The Role of Near Adaptation in Myopia Development

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Abstract

Prolonged near work is associated with myopia development in children and young adults but the reason underlying this association is unknown. Two potentially important factors are the near work induced ocular adaptations of contrast and accommodative adaptation. This study measured the degrees of contrast and accommodative adaptation during and following reading in myopic and emmetropic children and young adults in Singapore, where myopia is highly prevalent.

Reading caused significantly greater contrast and accommodative adaptations in myopic children and myopic young adults compared to that measured in emmetropes of comparable ages. The adaptations were greater in magnitude in children than young adults, suggesting that children are more susceptible to ocular changes induced by reading and thus are potentially at greater risk of adverse refractive outcomes from these adaptations.

In addition to the magnitude of the adaptations the regression time of these adaptations, (i.e. their durations) are also important. Longer accommodative adaptation regression times were measured for myopic children than for emmetropic children. Although the regression of contrast adaptation was not measured, its duration may likewise be important. The refractive effects of both of these adaptations are likely to be cumulative across the day and this could promote myopia in susceptible individuals performing considerable amounts of near work.

Whether the type of text read affected the magnitude of the adaptations was also explored. Given the high prevalence of myopia in Chinese children and the fact that Chinese text is more complicated to write than English text, it was hypothesized that Chinese text would induce greater adaptation. However, both Chinese and English text produced similar amounts of accommodative and contrast adaptation in young adult subjects.

We propose that children who spend prolonged periods reading at a young age are most vulnerable to near work induced adaptations and hence near work induced myopia. Both Chinese and English texts produce these effects and we propose that these adaptations are likely to occur for all types of common reading texts.

Statement of Original Authorship

This is to certify that the work contained in this thesis represents my own work. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made. The work in this thesis has not been previously submitted for a degree or diploma at any other higher education institution.

Yeo Chwee Hong (Anna)

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CHAPTER1

INTRODUCTION AND LITERATURE REVIEW

1 Introduction

The rapid increase in the prevalence of myopia in developed countries with intensive and competitive education systems indicates that there is a strong environmental impact on refractive development (Lin, Shih, Tsai et al. 1999; Lin, Shih, Hsiao et al. 2001). Epidemiological correlation based studies suggest that lengthy periods spent performing near work is likely to be a contributory factor to the high myopia levels that are observed (Saw, Hong, Zhang et al. 2001; Saw, Wu, Seet et al. 2001). Here, the distance at which the near work is performed and the duration of the reading task appear to be critical factors (Ip, Saw, Rose et al. 2008).

Animal studies demonstrate that a good quality visual signal is crucial for normal visual development, as visual image deprivation created by diffusers or defocus produced by lenses at the critical stage of development induce myopia. It is believed that form deprivation open-loops the emmetropization system, preventing critical retinal error signals that fine-tune eye growth, thus leading to uncontrolled axial elongation [reviewed in (Wallman and Winawer 2004)]. Emmetropization is the process of eye development in both humans and other animals that involves an active matching of the axial length of the eye to the optical power of the cornea and lens [reviewed in (Wildsoet 1997)]. This process should act to control eye growth and prevent the development of refractive error in the first few years of the animal's life (Gwiazda, Thorn, Bauer et al. 1993a). However, this process can be disrupted by environmental factors. For example to demonstrate the compensatory eye growth in animals using concave lenses, for a measurable change in eye growth to occur, the defocus durations must last at least 2 to 3 min (Zhu, Park, Winawer et al. 2005; Zhu and Wallman 2009). This finding has led to the suggestion that the retinal defocus signal is integrated over time (Wallman and Winawer 2004). The possible candidates for the retinal defocus integrator are retinal contrast and spatial frequency channel processes (Diether and Schaeffel 1999).

Contrast and spatial frequency adaptation is a phenomenon where prolonged inspection of high contrast gratings increases the contrast threshold for detecting gratings of similar spatial frequency and orientation and reduces the perceived contrast of subsequently presented gratings (Blakemore and Campbell 1969; Greenlee and Heitger 1988). This type of perceptual adaptation is paralleled by decreases in firing rates of the cortical neurons (Movshon and Lennie 1979; Albrecht, Farrar and Hamilton 1984). If the decreases in neuronal response occurred simultaneously at all contrast levels, the response gain would decrease and this would have a detrimental effect on vision, simply reducing sensitivity to all contrasts. However, experiments on animals show that there are some beneficial effects of contrast adaptation. These studies on single-unit neurons in the striate cortex of anesthetized cats (Ohzawa, Sclar and Freeman 1982; Ohzawa, Sclar and Freeman 1985; Sclar, Ohzawa and Freeman 1985) and monkeys (Sclar, Lennie and DePriest 1989) showed that contrast adaptation can shift the sensitivity such that the visual system re-centres its contrast response curve around the time-averaged contrast level, allowing neurons to encode contrasts that are relevant to the scene being viewed. (Gardner, Sun, Waggoner et al. 2005). This means adaptation allows the visual system to adjust response characteristics of cells to suit the prevailing stimulus conditions, thus providing improved discrimination at the cost of absolute intensity discrimination (Heinrich and Bach 2002a).

Due to the reduced contrast sensitivity and decrease in neuron firing rate that occurs, contrast adaptation has often been considered in terms of 'visual fatigue' (Maffei, Fiorentini and Bisti 1973; Barlow, Macleod and Meeteren 1976; Georgeson and Harris 1984) or 'neural fatigue' (Goldstein 2007) when the visual system is desensitized as a function of its own activity. The reduced neuronal activity implies a reduced retinal activity which stimulates a retinal error signal involved in the aetiology of myopia (Diether, Wallman and Schaeffel 1997). Since a good quality visual signal and high retinal activity (Norton 1990; Napper, Brennan, Barrington et al. 1997) is crucial for normal visual development, contrast adaptation may affect normal development of the eye if it is persistently experienced.

Near work tasks such as reading text involves looking at high contrast letters, which forms lines or rows of words. Viewing of this type of prolonged unchanging stimuli could induce contrast adaptation (Chen, Brown and Schmid 2006). It is thus possible that the contrast adaptation induced by prolonged reading could reduce the perceived image quality sufficiently to affect the emmetropization system and thus produce myopia and its progression in children. Contrast adaptation may be a transient response adapted to reading text, but with longer reading time and repeated near work, it may become a persistent retinal error signal in myopia development.

Another visual adaptation that is observed during near work is accommodative adaptation (where complete relaxation of the accommodation system fails to occur following prolonged near work) and this has also been suggested to play a role in myopia development [review in (Ong and Ciuffreda 1995; Chen, Schmid and Brown 2003)]. Near work induced accommodation effects are greater in myopes, with higher degrees of near work-induced transient myopia (NITM) and longer dissipation times measured than for emmetropes. Prolonged NITM creates distance blur and thus degrades the retinal image quality. Hence, accommodation adaptation has been suggested to be a possible reason for the association between near work and myopia development (Ong and Ciuffreda 1995; Ciuffreda and Vasudevan 2008).

