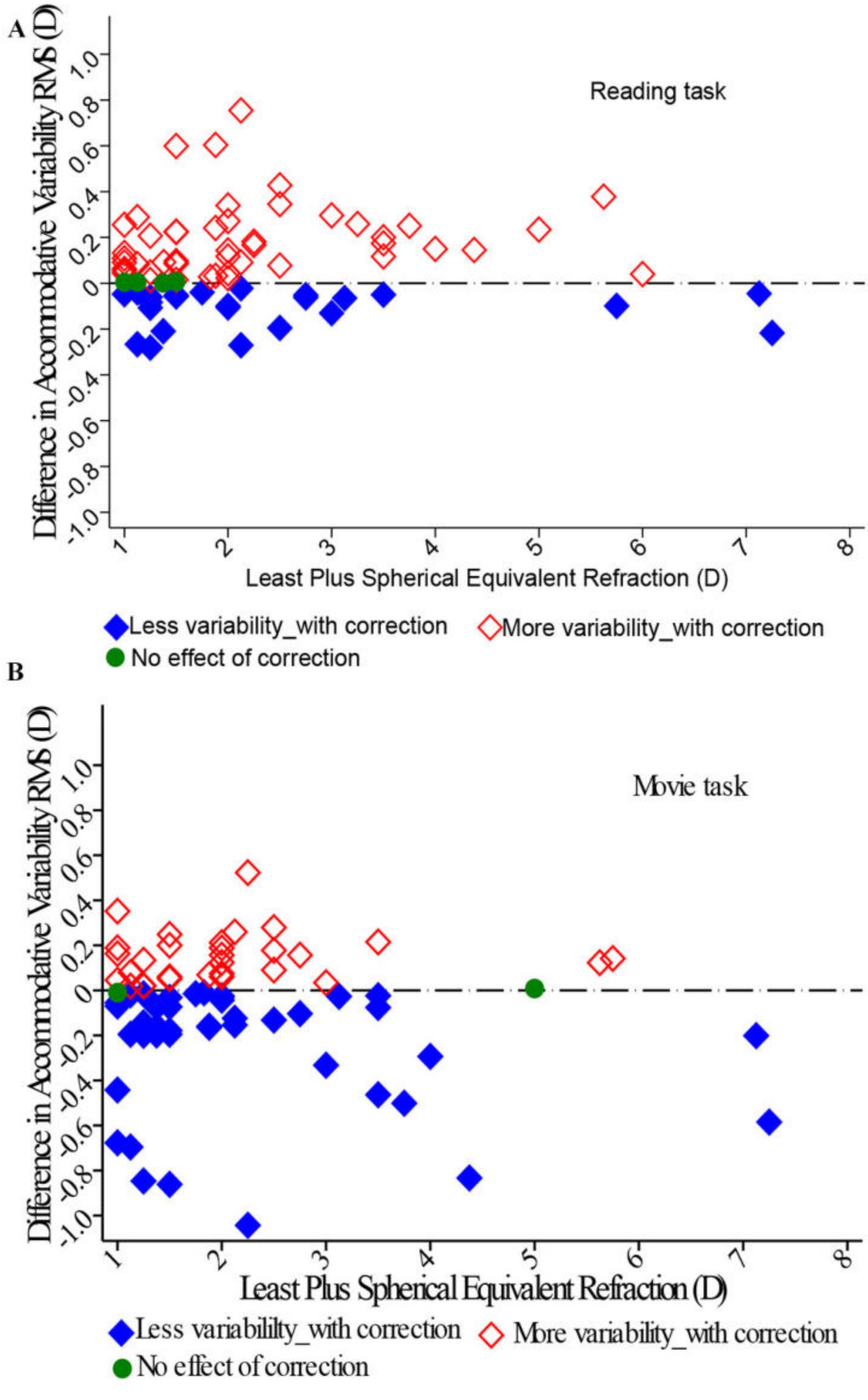


Figure 6.3.3 Scatterplots showing (A) difference in variability of accommodative response (RMS) with least plus spherical equivalent refraction in reading task, (B) difference in variability of accommodative response (RMS) with least plus spherical equivalent refraction in movie task. Difference in variability represents (RMS value with correction – RMS value without correction). Long dashed black line represents no difference in variability with and without correction.

Across the two tasks, there were statistically significant associations between accommodative variability with correction and accommodative response with correction, being stronger for the reading task compared to the movie task (r=0.40, p=0.0003, and r=0.25, p=0.033 for reading and movie tasks respectively). See also Figure 6.3.4.

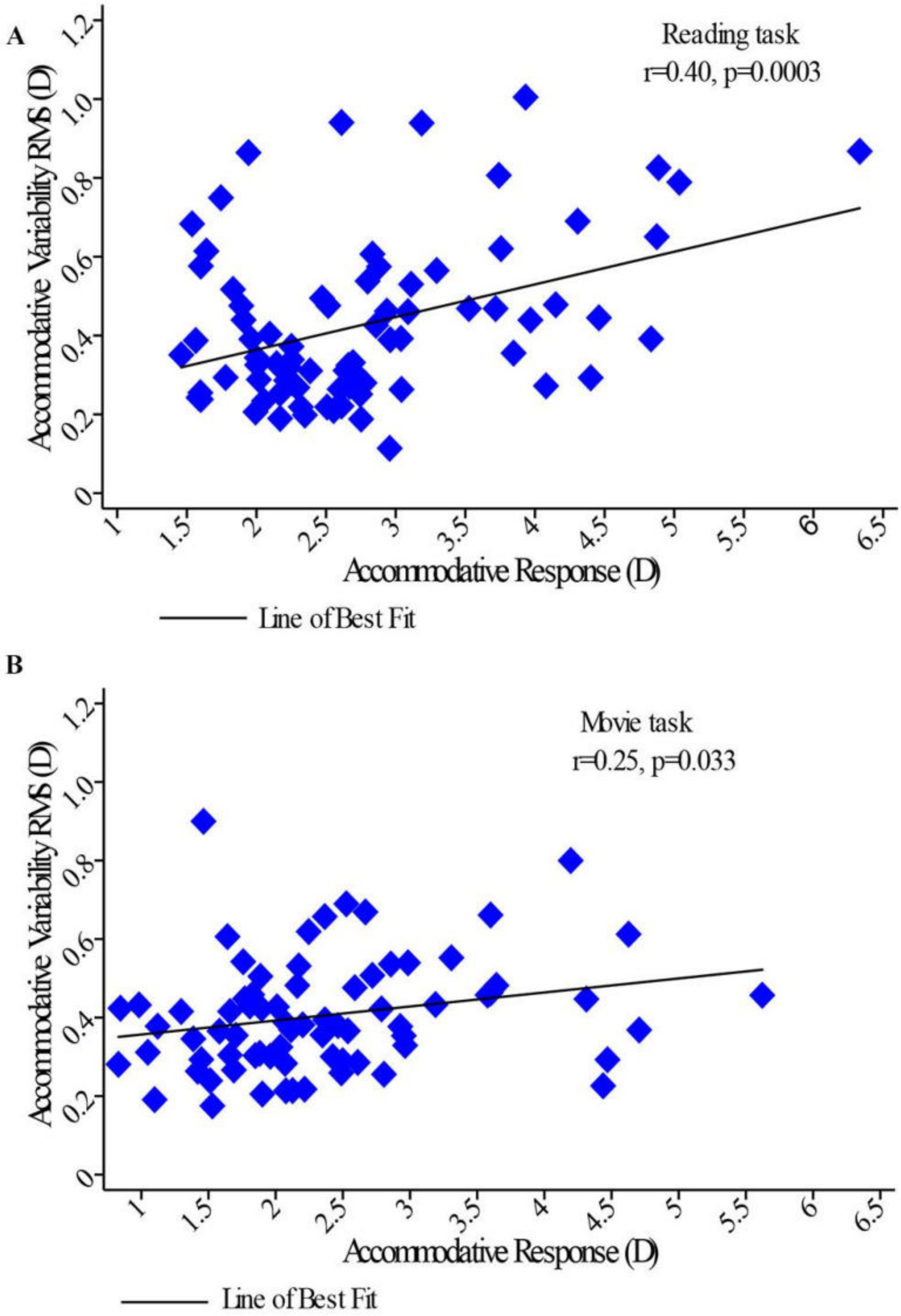


Figure 6.3.4 Scatterplots showing (A) accommodative variability with spectacle correction and mean accommodative response during reading task, (B) accommodative variability with spectacle correction and mean accommodative response during movie task.