This thesis explores the impact of these two near work induced adaptations (contrast and accommodation) on the visual function. The magnitudes of contrast and accommodative adaptation were measured for both emmetropes and myopes during reading. It also investigates the effect of different texts (Chinese vs English) on these adaptation processes since myopia prevalence tends to be high in South East Asian countires. As background to this research, myopia prevalence and its possible aetiology and the physiologic mechanisms of contrast adaptation and accommodative adaptation are reviewed.

1.1 Myopia definition, classification, socio-economic cost and aetiology

1.1.1 Definition of Myopia

Myopia is a refractive condition in which the images of distant objects are formed in front of the retina when the eye is in the un-accommodated or relaxed state (Figure 1.1). It occurs when the eyeball is too long or the refractive power is too great or a combination of both (Edwards and Lam 2004). More commonly, the axial length elongation is caused by vitreous chamber expansion (Grosvenor and Goss 1999).

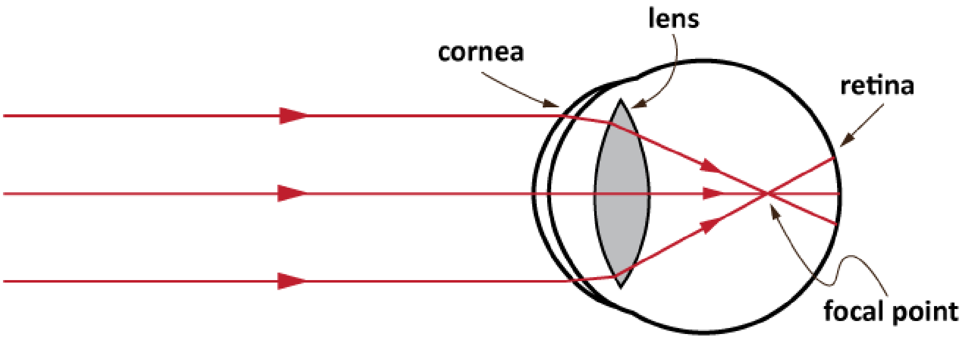


Figure 1.1 Myopia: the power of the eye's optical system is greater than is required to focus the light on the retina, and consequently the focal point is in front of the retina.

1.1.2 Classification of Myopia

There are several different ways to classify myopia (e.g. based on age of onset, clinical entity or progression pattern). Goss and Eskridge (Goss and Eskridge 1987) classified myopia based on clinical characteristics. They included simple myopia, night myopia, pseudo-myopia, pathologic myopia and induced myopia. Simple myopia is the most common type where there are no ocular structure anomalies other than the presence of small myopic temporal crescents. Night myopia refers to the shift towards myopia that occurs in darkness or under low illumination conditions. Pseudo-myopia is due to un-relaxed accommodation system or ciliary muscle spasm.

Pathological myopia usually refers to high myopia associated with degenerative changes at the posterior pole and/or retinal periphery. Induced myopia refers to myopia that is caused by external factors such as pharmaceutical agents or disease.

Grosvenor and Goss (1999) re-classified myopia on the basis of age-related onset, progression pattern and degree of myopia. Their four major types of myopia were congenital myopia (myopia present at birth, usually very high in degree), youth-onset myopia (onset at 5 or 6 yr of age, medium to high levels of myopia, stable from mid to late teens), early adult onset (onset after puberty but before 40 yr, low to medium levels of myopia) and late adult onset myopia (onset after 40 yr, associated with crystalline lens changes).

Other researchers (McBrien and Millodot 1986b; Gilmartin and Bullimore 1991; Strang, Winn and Gilmartin 1994) categorized myopia into two types: early-onset myopia (myopia develops before the age of 15 yr), and late onset myopia (myopia develops after the age of 15 yr) (Goldschmidt 1968). Some studies suggest that young adult myopes should be more appropriately classified as either progressing or stable to enable the study of factors that may be associated with myopia progression (Abbott, Schmid and Strang 1998; Vera-Diaz, Strang and Winn 2000). Morgan and Rose (2005) have termed the simple myopia that occurs in childhood, particularly during the school years in economically developed societies, as school myopia. This myopia has high prevalence rates in South East Asian countries such as Taiwan, Hong Kong and Singapore.

In the experiments that comprise this thesis, children and young adult myopes will be classified as progressing or stable. The myopia in children (age up to 12 yr) is by its very nature of early onset and progressing with the myopia usually stabilizing when young adulthood is reached. In this review of literature and discussion sections of the experiments, early-onset myopia (EOM) and late-onset myopia (LOM) which are common classifications used by other myopia researchers will be discussed.

1.1.3 Prevalence of Myopia

There are difficulties in comparing myopia prevalence values across studies because of differences in the age of participants, definitions of myopia, inclusion criteria and research methodology. Given this limitation, myopia prevalence data can give an indication of the effects of factors such as age, ethnicity, occupation and educational demands. The Baltimore Eye Survey and the Beaver Dam Study in the USA reported the prevalence of myopia in adults (aged 40-89 yr in the Baltimore Eye Survey and aged 43-84 yr in the Beaver Dam Study) to be 23% and 26%, respectively. However, more recent data published from the United States reported a higher prevalence of 38.4% among 20 to 50 yr old group (Vitale, Ellwein, Cotch et al. 2008). This is comparable to what was found in Singapore. In Singapore the prevalence rate was at 39% in a population of adults of slightly older age group (40 to 79 yr) (Wong, Foster, Hee et al. 2000). The prevalence of myopia among a group of young adult males, military conscripts (aged 16-25 yr) of different ethnic groups living in Singapore was 69% in Indians, 65% in Malays and 82% in Chinese (Wu, Seet, Yap et al. 2001). In contrast, the myopia prevalence of Finnish army conscripts was only 22% (Vannas, Ying, Stone et al. 2003). These prevalence data (summarized in Table 1) highlight the fact that sensitivity for myopia development varies with ethnic origin and education level.

In East Asian countries, it has been reported that myopia develops in children as young as 4 yr of age. This early development appears to be linked to educational demands and the commencement of schooling (Tan, Saw, Lam et al. 2000; Saw, Tong, Chua et al. 2005). By the time young adults go to university at 17 to 18 yr, the prevalence of myopia is an alarming 70% to 80% (Lam and Goh 1991; Matsumura and Hirai 1999; Lin, Shih, Hsiao et al. 2001; Saw, Tong, Chua et al. 2005). In addition, the higher the educational level attained, the higher the observed myopia prevalence (Chew, Chia and Lee 1988; Wu, Seet, Yap et al. 2001). Associated with the early age of onset, there is a corresponding increase in the prevalence of high and pathological myopia which has significant public health implications (Seet, Wong, Tan et al. 2001).

Table 1.1 Prevalence of Myopia and Risk Factors

Study (year)	Study Group / Location	No of Subjects	Age (year)	Prevalence	Possible Associating Factor
(Chow, Dhillon, Chew et al. 1990)	Singapore medical students	128	20-22	82%	IQ and near work
(Tay, Au Eong, Ng et al. 1992)	Singaporean males	421,116 (based on medical classification)	15-25	26% in 1974-1978; 43.3% in 1987-1991; Overall 30.4%	Education
(Lam, Goh, Tang et al. 1994)	Hong Kong Chinese	220	40-44 45-49 50-54 55-59 60-64	46.2% 30% 31.6% 30.8% 22.2%	Not determined
(Wang, Klein, Klein et al. 1994)	Adult American	4926	43-84	26.2%	Not determined
(Katz, Tielsch and Sommer 1997)	Black and White American	5028	40-89	19.4% Black; 28.1% White	Education (for younger subjects only)
(Lam, Edwards, Millodot et al. 1999)	Hong Kong school children	142	6-17	62%	Not determined
(Zhang, Saw, Hong et al. 2000)	Xiamen countryside, China Xiamen city, China Singapore	132 104 146	6-7	3.9%, 9.1% 12.3%	Environment
(Wong, Foster, Hee et al. 2000)	Adult Singaporean Chinese, Tanjong Pagar District	1232	40-79	38.7%	Education

(Mavracanas, Mandalos, Peios et al. 2000)	Greek students	1738	15-18	36.8%	Hereditary but correlates with education level, intelligence and excessive near work
(Wu, Seet, Yap et al. 2001)	Singapore military conscripts	15,095	16-25	79.3%	Education
(Lin, Shih, Hsiao et al. 2001)	Taiwan school children	10889	7 12 15	20% 61% 81%	Rigorous education system
(Vannas, Ying, Stone et al. 2003)	Finnish army conscripts	3524	17-30; mean 19.2±1.2	22.2%	Education attainment and parental myopia
(Villarreal, Ohlsson, Cavazos et al. 2003)	Monterrey, Mexico	1035 school children	12-13	37%	Interaction between genetics and environmental factors
(Goh, Abqariyah, Pokharel et al. 2005)	Malaysian school children	4634 (70.3% Malay, 16.5% Chinese, 8.9% Malay)	7 (Chinese) 7 (All) 15 (Chinese) 15 (All)	20.9% 9.8% to 10% 65.4% 32.5% to 34.4%	Chinese race, gender, age, parental education
(Fan, Lam, Lam et al. 2004)	Hong Kong school children	7560 school children	Total 7 8 9 10 >11	36.71 ± 2.87% 28.9% 37.5% 43.1% 48.2% 53.1%	Interaction between genetics and environmental factors

In summary, myopia prevalence is higher in people of Chinese descent compared with people of other ethnicity. The age of onset seems to be getting younger amongst children living in countries with higher educational demands and earlier commencement of schooling. Myopia prevalence is greater in children living in these countries than those living in still developing countries and countries where less competitive educational demands are placed on children.

1.1.4 Socio-economic Cost of Myopia

The cost of myopia both to individuals and societies is enormous and includes both direct costs, such as spectacles, contact lenses and refractive surgery to correct myopia, and indirect costs, such as vision loss due to associated pathologies. In the US, the cost of myopia in 1990 was estimated to be US$12.8 billion (Javitt and Chiang 1994). Due to the high prevalence of myopia in Singapore, the socio-economic cost of myopia in this country is also very high. It has been estimated that myopic Singaporeans spend US$90 million annually on spectacles alone and US$2.5 million annually on refractive surgery (Seet, Wong, Tan et al. 2001). These figures are expected to increase as the population of Singapore rises from 4.5 to 6.5 million in the next 40 to 50 years.

The indirect costs are related to ocular complications associated with myopia, such as peripheral retinal changes (Pierro, Camesasca, Mischi et al. 1992), open-angle glaucoma (Mitchell, Hourihan, Sandbach et al. 1999), cataract (Lim, Mitchell and Gumming 1999) and ocular complications that arise from myopia treatments (e.g. complications from refractive surgery). This amount is estimated to be US$2 to 2.5 million annually in Singapore (Seet, Wong, Tan et al. 2001). It is thus important to determine the aetiology of myopia so that the high prevalence rate and hence the socio-economic cost can be reduced.

1.1.5 Aetiology of Myopia

Despite the many risk factors (discussed in 1.1.5.1 and 1.1.5.2) that have been identified (Saw, Wu, Seet et al. 2001; Saw, Chua, Hong et al. 2002a; Saw, Chua, Hong et al. 2002b; Saw, Tan, Fung et al. 2004; Chong, Liang, Tan et al. 2005), the underlying causative factors involved in myopia development remain obscure. Conflicting theories exist as to the possible causes of myopia. These theories can be broadly grouped as genetic theories and environmental theories, and include genetic predispositions to environmental factors. The environmental factors that have received the most attention are near work and reading, and more recently, outdoor activities have been found to perhaps, be protective against myopia (Rose, Morgan, Ip et al. 2008). Epidemiological studies in Singapore associate high myopia prevalence with near activities and tuition classes during elementary school (Saw, Wu, Seet et al. 2001; Saw, Chua, Hong et al. 2002a).

1.1.5.1 Genetic Factors

There is a familial association between myopia and eye size, i.e., children with myopic parents tend to have longer eyes (Zadnik, Santariano et al. 1994) than children whose parents are non-myopic and children are more likely to be myopic if their parents are myopic as compared to children whose parents are non-myopic (Yap, Wu, Liu et al. 1993; Zadnik 1995; Pacella, McLellan, Grice et al. 1999; Mutti, Mitchell, Moeschberger et al. 2002a; Saw, Shankar, Tan et al. 2006). The correlations in refractive error between monozygotic twins are higher than those seen in dizygotic twins who are less genetically similar (Hammond, Snieder, Gilbert et al. 2001). However, twin studies on myopia and studies on within-family correlations in refractive errors have the confounding factor of shared environments and therefore it is not correct to claim from the findings of these studies that the cause of myopia is purely genetic in nature (Morgan and Rose 2005).

The discovery of potential gene loci associated with high myopia has increased the importance of genetic influences for this type of myopia (Young, Ronan, Alvear et al.

1998; Young, Ronan, Drahozal et al. 1998; Han, Yap, Wang et al. 2006; Hornbeak and Young 2009). There are at least 18 named loci that have been identified to be associated with myopia (Mutti 2010). Several loci have attached candidate genes that are related to collagen type, growth factors, mitochondrial function and early ocular organization (Mutti 2010). For example, a recent study found that insulin-like growth factor-1 gene polymorphisms were genetically associated with high degree (> -5.00 D) of myopia in a Caucasian family-based dataset (Metlapally, Ki, Li et al. 2010). Some of the myopia loci have been associated with refractive error as a continuous trait across a spectrum rather than just pathological amounts, but so far no candidate genes have been shown to account for even a modest fraction of the familiar risk of myopia, and most of the data are conflicting about whether a true association exists (Hornbeak and Young 2009). Furthermore, the precise functional significance of how any of these loci or candidate genes is related to myopia is unknown (Mutti 2010).