6.3.3 Discussion of influence of spectacle correction on accommodative response

In the present study, participants with varying levels of uncorrected hyperopia, ranging from low hyperopia (up to but not including +2D) to high hyperopia (>4D), were fully corrected with spectacles while they engaged in sustained reading and movie tasks. Results of the study show that spectacle correction of uncorrected hyperopia had a positive effect ("better accommodative response") on the mean accommodative response across the two sustained tasks. In the reading task, this effect was bidirectional – glasses reduced/relaxed excess accommodation or improved a low response by at least 0.25D in participants. In the movie task, where hypoaccommodation was exhibited without correction (chapter 5), the effect of spectacle correction tended to mainly improve the mean response than aiding relaxation of accommodation. Spectacle correction of hyperopia would be expected to relieve the eyes of the additional accommodative effort needed to correct any underlying refractive error, and thereby result in greater amount of accommodation available for use during a sustained near task (Cregg *et al.* 2001). This could explain, in part, the significant improvement in the accommodative response observed during the movie task. Similarly, spectacle correction could improve the accommodative response in the subgroup of participants who were classified as "poor accommodators" during the reading task without correction (chapter 5), though this was not statistically significant (probably due to the small number of "poor accommodators" n=11). Moreover, results of this study show that full correction of hyperopia aided relaxation of accommodation. This finding was anticipated as the need for greater accommodative effort to correct any underlying refractive error would have been eliminated by correction, allowing for only accommodation to the target demand. This finding which was observed in the reading task, has public health significance, particularly in the area of patient education on compliance with spectacle wear, as the hyperopic child could benefit relief from the strain on their accommodative system while they engage in sustained near tasks at school such as reading and writing, which in education would be typically of 4 to 5 hours duration daily (Ritty *et al.* 1993). These results further add to the evidence of benefits of spectacle correction on important visual functions such as visual acuity and contrast sensitivity, already described in some studies (Mutti 2005; Mutti 2007; Leat 2011). It has been suggested that because the critical period for significant emmetropisation is up to about age six, optical correction of hyperopia during this period depends on whether it will impede or slow this process. However, for older children in the school years, spectacle correction of hyperopia is more for improved function than for other considerations such as emmetropisation (Gwiazda *et al.* 1993; Leat 2011). Therefore, this study's results add to the evidence of improved visual function (accommodation) with spectacle correction in hyperopic children in the school years, which could be used to guide prescribing.

In the management of hyperopia in children, some clinical practice guidelines suggest that correction for hyperopia should be limited to higher levels of hyperopia (greater than 4.50D) because of its potential role in reducing the risk of abnormal visual development (*Preferred Practice Pattern, Paediatric Eye Evaluations, American Academy of Ophthalmology, p. 13*), however, the question of when to correct low to moderate amounts of uncorrected hyperopia has largely not been addressed. Recommendations in the literature suggest that for children in the school years, hyperopia of ≥1.50D magnitude, accompanied by other symptoms should be prescribed (Ciner 1990; Cotter 2007; Leat 2011). However, these recommendations are mostly based on the clinical experiences and philosophies of clinicians, with little input from robust research findings. In the present study, the observed positive effect of spectacle correction across the two sustained tasks was independent of the refractive group of the participant (see Figure 6.3.1). While this result does not necessarily answer which amount of hyperopia requires correction, it is interesting to find that spectacle correction has the potential to improve the accommodative response across the hyperopia spectrum (including low, moderate, to high levels of uncorrected hyperopia), for which reason its prescribing may be indicated even for low amounts of hyperopia, particularly when such cases are presented with other factors such as asthenopia.

The observed positive effect of spectacle correction on the accommodative response during sustained near tasks in the present study, is inconsistent with previous studies which have measured accommodative response with spectacle correction under different experimental protocols such as in participants with Down Syndrome who were predominantly hyperopic (Cregg *et al.* 2001); and in infants and children drawn from different populations with various binocular vision problems (Cregg *et al.* 2001; Horwood and Riddell 2011). Although the characteristics of the oculomotor system may not be entirely similar for children with Down Syndrome and typically developing children to warrant comparison, the study by Cregg *et al.* (2001), observed the same level of underaccommodation with and without spectacles in their hyperopic Down Syndrome participants. They suggested that deficits in the neural control system in Down syndrome could be responsible; a factor which would be absent in normally developing children like those who sat in the present study, which could account for the differences in study results. In the study by Horwood *et al*. (2011), participants included those with strabismus as well as visually normal participants whereas participants in this study were binocularly normal without any strabismus or amblyopia. It is possible that differences in participants' binocular vision characteristics, which represent different sensory experience, could account for the lack of effect of spectacle correction on the accuracy of the accommodative response in that study. Moreover, it is possible that participants in the two previous studies had adapted to their habitual spectacle correction, and therefore, the effects of the correction may have been minimised. Consequently, it would be interesting to know whether the observed positive effect of spectacle correction on accommodative response during sustained near testing in this study, would have long term-effects, as it is unclear whether participants could adapt to these glasses with time thereby minimising any observed effect.

In the present study, spectacle correction of hyperopia resulted in increased variability (microfluctuations) in accommodative response in the reading task. This increased variability in the accommodative response with spectacle correction, was associated with increasing accommodative response (Figure 6.3.3, panel A). There is generally, little or no data on the effect of distance spectacle correction on the variability of accommodative response in hyperopia. However, a previous study in myopes reported that distance single vision spectacle correction increased accommodative variability in myopes compared to emmetropes, and when participants wore plus lenses (near addition) for a near task, the accommodative variability significantly reduced in myopes but not in emmetropes (Sreenivasan *et al.* 2011). It is unclear why the accommodative variability increased with spectacle correction during the sustained reading task. It would have been expected that with full correction of hyperopia, the high accommodative demand due to uncorrected hyperopia would have been eliminated, and thus reducing the activity of the accommodative plant (crystalline lens movement), which would result in a more stable accommodative response. On the other hand, the high correlation between the RMS of accommodative variability and the mean accommodative response during the reading task suggests that perhaps with spectacle correction, microfluctuations of accommodation increased as way of providing temporal directional sign for the accommodative controller to produce appropriate response. Perhaps, spectacle correction of hyperopia increases the sensitivity of the sensorimotor system (accommodative system) to maximize error detection which causes more fluctuations (Yao *et al.* 2010). In the movie task, however, there was a trend towards less variability in the accommodative response with spectacle correction, although this was not statistically significant. It may be that differences in such factors as cognition, and investigation of pupil sizes may partially explain the inter-task differences in accommodative variability with spectacle correction in this study. It is unclear whether image magnification due to positive lens wear could influence the observed variabilities in the accommodative response in this study. A recent study has suggested that lens magnification of the luminance profiles in the pupils could affect refractive error/accommodative estimates in photorefraction (Bharadwaj *et al.* 2018). However, for the relatively low magnitude of refractive errors in this study, such magnification effects are unlikely to account for these differences. Further studies are needed to understand the mechanism underlying the effect of spectacle correction on the stability of accommodative response in hyperopia, including the inter-task differences.

6.4 Effect of spectacle correction on sustained vergence functions

6.4.1 What is the effect of spectacle correction on vergence response during sustained reading and movie tasks?

A two-way ANCOVA (factor- refractive group, covariate being mean vergence response without correction) was used to assess the effect of spectacle correction on the vergence response. Across the two tasks, there was no interaction between refractive group and covariate ($p= 0.63$), and there was no difference between the vergence response with and without correction across the two tasks [$F_{(1,70)} = 0.30$, $p=0.58$, and $F_{(1,66)} = 0.02$, $p=0.89$ for reading and movie tasks respectively]. See also Figure 6.4.1