One challenge in the study of genes is the inability to correlate genotypic data with the histopathology in tissues such as human retina/sclera. Therefore animal models of myopia have been developed to be used as surrogates (Hornbeak and Young 2009). It is unclear how close experimentally induced myopia in animals may be to physiologic myopia in humans.

1.1.5.2 Environmental Factors

The increased prevalence of myopia among younger age children in East Asia countries indicate an early impact of environmental factors (Morgan and Rose 2005). The age of myopia onset is becoming earlier and the progression rate much faster than previously observed (Saw, Tong, Chua et al. 2005). The environmental factors most strongly linked to myopia are the competitive educational system such as tuition classes during the elementary school and the increased near work activities in children (Saw, Wu, Seet et al. 2001; Saw, Chua, Hong et al. 2002a).

In addition to near work, other environmental factors have been proposed to be involved in myopia. Foods made of refined cereals and sugars are thought to interact with hormonal regulation and increase vitreous chamber growth (Cordain, Eaton, Brand Miller et al. 2002). It has been suggested that early exposure to night lights is myopigenic (Quinn, Shin, Maguire et al. 1999), but this finding was not replicated in later studies (Gwiazda, Ong, Held et al. 2000; Zadnik, Jones, Irvin et al. 2000; Saw, Wu, Hong et al. 2001; Saw, Zhang, Hong et al. 2002). One factor suggested recently to be protective is outdoor activities as an increased amount of time spent outdoors was found to be linked to less myopia (Rose, Morgan, Ip et al. 2008). This suggests that high light levels, with resulting pupil constriction and associated increased depth of field (lessening blur) and increased retinal dopamine release, may be an important factor to ameliorate myopia development (Morgan and Rose 2005; Rose, Morgan, Ip et al. 2008).

1.1.5.3 Genetic Susceptibility to Environmental Factors

A theory that may reconcile genetic and environmental evidence is that common myopia occurs due to a genetic susceptibility to the effects of near work activity. For instance, a susceptible child who performs the same level of near work as a non-susceptible child has a higher risk of myopia development. In this case, both heredity and environment are important, but the trait inherited is sensitivity to the myopigenic effects of near work rather than myopia itself (Goss 2000; Mutti, Mitchell, Moeschberger et al. 2002a). However, recent findings on environmental factors seem to change the belief that reduced involvement in outdoor activities is more important a risk factor than near work in myopia development or progression (Rose, Morgan, Ip et al. 2008; Mutti 2010). Therefore, while searching for a genotype in increased myopia susceptibility, consideration is needed to assess the interactions between genetic influences and environmental factors such as early age near work and now outdoor activities (Hornbeak and Young 2009).

1.2 Emmetropization and Myopia Development

Myopia research conducted using animal models has contributed to the understanding of normal eye growth processes and the impact of environment on refractive error development. In all vertebrate species, the eyes at birth or hatching are ill matched to the focal lengths of their optics [reviewed in Wallman and Winawer (2004)]. All eyes grow to emmetropia during the postnatal period - this process is called emmetropization. However, this process can be both modified (e.g. using lenses) and disrupted (e.g. using diffusers). For example, putting a concave lens in front of a young animal's eye shifts the image plane behind the retina. In order to regain sharp focus, the eye elongates to shift the image plane back to the retina, thus resulting in myopia (Figure 1.2). Eyes that experience poor vision due to form deprivation and hyperopic defocus show changes in the normal pattern of eye growth [reviewed in Wallman and Winawer (2004)]. Therefore, for normal visual development, a good quality visual signal is critical.

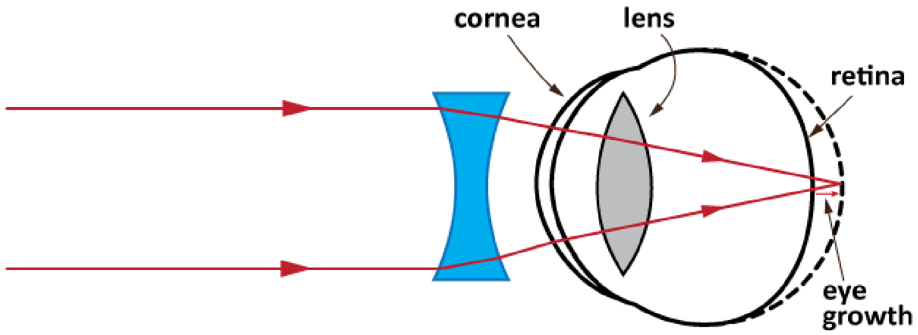


Figure 1.2 A concave lens placed in front of the eye pushes the image plane behind the retina, resulting in a hyperopic defocus. To regain sharp focus, the eye is lengthened by increasing the rate of growth or by remodelling of the sclera at the posterior pole of the eye, and the retina is pulled back by the thinning of the choroid.

Conditions that affect the quality of the retinal image such as neonatal ptosis, fused eyelids and corneal opacification are associated with myopia. The visual deprivation that results from these conditions is thought to disrupt the normal emmetropization process and leads to excessive eye size, causing myopia (Robb 1977; Hoyt, Stone and Fromer 1981; Gee and Tabbara 1988). There is also evidence of changes to ocular dimensions in young adults eyes associated with the progression of myopia. Thus, the young adult eye is still subject to visually guided growth – although to a lesser degree than the neonatal eye (McBrien and Adams 1997; Troilo, Nickla and Wildsoet 2000).

That form deprivation results in myopia is strongly supported by animal studies, including studies involving the use of lid suture and diffusers in chickens and non-human primates to produce myopia (Wiesel and Raviola 1977; Wallman and Turkel 1978; Troilo and Judge 1993; Siegwart and Norton 1999; Smith and Hung 2000) In chicks, as long as vision is obscured, the vitreous chamber will continue to elongate - becoming up to 25% longer than normal (Wallman and Adams 1987). When diffusers are removed, the choroid thickens, the rate of ocular elongation slows and refractions return to normal (Siegward and Norton 1999; Smith and Hung 2000).

Further observations indicate that such control is largely local, i.e. predominantly occurs within the eye. For example, form deprivation myopia in both monkeys and chicks takes place even after optic nerve section interrupts the direct pathway from retina to brain (Raviola and Wiesel 1985; Troilo, Gottlieb and Wallman 1987). Partial diffusers induce excessive eye growth only along the ocular direction corresponding to the occluded visual field (Hayes, Fitzke, Hodos et al. 1986; Wallman, Gottlieb, Rajaram et al. 1987). Therefore, control of eye growth seems to come from the retina. The retina encompasses an entire sensorimotor apparatus which may both encode the blur and move itself forward and backward within the eye by expansion and contraction of the choroid (Wallman and Winawer 2004).

1.2.1 Defocus Signalling in the Retina

Since the control of eye growth is thought to start at the retina, it has been proposed that the signals for growth produced by the retina through the choroid to the sclera form a signaling cascade - amacrine cell processing has been implicated in this (Wallman and Winawer 2004). Amacrine cells have complex visual responses in that they release neurotransmitters (glycine and GABA) and neuromodulators such as dopamine, serotonin, acetylcholine, adenosine and nitric oxide (Kolb 2003). The amacrine cells have profound effects on eye growth when they are selectively disabled with pharmacological treatments (Wildsoet and Pettigrew 1988; Fischer, Morgan and Stell 1999).