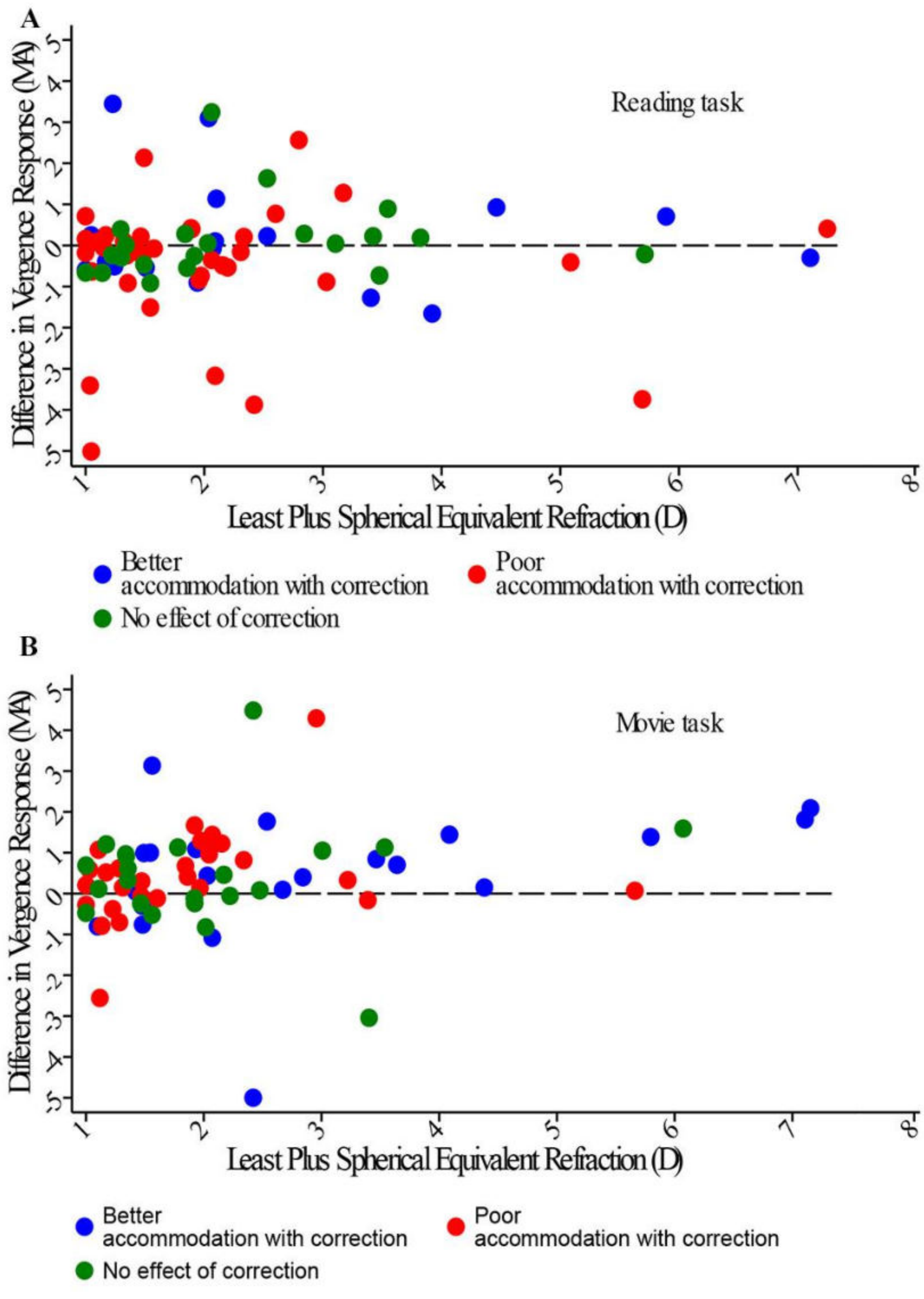


Figure 6.4.1 Scatterplots showing (A) difference in vergence response with least plus spherical equivalent refraction in the reading task, (B) difference in vergence response with and without spectacle correction with least plus spherical equivalent refraction in the movie task. Difference in vergence response represents (vergence response with correction – without correction). Long dashed line represents no difference between vergence response with and without correction. Colour coded individual data points show relationship with accommodative data with correction

– that is, for example whether individuals who had improved accommodation with correction also improved vergence response with correction.

6.4.2 What is the effect of spectacle correction on the stability of vergence response during sustained reading and movie tasks?

The stability of vergence response with spectacle correction was examined using the sample standard deviation of the vergence response during sustained testing with correction. In a two-way ANCOVA (using refractive group as factor, and mean vergence stability without glasses as covariate), there was no significant interaction between refractive group and covariate across the two tasks (p=0.21), and there was no difference in the stability of the vergence response with and without spectacle correction in both tasks [($F_{(1,70)} = 0.04$, p=0.83, and $F_{(1, 65)} = 0.07$, p=0.79) for reading and movie tasks respectively]. See also Figure 6.4.2.

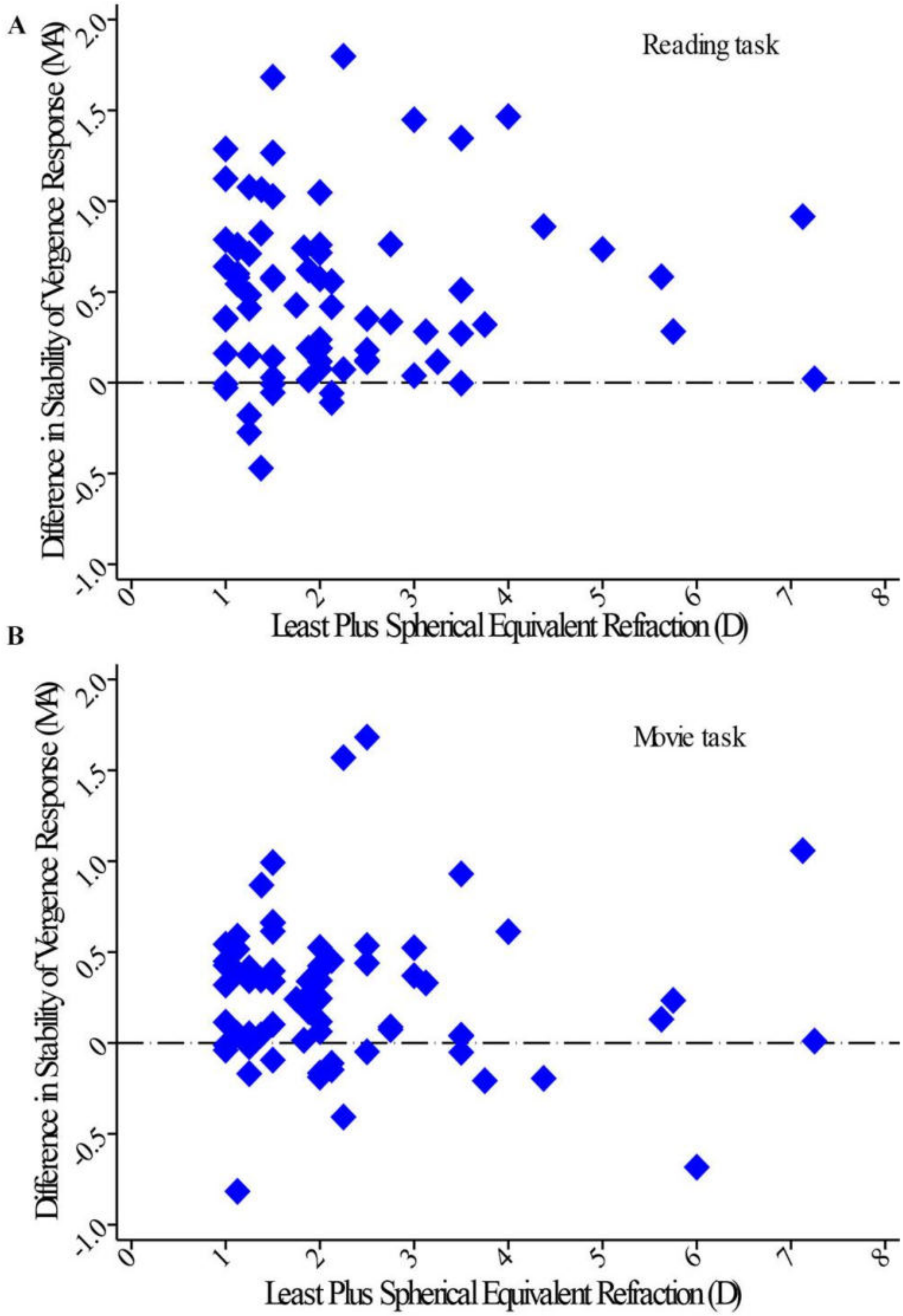


Figure 6.4.2 Scatterplots showing (A) difference in stability of vergence response with least plus spherical equivalent refraction in the reading tasks, (B) difference in stability of vergence response with least plus spherical equivalent refraction in the reading tasks Difference in stability of vergence response represents (stability of vergence response with correction – without correction). Long dashed line represents no difference in stability of vergence response with and without correction. Values above the long-dashed line indicate greater instability and those below the line indicate less instability.

6.4.3 Discussion of effect of spectacle correction on the vergence response

Results of the present study did not find a statistically significant effect of spectacle correction of hyperopia on the mean vergence response in both reading and movie tasks. It would be expected that increased accommodative response with correction, should have resulted in increased vergence response, given that the two systems are yoked. In the movie task, where the accommodative response did increase with spectacle correction, the vergence response increased as well, although not statistically significantly (Figure 6.4.1, panel B). Similarly, although increased variability in the vergence response was observed with correction, these were not statistically significant. It does not appear that the lack of statistical significance in the vergence response with correction may be due to sample size as the sample size of participants who were corrected was fairly adequate (n=78). Furthermore, there is paucity of studies on the effect of spectacle correction on vergence response in general, and hyperopia in particular, for comparison. Regardless, there may be factors such as participant's baseline fixation disparity, fusional reserve before glasses were worn, and AC/A ratio which could all possibly affect the vergence response with correction (Jiang *et al.* 2007; Sreenivasan *et al.* 2011). However, the majority of participants in this study were orthophoric at distance (97%) and near (54%), and for those with phoria at near, majority of the phorias was of magnitude less than 10 ΔD. They all also had good control/ recovery movement. Therefore, the influence of baseline near phoria on the vergence response with correction would likely be low. Differential prismatic effect was discussed in chapter 3. Its impact on vergence is likely to be low as the highest prismatic effect recorded was 0.09 ΔD base-in. Further studies are required to explore factors which influence the effect of spectacle correction on the vergence response.

6.5 What is the effect of spectacle correction on the rate of reading score?

A two-way ANCOVA (dependent variable – rate of reading score with correction; factor – refractive group; and covariate – rate of reading score without correction) was used to determine the effect of spectacle correction on rate of reading score. There was no significant interaction between the factor and covariate ($F_{(3,89)} = 1.40$, $p=0.25$), and the rate of reading score with spectacle correction was significantly higher than without correction ($F_{(1,89)} = 149.14$, $p<0.0001$), independent of the refractive group of the participant ($F_{(3,89)} = 1.18$, $p=0.32$). See also Figure 6.5.1. To assess the possible effect of learning on the outcome of the rate of reading test with spectacle correction, a two-way ANCOVA analysis was performed (with covariate being the rate of reading without correction, and factor being a binary variable indicating whether rate of reading was performed with correction first, or without correction). There was no significant interaction between the covariate and factor ($p=0.12$), and there was no effect of learning on the rate of reading score with or without correction ($F_{(1,93)} = 3.28$, $p = 0.07$). The association between rate of reading score with correction and the vergence response with correction was negative and not statistically significant ($r=-0.16$, $p=0.23$).

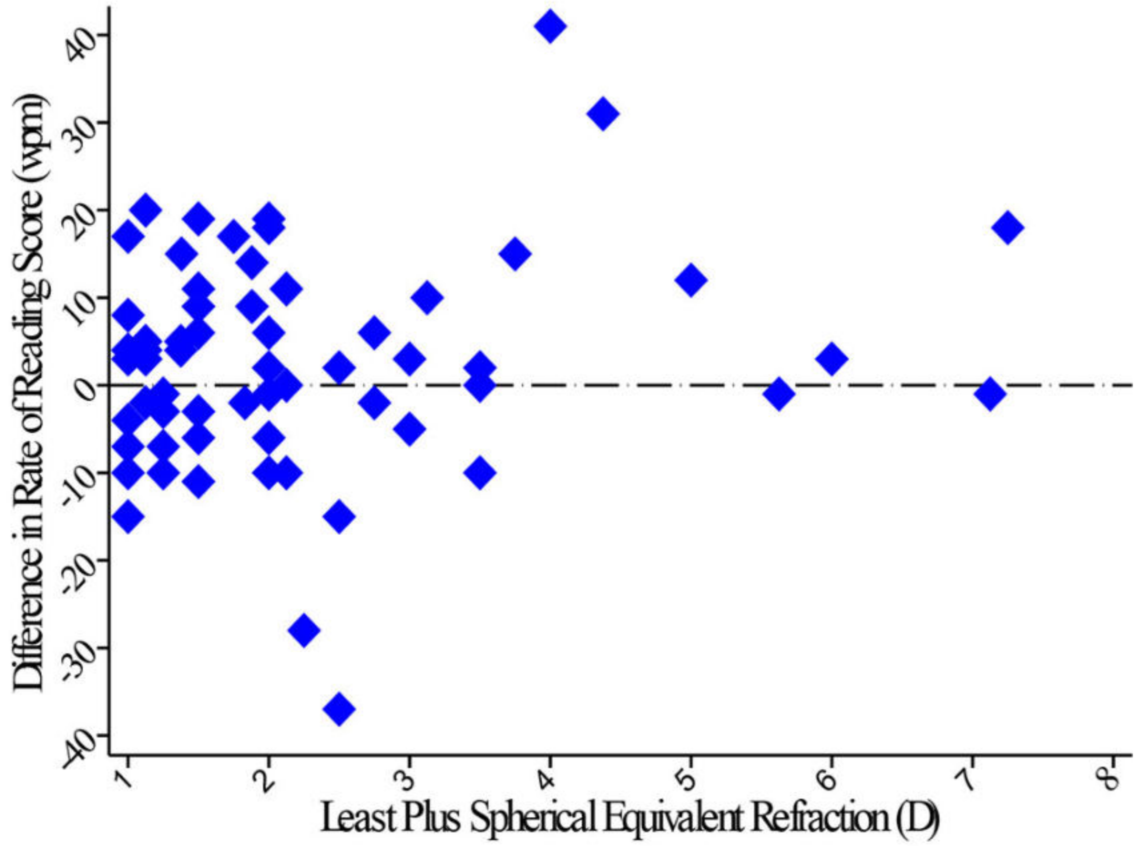


Figure 6.5.1 Scatter plot of difference in rate of reading score with least plus spherical equivalent refraction. Difference in rate of reading score represents (rate of reading score with correction – without correction). Long dashed line represents no difference in rate of reading score with and without correction. Scores above the long-dashed line suggest improved rate of reading and those below the line reduced rate of reading with spectacle correction. Wpm: words per minute.

6.5.1 Discussion of the effect of spectacle correction on the rate of reading test

Results of the present study show that spectacle correction significantly improved the rate of reading score in children with hyperopia. This result is consistent with previous work by van Rijn *et al.* (2014), who reported that spectacle correction significantly improved reading speed in their hyperopic participants compared to participants who were myopic. Despite methodological differences between their work and the present study, including age range of participants, and rate of reading test kit, agreement between the results of the two studies may indicate that the rate of reading test may be a more sensitive, and pragmatic measure of the benefit of spectacle correction for the hyperopic child, with relevance for their educational attainment. The Wilkin's rate of reading test kit measures rate of reading over one minute, is a "real-world" task, very easy to use and easily accessible to practitioners, which could be used to test children with hyperopia who can benefit from their spectacle correction, although its application in younger cohorts (< 7 years) may be limited, due to the level of reading ability in pre-schoolers. Improvement in visual function measures with spectacle correction forms one side of the evidence required for spectacle prescribing in hyperopia in school-aged children. On the other side, the evidence required depends on the benefit of spectacle correction to academic (literacy) performance of the hyperopic child. Reading performance includes reading speed, accuracy, and comprehension (van Rijn *et al.* 2014; Narayanasamy *et al.* 2015; Harvey *et al.* 2016). Although fluency may not necessarily represent comprehension, improved reading speed with spectacle correction may be an important tool for use by clinicians to reassure/motivate parents of the benefits of glasses to their child's reading performance. Against the background of emerging evidence of the association between uncorrected hyperopia and decreased literacy scores, evidence of improved reading speed with spectacle correction will be well received by parents, teachers and other stakeholders. The result of the present study also shows that this observed positive effect of spectacle correction on reading speed was not limited to any amount of hyperopia, suggesting that even low amounts of uncorrected hyperopia may benefit from improved reading speed with spectacle correction. Moreover, there was no effect of learning on spectacle correction improving the rate of reading score. This may be due to the fact the instructions at the start of both visits were the same. Also, randomisation of the reading sheets (versions A, B, C, D) minimised familiarity with a particular reading sheet.

Correction of hyperopia would be expected to make the words on the reading test clearer. However, as discussed in chapter 5, and accords with previous work, it appears that less accommodative effort is required to read fluently as long as the print size is large enough (Chung *et al.* 2007). Further discussion on the rate of reading in chapter 5, addressed the association between vergence response and rate of reading score, where it was speculated that the vergence response (or accurate binocular eye movement/status) may be the visual factor related to better reading fluency, to which optical intervention may be targeted. However, the present result shows that vergence response did not significantly increase with spectacle correction, and the association between vergence response with spectacle correction and rate of reading was negative and not significant. Results of chapter 4 showed that near VA was associated with the rate of reading score. Although near VA was not tested with and without spectacle correction, it may be that spectacle correction enabled hyperopes to see more clearly during the rate of reading test. Further period of adaptation with the correction might even potentially increase the scores. Further study is needed to identify which visual factors improve with optical correction, and at the same time, may be associated with increased reading speed.

6.6 Effect of Simulated Hyperopia on Sustained Accommodative and Vergence Functions

6.6.1 Brief recap of simulated hyperopia design

For participants who were emmetropic (n=31), minus lenses were used to simulate hyperopia during their return visit. These lenses ranged from -3.00D to -0.50D (depending on initial refractive error) to obtain a 3D hyperopic demand. Full aperture trial lenses were worn while sustained accommodative and vergence responses were measured with the PowerRef 3™.

6.6.2 Effect of simulated hyperopia on sustained accommodative response

The mean accommodative response with simulated lenses was higher than habitual response across the two tasks in emmetropic participants [(3.12±0.78 D (with simulation) vs 2.95±0.62 D (without simulation) in the reading tasks. In the movie task, a similar pattern was observed [(2.28±0.92 (with simulation) vs 2.22±0.81 D (without simulation)]. However, these differences in response were not statistically significant [(F (1, 22) = 0.13, p=0.72, and F (1, 23) =1.36, p=0.25 for reading and movie tasks respectively (two-way ANCOVA (mean accommodative response without simulation, and magnitude of simulated hyperopia as covariates)].

6.6.3 Effect of simulated hyperopia on accommodative variability

The mean accommodative variability with simulated lenses was higher than habitual response across the two tasks [(0.49±0.32 D (with simulation) vs 0.34±0.14 D (without simulation – reading task), and (0.53±0.36 D (with simulation) vs 0.37±0.13 D (without simulation – movie task)]. These differences in variability were not statistically significant [(F (1, 22) = 0.18, p=0.38, and F (1, 23) =0.69, p=0.42 for reading and movie tasks respectively, two-way ANCOVA (accommodative variability without simulation, and magnitude of simulated hyperopia as covariates].