The most studied candidate retinal neuron for myopia development is the dopaminergic amacrine cell. Form deprivation in both monkey and chick leads to decreased dopamine production (Luvone, Tigges, Fernandes et al. 1989; Stone, Lin, Laties et al. 1989). In addition, a dopamine agonist reduces form-deprivation myopia to some extent in monkeys and in chicks (Stone, Lin, Laties et al. 1989; Luvone, Tigges, Stone et al. 1991; Schmid and Wildsoet 2004), and a dopamine antagonist enhances it (Schaeffel, Bartmann, Hagel et al. 1995). It has been proposed that retinal amacrine cells release dopamine, affecting the retinal pigment epithelium, which then determines eye growth (Ohngemach, Hagel and Schaeffel 1997). However, several pieces of evidence speak against the importance of dopamine in myopia development. Firstly, dopamine concentration did not change in opposite directions in response to positive and negative lens defocus (Bartmann, Schaeffel, Hagel et al. 1994; Schaeffel, Bartmann, Hagel et al. 1995). Secondly, when diffusers were removed from form deprived eyes, ocular elongation stopped abruptly but dopamine levels returned to normal only slowly (Pendrak, Nguyen, Lin et al. 1997). Finally, complete depletion of dopamine did not prevent the response of either myopic or hyperopic blur, but caused an overall reduction of the eye size in fish (Kroger, Hirt and Wagner 1999).

Two other retinal molecules that show opposing changes in their concentrations in response to the signs of defocus are retinoic acid and glucagon. Retinoic acid concentration increases in form deprived chicks (Seko, Shimizu and Tokoro 1998) and in negative lens induced myopia but decreases in guinea pigs exposed to positive lens induced hyperopia (McFadden, Howlett and Mertz 2004). Injecting the eye with a glucagon agonist inhibits negative lens compensation, whereas a glucagon antagonist inhibits positive lens compensation (Feldkaemper and Schaeffel 2002).

Even though there are many studies investigating the neuro-transmitters and neuro-modulators in eye growth, the mechanism of eye growth remains obscure. The proposed model is that the time integrated change in retinal defocus provides a signal for modulation of neuromodulator release. An increase in retinal defocus over time decreases the rate of retinal neuromodulators release which in turn decreases the rate of proteoglycan synthesis and reduces scleral structural integrity, thus resulting in axial elongation and myopia (Hung, Fiedler and Ciuffreda 2010). This is the type of change expected in mammals. The chick mechanism would probably differ.

1.2.2 Importance of Contrast and Spatial Information in Eye Growth

Since emmetropization is visually guided, the quality of the visual image during the critical eye growth period is very important. Visual images within the environment are made up of a variety of spatial frequencies and contrasts which form the fundamental information that is vital to emmetropization (Bartmann and Schaeffel 1994; Schmid and Wildsoet 1997a; Schmid, Brinkworth, Wallace et al. 2006).

In form deprivation myopia, the amount of myopia that develops is directly related to the extent of image degradation as measured in terms of both contrast degradation and differential loss of spatial frequency information (Bartmann and Schaeffel 1994). Chicks wearing the densest diffuser (of modulation transfer of 10% at spatial frequency > 4 cpd) produced about 12.50 D of myopia, while with the least dense diffuser (with modulation transfer of 30% at spatial frequency > 4cpd) produced 4.0 D of myopia (Bartmann and Schaeffel 1994). Modest reductions in object contrast from 0.1 log units at 0.125 cpd to 0.75 log units at 8 cpd produced by diffusers for a 95% contrast target were sufficient to cause deprivation myopia of up to 4 D in 2 out of 3 monkeys (Smith and Hung 2000). In terms of preventing form deprivation myopia when chicks were exposed to a restricted high contrast environment (78%) during a short period of diffuser removal, they became 1.5 D less myopic compared to when they were restricted to a low contrast (9%) environment (Schmid and Wildsoet 1997a). Using a similar protocol, Schmid and

Wildsoet found that the mid spatial frequency 0.86 cpd target prevented more myopia than targets of lower (0.086 cpd) and a higher (4.3 cpd) spatial frequency, and they hypothesised that to account for this, the mid spatial frequency target might produce more retinal activity (Schmid and Wildsoet 1997a).

It has been suggested that the contrast of a target must reach a threshold value for the emmetropization signal to function. In their study on chicks, Schmid, Brinkworth, Wallace et al (2006) reported that for contrast levels of 4.2% and lower, a 1.6 cpd square-wave grating target produced relative high myopia similar in degree to that produced by a blank (0%) target. For the range of contrasts between 8.5% and 33.5%, relative myopia occurred in 65% of animals. Targets in this contrast range should be visible as the contrast threshold of chicks was found to be 4.2% (Schmid, Brinkworth, Wallace et al. 2006), yet myopia developed in more than half of the animals.

1.3 Contrast Sensitivity Function

Since contrast and spatial frequency are important parameters in visual information, contrast sensitivity function (CSF) measurement is important to determine their effects on myopia. CSF is obtained by measuring the contrast sensitivity for sine wave gratings at a range of spatial frequencies. The chief merit of the human CSF is that it provides considerably more information than visual acuity: the CSF is a description of the visual system's sensitivity to coarse, medium and fine detail, while visual acuity quantifies sensitivity to fine detail only.

Contrast is expressed as a percentage from 0% to 100%. It is often measured using the Michelson definition, which is

$$contrast = \frac{Lmax - Lmin}{Lmax + Lmin}$$

where Lmax and Lmin are the maximum (white bars) and minimum (black bars) luminances of the grating. Similarly, if letter charts are used to test for letter contrast, Lmin is usually referred to the dark letters and Lmax is the white background.

The amount of contrast a person needs to see a grating target is called the contrast threshold. Contrast sensitivity is the inverse of the contrast threshold. Usually, contrast threshold and contrast sensitivity are expressed on logarithmic base 10 scales. Thus, a contrast threshold of 0.01 (1%) corresponds to a log contrast threshold of -2, a contrast sensitivity of 100, and to a log contrast sensitivity of 2.