6.6.4 Effect of Simulated Hyperopia on mean vergence response

The mean vergence response with simulated lenses was lower than response without simulation across the two tasks [(2.49±0.90 MA vs 2.85±0.54 MA for reading task and (2.12±1.49 MA vs 2.69±0.63 MA for movie task)]. These differences in responses were not statistically significant (two-way ANCOVA (vergence response without simulation, and magnitude of simulated hyperopia as covariates [$(F(1, 22) = 0.57, p=0.50$, and $F(1, 23) =1.24, p=0.28$ for reading and movie tasks respectively, with no significant interaction between covariates in both tasks $p>0.05$].

6.6.5 Effect of hyperopia simulation on the stability of vergence response

The mean vergence variability with simulated lenses was higher than in the habitual condition across the two tasks [(0.69±0.38 D vs 0.22±0.12 D and (0.66±0.47 vs 0.28±0.16 D) in the reading and movie tasks respectively]. and these differences in variability were not significant (two-way ANCOVA (without correction RMS and magnitude of simulated hyperopia as covariates [$(F(1, 22) = 0.23, p=0.64$, and $F(1, 23) =0.01, p=0.94$, with no significant interaction between covariates in both tasks $p>0.05$].

6.6.6 Discussion of effect of simulated hyperopia on accommodative and vergence measures

Some recent studies have reported on the impact of simulated hyperopia on academic-related measures (Narayanasamy *et al.* 2014; Narayanasamy *et al.* 2015). These studies observed that participants in whom hyperopia was simulated performed worse on several reading tests. These findings have been attributed to the increased accommodative and vergence demand associated with hyperopia (Simons and Gassler 1988; Narayanasamy *et al.* 2014). In the present study, 3 D of hyperopia was simulated in participants with emmetropia ranging from -0.25D to less than 1D. There was a general trend towards higher accommodative response with simulated hyperopia across the two sustained tasks, although this was not statistically significant. This finding accords with the results of sustained accommodative response in uncorrected hyperopia which was described and discussed in chapter 5. The mechanism underlying the relatively higher accommodative response in uncorrected hyperopia during sustained near task is currently poorly understood; however, it is possible that hyperopes may have lower blur detection thresholds, which allows them to use blur cues efficiently to drive a response. Outputs of the slow, blur-driven accommodation may also influence the higher accommodative response in hyperopia during sustained reading and movie tasks (Rosenfield and Gilmartin 1998). Similarly, simulated hyperopia caused an increase in the variability of accommodative and vergence response, although these results were not statistically significant. The lack of statistical significance in these measures could be due to small sample size (n=27) used for simulating hyperopia. It is also possible that if higher minus lens powers had been used for simulation, a significant effect could have been detected. In the present study, participants were simulated with minus 3 DS of lenses.

6.7 Chapter Discussion

While several studies have looked at the impact of uncorrected hyperopia on the accommodative response (Horwood and Riddell 2011; Candy *et al.* 2012; Kulp *et al.* 2014; Ciner *et al.* 2016; Roberts *et al.* 2018a; Roberts *et al.* 2018b), this study provides further scholarship on the subject by measuring the effect of spectacle correction on the accommodative and vergence functions (in terms of the response and stability of the response). Using state-of-the-art photorefraction technology, simultaneous, continuous and binocular measurements of accommodation and vergence were made while children (n= 78) with varying levels of hyperopia engaged in sustained reading task, simulating a literacy activity in the classroom; as well as watching an animation movie, which mimicked a naturalistic, every day recreational activity. Observed effects of spectacle correction, therefore, have practical application to the child's learning and social wellbeing. Although the order of task introduction while children wore their correction was not randomised, the result of counterbalancing technique in a subgroup of participants, revealed that there was no "order effect" (order of task introduction) on the results of accommodative and vergence functions with spectacle correction. The present study finds that spectacle correction, which is the mainstay in the management of refractive errors, particularly in children with hyperopia (Morjaria *et al.* 2016), had a positive effect on the accommodative response in terms of improving the response where there was hypoaccommodation, and also aiding relaxation of accommodation where there was excessive accommodation. Furthermore, there was improved reading speed with spectacle correction of hyperopia. These findings could be used for health promotion/education on benefits of spectacle correction in children, which might help with compliance.

Several studies have evaluated the lag of accommodation using the photorefraction technique while participants wore spectacle correction (Seidemann and Schaeffel 2003;

Horwood and Riddell 2011; Doyle *et al.* 2016; Doyle *et al.* 2017). However, a recent study by Bharadwaj *et al.* (2018), asserts that the use of spectacle correction while obtaining photorefractive estimates of refractive error/accommodation could underestimate the results due to image magnification of the luminance profile in the pupils. They further report that this effect is compounded by large vertex distance of the spectacle from the corneal plane. In the present study, constant vertex distance (12mm) while wearing spectacles was checked and maintained by fixing adhesive nose pads on the glasses of each child, which would have likely reduced any effects from variable vertex distance. Also, the range of lenses used (mostly +1.00D to +4.00D) would make any magnification effects less. Nonetheless, the results of the sustained accommodative functions in hyperopes who were corrected with spectacles in this study, are to be interpreted in light of the observation by Bharadwaj *et al.* (2018) on the potential impact of image magnification.

In the present study, participants wore full correction while they engaged in the two sustained near tasks. No subjective assessment of comfort with the spectacles was made, but it is recognised that in routine clinical practice, spectacle prescription is a function of objective end-point and subjective tolerance. Consequently, improved performance with full correction (as was observed in the present study) may not be tolerated in some individuals during everyday wear, and whether under-correction of hyperopia by various amounts would accord with the results of the present study too, cannot be addressed by the current results.

6.8 Chapter Summary

- **There was a positive effect of spectacle correction on sustained accommodative response during the reading and movie tasks.**
- **The effect of spectacle correction on accommodative variability was mixed across the two tasks; being statistically significantly higher in the reading task, but no significant effect observed in the movie task.**
- **There was an improved rate of reading score with spectacle correction compared to without correction.**
- **There was no effect of spectacle correction on sustained vergence response and stability.**
- **Simulated hyperopia in emmetropic controls resulted in high mean accommodative response and variability in the response, although these were not statistically significant.**

Chapter 7: Thesis Conclusions and Recommendations for Further Research

7.1 Introduction

Uncorrected hyperopia is the most common refractive error in young children. Despite this, it is often undetected unless a child attends a routine eye examination, or it is identified during a screening programme. Uncorrected hyperopes, typically those with low to moderate amounts, are usually able to use accommodation to overcome any blur due to the uncorrected refractive error for distance viewing. Consequently, when near work is required, extra accommodative effort is required to see clearly close-up. Compared to myopia, there are few studies which have investigated the characteristics of the accommodative function in hyperopia. However, of the few studies reported, the consistent finding in the literature is that children with uncorrected hyperopia tend to hypoaccommodate (or demonstrate significant accommodative lags), and that those with reduced and variable lags, who tend to be those with higher magnitudes of uncorrected hyperopia, are at risk for abnormal visual development including strabismus and amblyopia (Candy *et al.* 2012; Kulp *et al.* 2014; Ciner *et al.* 2016). However, it is still unclear when, and at what magnitude of hyperopia, refractive intervention is necessary. Furthermore, there is a gap in our current understanding of the accommodative characteristics of the uncorrected hyperopic child. The question of sustained accommodative response, which reflects what happens naturally when, for example, the hyperopic child engages in near work at school for a prolonged period of time, is yet to be addressed in the literature. Beyond conventional school tasks, the advent of portable electronic devices such as smartphones and tablets, and their prolonged use by children for both educational and recreational reasons, suggest that accommodation will often be engaged for sustained periods in children. There is therefore a need to assess the response profile of accommodation over prolonged periods. It is possible that an uncorrected hyperope may initially demonstrate a significant lag of accommodation, but then improve during sustained response. Moreover, whether the accommodative response exhibited by the uncorrected hyperope is stable over time is yet to be ascertained. It is well known that the accommodative and vergence systems are neurally coupled (Zhang *et al.* 1992; Gamlin 1999). However, in the few studies that have investigated the dynamic relationship between vergence and accommodation, uncorrected hyperopes simultaneously demonstrated accurate vergence responses alongside significant accommodative lag (Horwood and Riddell 2011). No previous study has concurrently investigated the characteristics of uncorrected young hyperopes' accommodation and vergence responses, in terms of accuracy and stability, during sustained near vision tasks. Unlike myopia, where a -0.50D correction for a -0.50D myope will result in significant improvement in vision and therefore warrant spectacle correction, the case for hyperopes is not a straightforward one, as correction would not necessarily always improve vision. Currently, optical management of the hyperopic child relies mostly on clinical consensus and the practice guidelines of professional bodies such as the American Academy of Optometry and American Academy of Ophthalmology. The American Academy of Ophthalmology, for example, recommends optical correction only for hyperopia greater than 4D because it is purported that hyperopic children who fall above that threshold are at greater risk of developing strabismus and amblyopia. However, recent evidence suggest that even moderate amounts of uncorrected hyperopia can affect measures of visual function such as visual acuity and accommodation (Kulp *et al.* 2014; Suh *et al.* 2016), as well as potentially adversely affect educational attainment (Williams *et al.* 2005; Kulp *et al.* 2016). A recent study investigating the outcomes of young hyperopes assigned to spectacle correction or observation without correction was not sufficiently powered at conclusion to make firm conclusions about the impact of early spectacle correction. They summarise the findings from the trial (which closed early due to poor recruitment) as showing a small to moderate benefit or no benefit of immediate glasses compared with careful observation and spectacles if deterioration of visual status i.e. onset of strabismus or reduced vision, occurs (Kulp *et al.* 2019).

The effect of spectacle correction on measures of sustained accommodation and vergence functions has not been previously reported in the literature, and knowledge of this could be very useful for clinicians in every day clinical practice when deciding whether, and what strength, of refractive correction to prescribe.

To answer these questions, this PhD study examined sustained accommodative and vergence functions in a population of children with varying levels of hyperopia, and emmetropic age-matched controls. The effect of spectacle correction on these measures was also investigated using a current version of a slope-based, eccentric photorefractor – the PowerRef 3™. Participants engaged in two near tasks: reading on a Kindle Paperwhite and watching a stop-clay animation movie on an LCD screen for 15 minutes at 25 cm while the PowerRef 3™ measured their refraction, vergence and pupil sizes (near triad). Full refractive error status was known from prior cycloplegic refraction. Measurements of the near triad were made under two experimental conditions; a) with habitual refractive status (participants either wore their habitual corrective glasses or were assessed without glasses for those who did not normally wear correction), and b) with altered refractive condition (where habitual wearers temporarily forwent their correction, while those without correction were given temporary correction for their hyperopia). The altered refractive condition was tested one week following the first habitual measure. Prior to undertaking these measures, a calibration of defocus (refraction estimates) and gaze position estimates of the PowerRef 3™ were undertaken. This is a critical step required to ensure the accuracy of estimates of the instrument (Blade and Candy 2006; Jagini *et al.* 2014). Particularly for gaze position calibration, there have been no previous studies in the literature comparing the relative accuracy and repeatability of various gaze position calibration techniques. This study addressed this gap by investigating three gaze position calibration techniques previously used to calibrate first Purkinje image-based (PI) eye trackers; *eccentric viewing, prism-based and theoretical techniques.*

7.2 Summary of Main Findings

- Accommodative and vergence responses during sustained near tasks do not differ significantly between uncorrected hyperopes and emmetropes.
- However, the stability of accommodative response worsens with increasing hyperopia.
- Vergence stability was also worse for hyperopes, and this is an often-overlooked factor which could contribute to asthenopia.
- Hyperopic spectacle correction is beneficial to optimise the accommodative response.
- Spectacle correction was also associated with improved rates of reading.

This PhD study found the mean accommodative response during sustained reading and movie tasks was not significantly related to magnitude of refractive error. Uncorrected hyperopes accommodated comparably to emmetropic controls. Moreover, when the response under consideration is the total accommodative effort required to correct at any underlying refractive error and to focus at 25 cm, uncorrected hyperopes actually produced more accommodation. These findings are inconsistent with what has been previously reported (Horwood and Riddell 2011; Candy *et al.* 2012). The apparent disparity with the present results may relate to the fact that this study considered the characteristics of the accommodative response during sustained engagement for two everyday tasks (reading and watching a movie), reflecting the use of accommodation for naturalistic tasks, compared to the previous studies which tested with different targets and response durations.

The other aspect considered in the present study concerned the stability of accommodative response. The study found that increased amounts of uncorrected hyperopia were associated with greater instability in the accommodative response during sustained near work, particularly in the reading tasks. The functional role of accommodative variability during steady state fixation (microfluctuations) is yet to be fully elucidated. It has been suggested that microfluctuations may provide a directional cue (act as subthreshold blur detector) that can be used to drive the accommodative response (Kotulak and Schor 1986). Some investigators have also proposed a role for microfluctuations in myopia progression (Day *et al.* 2006; Harb *et al.* 2006; Langaas *et al.* 2008). However, the characteristics of microfluctuations in hyperopic refractive errors have not been fully explored, and no functional roles have been put forward yet. From the results of the present work, we can speculate that microfluctuations may be a factor related to asthenopia, known to occur commonly in uncorrected hyperopia (Junghans *et al.* 2010), with an increased degree of microfluctuations causing muscular fatigue after prolonged periods of near work.

A related finding from this work, which is being reported for the first time, was the association between vergence instability and uncorrected hyperopia. Vergence instability increased with increasing uncorrected hyperopia. Together, these two characteristics of the accommodative and vergence systems could act as trigger factors in the asthenopic symptoms experienced by some uncorrected hyperopes. These may also be implicated as factors contributing to the poorer academic performance other authors have reported for uncorrected hyperopes.

This work reports for the first time, the effect of spectacle correction on sustained accommodation. The study found a positive effect of spectacle correction on the accommodative accuracy; spectacle correction either reduced accommodative lead in some participants or improved the response in participants in whom lag was typical. The benefits of hyperopic correction, particularly in low to moderate hyperopia are often stated anecdotally. Consequently, this result may be relevant for evidence-based management of hyperopia in children, especially given that the observed positive effect of correction occurred independently of the magnitude of hyperopia. In addition, spectacle correction was associated with an improved rate of reading score in children with hyperopia, consistent with previous studies (van Rijn *et al.* 2014). Perhaps clinicians should consider including some kind of rate of reading test with refractive correction in situ, as part of the battery of tests carried out in a standard eye examination after refraction, to specifically quantify the benefit of spectacle correction in hyperopia. Rate of reading tests are quick to administer and can be useful in demonstrating the benefit of glasses to a hyperopic child's reading to parents and other stakeholders.

This PhD study also demonstrates for the first time that the prism-based calibration technique tended to overestimate the Hirschberg ratio (HR) of subjects compared to the eccentric viewing and theoretical techniques. The prism-based calibration technique also exhibited the poorest repeatability of the three techniques. This high variability in HR when the prism-based technique is used to calibrate gaze position estimates may be inherent in the use of prism for calibration, as variable prism orientation during different measurement sessions can lead to high variability in HR. The prism-based technique has previously been found to successfully calibrate gaze position estimates in infants and children from the PowerRef 2™ (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009). Regardless, results of this PhD study in adult subjects point to the need to carefully consider estimates derived by this calibration technique when used for 1st PI-based eye trackers.

7.3 Strengths and Limitations of study

The strengths of this PhD study have been highlighted earlier in the introduction section of this chapter; including the use of two everyday tasks – reading and movie, to measure accommodative and vergence response. The two tasks reflect natural use of accommodation in typically developing children. The differences in the two tasks such as attentional demand and spatial frequency content allowed investigation of the accommodation and vergence responses under two different task conditions. The use of photorefraction also allowed investigation of the effect of spectacle correction on sustained accommodative and vergence response for the first time. Continuous and binocular measurement of accommodation, vergence and pupil sizes using the photorefraction technology is a strength of this study as previous studies using techniques such as Nott retinoscopy and autorefractor only obtained monocular measures. Recruitment of a fairly large sample of children (n=117) with varying levels of hyperopia is another strength of the study. Nonetheless, there are some limitations to discuss.

Although the number of participants who took part in the main study (Chapter 3) was fairly large, the number of high hyperopes (> 4D) was small (n=8). Every effort was made to increase the number of this participant type, including widening recruitment to both the University Optometry clinic and community optometric practices. The small number of high hyperopes in this study reduced the power of some of the analyses, potentially masking real differences where no statistical significance was observed. On the other hand, the study findings reported a benefit to spectacle correction and decreased stability of accommodative response with increasing hyperopia: and one would anticipate that such effects would be strengthened with inclusion of more high hyperopic subjects.

Assessment of sustained accommodation was carried out on school premises within the school day. Classroom tasks, some of which could have been done at near prior to measurement of sustained accommodation could involve the use of accommodation.

Participants could thus come in accommodation-adapted. This effect was not ascertained. Nonetheless, participants underwent baseline testing before engaging in the two sustained tasks, by which time any such effects would have been minimised.

In the very young participants (< 7 years), despite the use of Velcro straps to stabilise their head for a steady fixation, micro head movements were apparent, especially when participants indicated that they wanted to stop the task. However, this was unlikely to have affected the results of the study as, for example, vergence results were not related to age, suggesting that the stability of the young participants' fixation was comparable to that of older participants while attending to the targets.

A minor limitation of this PhD work relates to the lack of randomisation for the task order and for the "treatment" or spectacle correction order. Randomisation of tasks or treatment effect is considered a gold-standard procedure for clinical trials and other experimental studies (Suresh 2011). However, in this PhD work, given the sustained nature of the two near tasks, it was anticipated that if participants watched the movie task (a livelier and more interesting task) before doing the reading tasks, there could be lower completion rates for the reading task. Therefore, in most cases, the accommodative and vergence measures were taken during the reading task before the movie task. Nonetheless, to evaluate the possible effect of task introduction order, the *counterbalancing technique* was introduced in a subgroup of the participants. The results of this study show that the inter-task differences observed were not related to the order in which the tasks were performed.