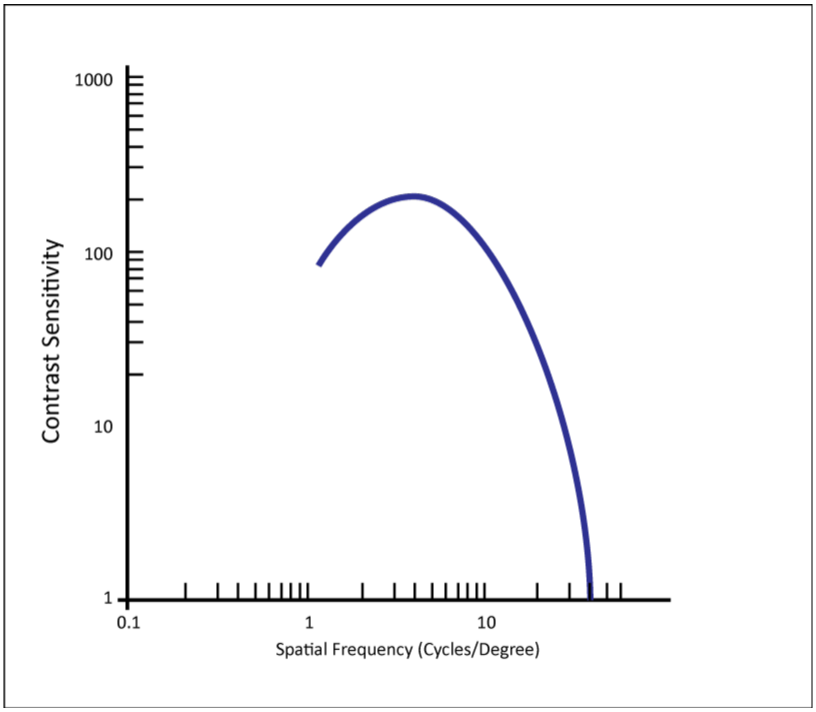


Figure 1.3 Contrast Sensitivity Function of a Human Subject. Adapted from Fig 7-8, (Schwartz 1999)

A typical contrast sensitivity function (CSF) of a human subject is a band-pass function (Fig.1.3) with the coordinates plotted in log units. Since a grating target consists of alternating bright bars and dark bars, the width of the bars is specified by the spatial frequency of the grating. The spatial frequency represents the number of cycles per degree (cpd) of visual angle, with 1 cycle comprising a bright bar and a dark bar. Spatial frequency with a high number, say 30 cpd, represents narrower bars than one with a low number, say 3 cpd. The peak contrast sensitivity of a human subject occurs in the region of 4 cpd. This means the human visual system will detect gratings of 4 cpd at a contrast lower than that required for the detection of other frequencies.

For a young, healthy adult, the high-frequency cutoff is 40-60 cpd. The high-frequency cutoff is limited by the inherent optical aberrations and the packing density of retinal photoreceptors (Schwartz 1999). The low-frequency drop off, on the other hand, is due to lateral inhibition (Schwartz 1999), a process by which responses in one region in a receptive field oppose the responses from another area (Levine and Shefner 1991). The shape of the CSF depends on a number of factors including the mean luminance of the grating (Levine and Shefner 1991; Regan 2000), whether the luminance profiles of the gratings are sinusoidal or square wave (Levine and Shefner 1991), the level of defocus (Woods, Strang and Atchison 2000) and the clarity of the media and the optics of the eye (Schwartz 1999).

Contrast sensitivity in young children is lower than in adults across all spatial frequencies (Beazley, Illingworth, Jahn et al. 1980; Bradley and Freeman 1982; Scharre, Cotter, Block et al. 1990). Children’s grating acuity has been reported to reach adult values at various ages, including by 6 yr (Ellemberg, Lewis, Liu et al. 1999), > 7 yr (Scharre, Cotter, Block et al. 1990), 8 yr (Gwiazda, Bauer, Thorn et al. 1997) and 9 yr of age (Adams and Courage 2002). A detailed review concluded that contrast sensitivity becomes fully mature between the ages of 8 to 19 yr (Leat, Yadav and Irving 2009). Since the range is large, it is still difficult to ascertain the ‘mature’ age for CSF. The reductions found in young children may be due to non-visual factors, such as attention, motivation and adopting different criteria in subjective testing (Abromov, Hainline, Turkel et al. 1984), or to immature neural development (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997).

1.4 Visual System as a Fourier Analyzer

The concept of contrast sensitivity formation led researchers to regard the visual system as acting like a Fourier analyzer. The visual system is thought to break the visual world down into its spatial frequency components (Figure 1.4), and then reassemble these components to produce a unified spatial percept (Blakemore and Campbell 1969). This concept was supported by an experiment conducted to determine an observer's contrast sensitivity after the observer had adapted to a grating with a similar orientation to the test grating at a specific spatial frequency (Blakemore and Campbell 1969). Blakemore and Campbell found there was a discrete reduction in sensitivity at the specific frequency to which the observer had adapted. The experiment was conducted at spatial frequencies of 3.5, 5, 7.1, 10 and 14.2 cpd and the adaptation characteristics showed relative threshold elevation at these spatial frequencies. When the contrast sensitivities were plotted at these frequencies, they resembled a number of narrow spatial frequency channels being enveloped by the contrast sensitivity function, an example of which is shown in Figure 1.4.

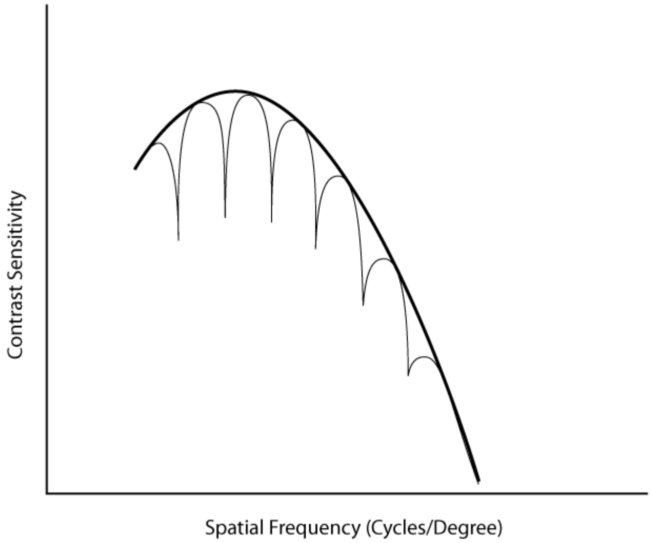


Figure 1.4 Contrast sensitivity function can be thought of as forming an envelope for encompassing a number of independent narrow spatial frequency channels. Adapted from Schwartz (1999)

This led to the hypothesis that there is a large number of separate channels in the visual system (Campbell and Robson 1968). Each of the hypothetical channels is "tuned" to a relatively narrow range of spatial frequencies. Thus, different channels are specific for low, mid and high spatial frequencies (Levine and Shefner 1991). Blakemore and Campbell also observed that a number of the properties of the adaptation effect correspond to the measured responses of the neurons of the visual cortex of the cat (Blakemore and Campbell 1969). These cortex neurons respond to elongated stimulus of a limited band of spatial frequencies (Campbell, Cooper and Enroth-Cugell 1969) and show orientation selectivity (Hubel and Wiesel 1962; Campbell, Cooper and Enroth-Cugell 1969); the adaptation effect is both spatial frequency and orientation specific. Thus, there is evidence of physiological correlates with the psychophysical experiments.