Similarly, it was difficult to randomise the treatment order (spectacle correction). For participants who were not habitual spectacle wearers, measurement of sustained accommodation with correction could only be carried out during a return visit, by which time their cycloplegic refraction had been determined. However, for habitual spectacle wearers, measurements were first made through their habitual spectacle correction, with the measurement without correction taken during the follow-up/second visit.

7.4 Recommendations for further research

7.4.1 Investigation of blur detection thresholds in uncorrected hyperopia

Retinal defocus is an important input to the accommodation feedback control system, with the accuracy of the accommodative response depending on the eye's ability to detect and utilise retinal defocus (Yao *et al.* 2010). The range at which retinal defocus may be tolerated perceptually and by the sensorimotor system (the accommodative system), has given rise to the terms subjective and objective depths-of-focus respectively (Wang and Ciuffreda 2006; Yao *et al.* 2010; Roberts *et al.* 2018a; Roberts *et al.* 2018b). Depth-of-focus, blur detection thresholds or blur sensitivity are terms frequently used in the literature but all denote the same concept (Yao *et al.* 2010). The subjective and objective depth-of-focus are affected by pupil size, luminance and spatial frequency of the target (Wang and Ciuffreda 2006; Yao *et al.* 2010). The objective depth-of-focus is reported to be smaller than the subjective depth-of-focus and represents the smallest detectable change in the accommodative response for a small change in the accommodative stimulus (Yao *et al.* 2010). Beyond the recent work of Roberts *et al.* (2018b), who reported no difference in blur detection thresholds between uncorrected hyperopic and emmetropic children, little is known about blur detection in uncorrected hyperopes. In the work of Roberts *et al.* (2018b), blur detection threshold was determined subjectively, which does not reflect the sensorimotor (accommodative system's) use of retinal defocus i.e. the objective depth-of-focus. Understanding the objective depth-of-focus may help to shed light on the high accommodative response of uncorrected hyperopes during sustained near work. The relationships between the subjective depth-of-focus, objective depth-of-focus and accommodative microfluctuations in uncorrected hyperopia, need to be explored further.

7.4.2 Investigation of the open-loop accommodation and vergence response

In the present PhD study, the accommodative-vergence interaction was investigated under closed-loop conditions. However, in order to understand this interaction further, and to quantify the relative contributions of blur-driven convergence (AC/A) and disparity-driven accommodation (CA/C), will require the measurement of accommodation and vergence functions under open-loop experimental conditions. Such a study will help build our understanding of which subgroup of hyperopes have flexible/inflexible cross-link interactions and are therefore more at risk for abnormal visual development such as the development of strabismus.

7.4.3 Investigation of the role of accommodative and vergence instabilities in patients' symptomatic experience of asthenopia

A definitive functional role(s) of accommodative microfluctuations is/are yet to be elucidated. In uncorrected hyperopia, the results of the present work demonstrate an increased instability in the steady-state accommodative response during two sustained near tasks. Moreover, there is increased vergence instability in participants with high uncorrected hyperopia. It would be interesting to explore further any potential associations between these measures of stability in the accommodative and vergence responses and the subjective experience of asthenopia.

7.4.4 Randomised controlled trial of the effect of spectacle correction in uncorrected hyperopia

This study has demonstrated the effect of spectacle correction on an important visual function measure: accommodation. This information is to be interpreted within the limitations outlined in the thesis. Further studies using the gold-standard technique of randomised, controlled trials are required to evaluate the long-term effect of spectacle correction on accommodation and other important visual function measures, such as stereoacuity and academic performance. A new randomised controlled trial study has just been published comparing early versus delayed intervention for hyperopia. It fails to find a definitive benefit of early hyperopia correction, but outcome measures were distance VA and near stereoacuity, but not accommodation or other near visual measures (Kulp *et al.* 2019).

7.4.5 Investigation of sustained pupillary response (pupil load) and uncorrected refractive error

A previous study has reported no relationship between pupil diameter and refractive error (Orr *et al.* 2015). However, it has been observed that the pupils dilate during increased cognitive/mental activity (Kahneman and Beatty 1966; Sirois and Brisson 2014; White and French 2017), as well as during increased sympathetic innervation (Gilmartin 1986). Pupillary behaviour to different target luminance has also been put forward as a potential instrument to measure attention and its effect on sensory processing (Binda and Murray 2015). It may be possible that a further study looking at sustained pupillary behaviour, including characteristics such as its variability in different tasks, may find differences in individuals with different refractive errors. Such information may reveal differences in attentional and sensory processing.

7.4.6 Assessment of the utility of the theoretical calibration protocol in children

Previous studies have calibrated the HR of both adults and child participants using eccentric viewing (Riddell *et al.* 1994; Hasebe *et al.* 1995; Hasebe *et al.* 1998; Jagini *et al.* 2014), and prism-based techniques (Bharadwaj and Candy 2008; Bharadwaj and Candy 2009; Doyle *et al.* 2016; Doyle *et al.* 2017). However, there is no current literature on the use of the theoretical calibration technique in children. Based on the results of this work, there appear to be several advantages of the theoretical calibration technique (presented in Table 2.1 of chapter 2) including its relative accuracy, making it attractive for use in children. Nonetheless, the ease of obtaining the two ocular biometric measures (anterior corneal curvature and ACD) for calibrating HR in this population needs to be investigated.

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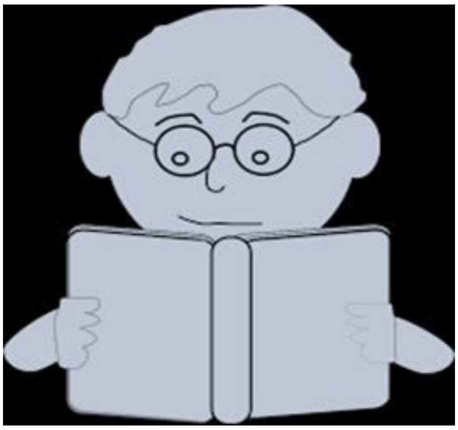
Appendix 1: Parent Information Sheet

What impact does using e-readers and tablets up close have on your child's eyes and focussing ability?



Parent/Guardian Information Leaflet (school route)

What are we doing?

We are inviting your child to take part in a research study. A lot of children use smartphones and tablets at a close distance from their eyes. We would like to measure how well your child focusses up close while reading or watching a movie on a tablet and measure how well their eyes cope with this over time. We are particularly interested in children who are long-sighted (hyperopic) because their eyes have to work especially hard to see clearly up close when they aren't wearing their glasses. We are asking your child to participate because we would like to study how well they focus during near work, with and without their glasses (if they have any). We have a specialised camera that allows us to do this. We will be testing over 100 children of different ages, some of whom are long-sighted, and others who are not. We will measure how well your child's eyes focus while they look at a tablet screen for 15 minutes; doing some simple reading activity or watching a suitable movie. Once your child has taken part in the study we will send you a short report so that you know what we found.

To help you understand what this research is about and what your child will be asked to do if they take part, please read the information provided in this leaflet and do not hesitate to contact us about anything that might not be clear to you.

Thank you for taking the time to consider this invitation.

What might happen to my child if they take part?

By taking part in this study, your child will get their eyes examined. They will also do some simple reading tasks and watch a short-animated movie on a tablet. While they are doing this our special camera will record how well their eyes are focussed on the tablet. As this is not a full eye examination, if any abnormalities of vision are detected, then we will recommend that your child attends his/her optometrist.

Who are we?

Dr Julie-Anne Little: Julie-Anne is an optometrist and the chief investigator for this study. She is part of the paediatric vision research team at Ulster University. She is highly experienced in examining children, both in clinical practice and research studies.

Prof Kathryn Saunders: Kathryn is an experienced optometrist with many years of providing vision care for children. She is part of the paediatric vision research team at Ulster University where she runs a paediatric and special needs clinic.

Michael Ntodie: Michael is an optometrist and a PhD student who has practiced for six years in Ghana. He has worked on research projects, including the Glass hopper project led by the Optical Foundation from the Netherlands, which examined the vision of school children in Ghana.

This study has received ethical approval from Ulster University Research Ethics Committee. There are no major risks associated with participation and all your child's details will be kept confidential. The procedures we will use in this study have all been used to test children's vision and are standard clinical procedures. If you are happy to let your child join the study, we will attend their school and do the testing at their school. Your child can withdraw from the study at any stage without any consequences to them.

What does the study involve?

For you-

- You will be requested to complete a short questionnaire, asking questions about your child's general health and vision, whether they wear glasses, and if they are prescribed any medications (some medications can affect focussing).

For your child-

- An initial check of your child's eyes to measure how well they see, how well their two eyes work together and how good their 3D vision is. These are all quick easy tests that are routinely conducted during a child's eye test.
- A specialised video camera will be used to measure your child's focussing accuracy while they do two tasks. In the first activity, your child will undertake a simple reading activity for a period of 10-15 minutes (we realise the length of attention time will depend on their age and cooperation) while the camera measures their focussing accuracy. The study will not be assessing the reading ability of your child, but their focussing accuracy while they are engaged in a sustained simple reading activity. In the second activity, your child will watch an animated movie and their focussing accuracy will be measured again by the camera during this task. We will ensure they have a break in-between these activities.
- In order to obtain an accurate measure of your child's long-sightedness, at the end of the visit an eye drop will be put into your child's eyes. The eye drops are routinely used by optometrists to test children's eyes – so your child may have had them before. After a break of 30 minutes we will measure the amount of long-sightedness by shining a small light into your child's eyes and placing some lenses in front of their eyes. This is a quick test and only takes a few minutes.

- We will come back to the school on another day and your child will do some of the same activities again, but this time we will ask them to do the activities without their glasses (if they wore glasses the first time) and with some temporary glasses if they usually don't wear glasses. This will help us determine how much differences glasses may make to focussing accuracy.

More information about the eye drops

The eye drops which will be used for this study are routinely used for eye tests on children. We have used these drops successfully in our vision research on children in schools over many years, as have a great deal of other researchers. The drops sting a little when they are put in the eyes, but this wears off very quickly. We will minimise the discomfort that this drop may cause by first instilling an anaesthetic eye drop. The drops take about 30 minutes to work. The effect of the drops is to make focussing more difficult for a few hours and your child's near vision is likely to be temporarily blurred. The drops also make the pupils larger, making your child a little more sensitive to bright light than usual. This effect wears off after about 24 hours.

Ulster University Procedures

It is very unlikely that something will go wrong during this study. However, you should know that the University has procedures in place for reporting, investigating, recording and handling adverse events and complaints from study volunteers. The University is insured for its staff and students to carry out research involving people. The University knows about this research project and has approved it. Any complaint should be made, in the first instance, to the Chief Investigator (Dr Julie-Anne Little). Any complaint you make will be treated seriously and reported to the appropriate authority.

What to do now?

Please talk to your child about this study. If you consent, and your child is happy to be part of the study, please complete and return the consent form and the questionnaire in the envelope provided and we will attend your child's school for their testing.

Thank you for taking time to consider this study.

If you have any questions, please contact us on:

Michael Ntodie: (02870123718) email: ntodie-m@email.ulster.ac.uk
Dr Julie-Anne Little: (028 70324374) email: ja.little@ulster.ac.uk
Professor Kathryn Saunders: (02870123047) email: kj.saunders@ulster.ac.uk

Appendix 2: Consent Form

Focussing on near work: the impact of uncorrected hyperopic refractive errors
Parent/Guardian Consent Form

Researchers: Dr Julie-Anne Little, Prof Kathryn Saunders, Michael Ntodie.

Please confirm you agree with each of the statement below by marking the boxes.

- I confirm that I have read and understood the information sheet provided for the above study and have had the opportunity to ask questions and receive answers to my questions. ☐
- I understand that my child's participation is voluntary and that they are free to withdraw at any time, without giving any reason and without their medical care or rights being affected in any way. ☐
- I understand that the researchers will hold all information and data collected during the study in confidence and all efforts will be made to ensure that my child cannot be identified as a participant of the study (except as required by law). I give permission to the researchers involved in the study to hold my personal data securely. ☐
- I give consent for a report to be written to me for my child for any eye problem that may be detected during the study, and for a referral to their health professional if necessary. ☐
- I give consent to be contacted in the future about this study. ☐
- For the purposes of describing the research and the methods used, the research team may take photographs during data collection. I give consent for a photograph to be taken of my child conducting the study. ☐
- I agree for my child to take part in the above study. ☐

________________________	________________	____________________
Name of parent/guardian	**Date**	**Signature**

Contact number: ____________________ **Email:** ________________________

Name of Child: ____________________

______________________	________________	____________________
Researcher's name	**Date**	**Signature**

Appendix 3: Medical and Eye History Questionnaire

Eye and Medical History Questions

We would be grateful if you could spend some few minutes to answer the following questions which seek to obtain information about your child's eye and medical health**.**

Child's age: ……………. **Gender:** Male ☐ Female ☐

Child's class: …………………… **Teacher's name: ……………………..**

Does your child currently wear glasses? Yes ☐ No ☐

If yes, do you know if their glasses are worn for: long-sight ☐ short-sight ☐

astigmatism ☐ not sure ☐

Does your child have any eye conditions? (E.g. a squint, or a lazy eye?)

If yes, please tell us about them ……………………………………………….

Do you have any concerns about your child's vision? Yes ☐ No ☐

If yes, please tell us about your concerns…………………………

Has your child reacted to any eye drops in the past? Yes ☐ No ☐

If yes, please tell us about what happened ……………….

Does your child have any medical history you would like us to know about?

…………………………

Are they currently taking any medications? Yes ☐ No ☐

If yes, please state them**………………………………………..**

Thank you for completing these questions.

Please return via the envelope provide

Appendix 4: UUREC Approval Letter

Ulster University
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ulster.ac.uk

Our Ref: NC:GOV

22 August 2016

Dr J-A Little
Room G159
School of Biomedical Sciences
Ulster University
Coleraine Campus

Dear Dr Little

Research Ethics Committee Application Number: REC/16/0061

Study Title: Focussing on near work: the impact of uncorrected hyperopic refractive errors

Thank you for your recent response to matters raised by the committee. This has been considered and the decision of the committee is that the research should proceed.

Please also note the additional documentation relating to research governance and indemnity matters, including the requirements placed upon you as Chief Investigator.

The committee's decision is valid for a period of three years from today's date (this means that the study should be completed by that date). If you require this period to be extended, please contact the Research Governance section.

1. **Please complete and return the Chief Investigator Statement of Compliance prior to commencing the study and keep a copy for your file.**
2. **Please retain all other documents.**

Further details of the University's policy along with guidance notes, procedures, terms of reference and forms are available on the Ulster University Portal.

If you need any further information or clarification of any points, please do not hesitate to contact me.

Yours sincerely

Nick Curry
Senior Administrative Officer
Research Governance
028 9036 6629

Appendix 5: Data Recording Form

Near work in Uncorrected Hyperopia Study

Date: ____________

Date of birth: ______________________

Age: ________

School/Class: ______________________

Gender:

1	Male
2	Female

Study ID ____________

Spectacle Rx

R: ________________

L: ________________

Spectacle Correction

1	Yes
2	No

How often are glasses worn?

1	Everyday
2	Once a week
3	Twice a week
4	> Twice a week

PCT:

Distant: ______________ Near: ______________

Eye movement (pendulum movement)

1	Excellent
2	Fair
3	Poor

Frisby Stereoacuity:

Uncrossed ________ @ ________ cm

Amplitude of Accommodation:

RE			
LE:			
BE			

NPC: ____________

Nott Ret @ 25cm: ____________

Sonksen logMAR test (single letter)

Distant (habitual)

BE: ________

Sonksen logMAR test (crowded letters

Distant — Near

BE: ________ BE: ________

RE: ________ LE: ________

Sustained Accommodation with PoweRef 3

Reading task

1st Visit

1 Yes @ ________ mins

2 No

2nd Visit

1 Yes @ ________ mins

2 No

Movie task

1st Visit

1 Yes @ ________ mins

2 No

2nd Visit

1 Yes @ ________ mins

2 No

Wilkins rate of reading test

Visit 1 ________ per minute

________ words missed

Visit 2 ________ per minute

________ words missed

Cyclo ret: Time of installation: ________

RE: ________ LE: ________

Calibration routine @ RE

Lens

1 Yes

2 No

Prism

1 Yes

2 No

Signature: ________________

Appendix 6: Lists of Publication and Conference Presentations

Accepted with minor correction:

Michael Ntodie, Shrikant R. Bharadwaj, Swaathi Balaji, Kathryn J. Saunders, Julie-Anne Little. **Comparison of Three Gaze Position Calibration Techniques in First Purkinje-Image Based Eye Trackers.** Optom Vis Sci. OVS17306R3.

Conference presentations (poster):

"Exploring the accuracy and repeatability of eccentric infrared photorefraction with the PlusOptix PowerRefractor III" British Congress of Optometry and Vision Science, Coleraine, 2016.

"Photorefraction measurements with the PowerRefractor III: comparison of calibration techniques to determine individual Hirschberg ratios". Child Vision Research Society, Coleraine, Northern Ireland, 2017. (Joint-winner, Best Poster presentation).

"What happens to the accommodative response after sustained near tasks in young uncorrected hyperopes?" The Association for Research in Vision and Ophthalmology annual meeting, Honolulu, Hawaii, 2018.

Conference (oral presentation):

Ten-minute oral presentation of PhD project to non-expert audience. "Life Beyond the PhD conference", Cumberland Lodge, Windsor, England, 2017. (Emerged winner of a competition organised by Ulster University Doctoral College to sponsor PhD student for this annual conference.