When we view a stimulus with a specific property (e.g. at a specific orientation and spatial frequency), neurons tuned to that property fire, and if viewing continues for long enough, these neurons adapt. The adaptation has two components: (1) the neuron's firing rate decreases, and (2) the neuron fires less when that stimulus is immediately presented again (Goldstein 2007). If these adapted neurons have anything to do with perception, adaptation of neurons that respond to a certain orientation, say horizontal, should result in the perceptual effect of becoming less sensitive to horizontal stimuli. The adaptation effect results in a decrease in the firing rate and this probably indicates firing fatigue in the neurons (Goldstein 2007). The adaptation of these neurons correlates well with the psychophysical properties of contrast adaptation, which is to be discussed in 1.5.

The best stimuli for studying selective adaptation are gratings. Gratings have a number of properties, including bar thickness: inversely relationed to spatial frequency, the orientation of the bars and the contrast between the bars. In this thesis, the term contrast adaptation is used for the selective adaptation to contrast, spatial frequency and orientation of the gratings.

1.5 Contrast Adaptation

1.5.1 Adaptation Effects

Contrast adaptation was first described by Gilinsky (1968), who reported that adaptation to a grating for about 5 s raises the identification threshold of spatial gratings with the same orientation that lasted for about 11 s. Subsequent studies confirmed that the reduction in perceived contrast is strongest for test stimuli that have the same orientation (Blakemore and Campbell 1969; Blakemore and Nachmias 1971) and spatial frequency (Pantle and Sekuler 1968; Blakemore, Muncey and Ridley 1973) as the adapter. Contrast threshold increases at spatial frequencies close to that of the adapting stimulus (Blakemore and Campbell 1969; Blakemore, Muncey and Ridley 1973; Georgeson and Harris 1984). The degree of adaptation is stronger for a higher contrast than a lower contrast adapting pattern (Blakemore and Campbell 1969; Blakemore, Muncey and Ridley 1973). For example, Blackmore and Campbell found that there was a temporary fivefold increase in contrast threshold after exposure to a high contrast grating of 1.25 log units above threshold as compared to a lower contrast gratings of 0.75 log units above threshold of the same orientation and spatial frequency (Figure 1.5).

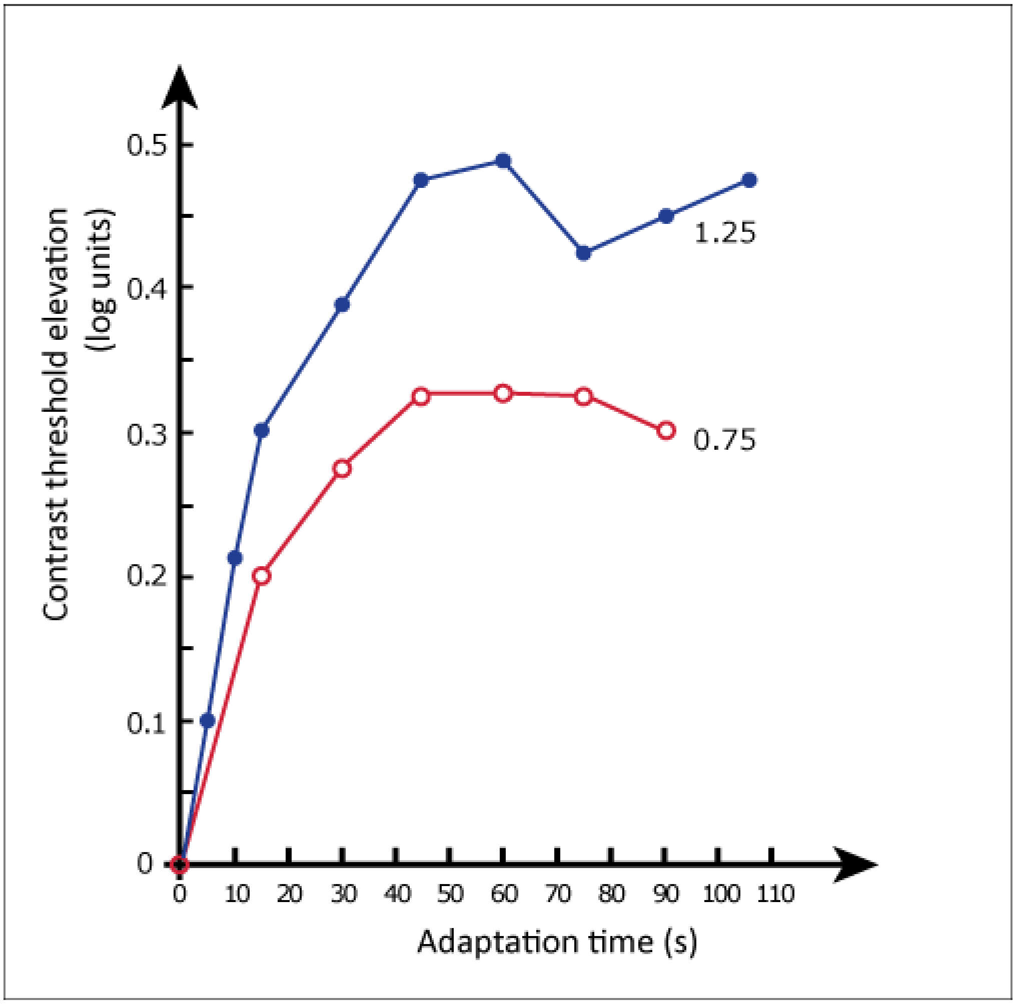


Figure 1.5 The initial elevation of threshold plotted against adaptation time of observer F.W.C. The adapting grating was 15 cpd at 1.25 and 0.75 log units above threshold, represented by filled and open circles respectively. The initial increase in threshold reached its maximum after 45 to 60 s adaptation. Both the adapting and test gratings were of the same spatial frequency and orientation (Adapted from Blakemore and Campbell, 1969).

In addition, adaptation is effective, although weakened, when the adapter and test stimuli are presented to different eyes (Blakemore and Campbell 1969; Maffei, Fiorentini and Bisti 1973). Both orientation specificity and inter-ocular transfer suggest a cortical locus for the perceptual effect because orientation tuning and binocular responses first occur in V1 (Blakemore and Campbell 1969).

Contrast threshold was also found to be elevated at spatial frequencies of 2, 3 and 5 cpd after reading single-spaced text on a video display unit (VDU) (Lunn and Banks 1986). Seven adult subjects were recruited to read stories displayed as single-spaced text on the VDU for 10 min. Adaptation, induced by reading the lines of text at 2.6 cpd, reduced sensitivity to spatial frequency in the range of 2 to 6 cpd. The authors suggested that the loss of sensitivity to these frequencies that control the reflexive accommodation systems would lead to the frequent complaints of VDU operators concerning blurred vision and difficulties in focusing after several hours of VDU-related work (Lunn and Banks 1986).

Another study found a similar positive contrast adaptation effect after 10 and 60 min reading of VDU displayed text (Magnussen, Dyrnes, Greenlee et al. 1992). The text was defined by the height of lower-case characters and the line spacing to form 1.45 cpd and the line elements of the individual character to form 4.5 cpd. Contrast thresholds were measured with sinewave gratings of these two spatial frequencies. Contrast sensitivity impairments in the order of 0.4 to 0.7 log unit were observed. The sensitivity impairment decayed as a power function of time, with time required to recover from adaptation approximately corresponding to the reading times. The authors proposed that the contrast adaptation might induce visual fatigue via sensitivity impairment of low-to-medium spatial frequency mechanisms which control the reflexive accommodative response of the eye to complex patterns.

1.5.2 Time of Adaptation and Recovery

Most studies agreed that recovery time increases with inspection or adaptation time (Blakemore, Muncey and Ridley 1973; Rose and Evans 1983; Magnussen and Greenlee 1985; Georgeson and Georgeson 1987), with longer recovery time found following prolonged inspection. Contrast adaptation could take up to hours to recover to baseline (Blakemore, Nachmias and Sutton 1970; Huggelund and Hohmann 1976; Mecacci and Spinelli 1976). For example, it takes about 90 min for the adaptation effect to recover to baseline level after a 20 min adaptation (Rose and Evans 1983) and several hours of recovery after 30 min adaptation (Blakemore, Nachmias and Sutton 1970). The recovery time between the two studies in the examples above was not proportionate because the testing environments were different. In the study of Rose and Evans, the contrast of the adapting grating was 0.4 while the adapting contrast in the study of Blakemore et al was 0.72. The higher adapting contrast leads to a stronger adaptation and probably a longer recovery time.

When comparing recovery time and time taken to reach saturation, recovery time depends on the saturation time (Magnussen and Greenlee 1985). The quicker a person takes to reach the maximum adaptation effect, the quicker the recovery time. Although it was originally suggested that the effect of adaptation to contrast saturates after as little as 40 s (Blakemore and Campbell 1969), Magnussen and Greenlee demonstrated that for an adapting contrast of 0.6, thresholds continue to rise for up to 30-60 min of adaptation (Magnussen and Greenlee 1985). The difference in saturation times found in the two studies described above could be due to the differences in the contrast of adapting stimuli, the method of contrast measurement and the subject's susceptibility to adaptation. In order to test the limit of contrast adaptation, Magnussen and Greenlee (1985) engaged 2 subjects to participate in a marathon adaptation. They found that individual growth and decay functions of the aftereffect have approximately the same slopes (solid and open circles in Figure 1.6). Decay functions following 2 and 10 min adaptation were also measured for subject RH (solid squares and triangles respectively), thus showing that adaptation and recovery appear to be fairly symmetrical.

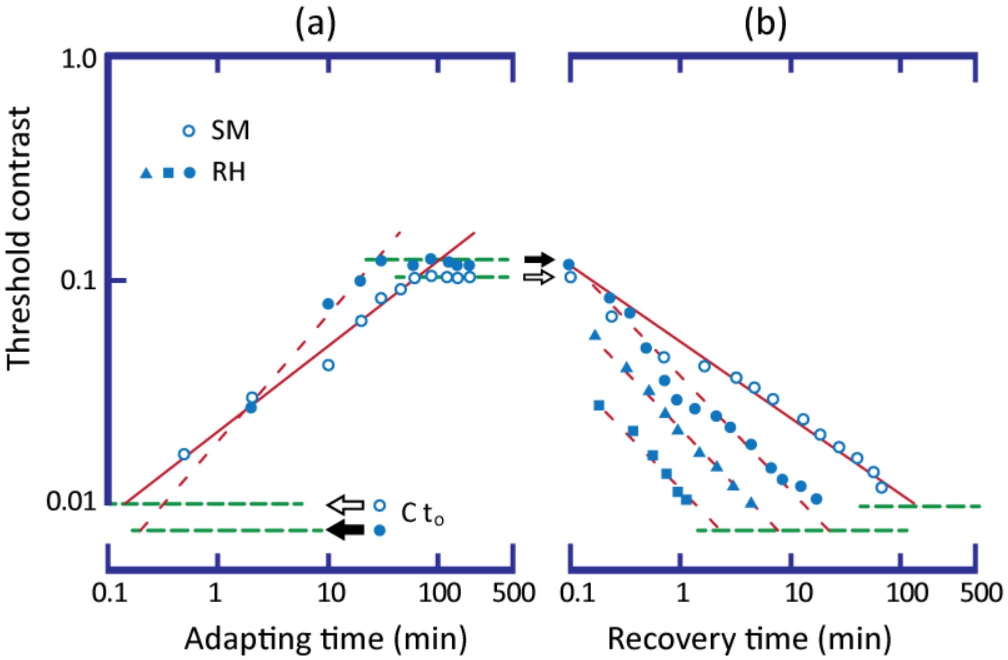


Figure 1.6 (a) Contrast required to detect a 6 cpd vertical grating as a function of time adapting to a high-contrast (0.6) grating of the same spatial frequency and orientation. Ct_0 indicate the un-adapted thresholds of 2 subjects, SM and RH.

(b) Time course of the recovery to normal sensitivity following adaptation.
Solid squares and triangles show the decay following 2 and 10 min adaptation measured for RH.
Adapted from Magnussen and Greenlee (1985).

Recovery time is affected if the eye is closed following the period of visual adaptation and the method of measurement. Adapting to a vertical grating for 1 hr (eyes stimulated between adaptation and test gratings) produced an effect that lasted for more than half an hour if the eyes were open and more than 3 hr if the eyes were blindfolded (Heggelund and Hohmann 1976). With varying adaptation duration of 30, 60 and 90 min, Mecacci and Spinelli (1976) found that contrast threshold recovered 2 hr after adaptation, which did not correlate with the evoked potential method, which recovered from adaptation 20 min later. Recovery time measured using a threshold adjustment method was also longer than the two-interval forced-choice paradigm due to the contamination by the response time required for the observer to adjust a setting (Greenlee, Georgeson, Magnussen et al. 1991).

1.5.3 Spatial Frequency Adaptation

In spatial frequency adaptation, the amount of threshold elevation is less if the orientation and spatial frequency of the test grating differs from that of the adapting grating (Pantle and Sekuler 1968; Blakemore and Campbell 1969; Blakemore and Nachmias 1971). This finding can best be explained by supposing that there are orientation-specific and frequency-specific channels in the human visual system, in which adaptation is not just an after-effect of prolonged excitation of a channel, but an after effect of prolonged inhibition by other channels or neurons (Dealy and Tolhurst 1974). This adaptation effect has also been taken as evidence for multiple separate channels in the visual system (see 1.4), each of which is sensitive to a narrow range of spatial frequencies (De Valois 1977; Goldstein 2007).

Greenlee and Heitger (1988) found no threshold elevation for spatial frequencies below 0.5 cpd after adaptation to various spatial frequencies from 0.09 to 9 cpd. The insignificant amplitude change in Visual Evoked Potential (VEP) and pattern electroretinogram (PERG) further confirmed that limited contrast adaptation occurs at 0.5 cpd (Heinrich and Bach 2002a).

In summary, initial magnitude of threshold elevation depends on the contrast and spatial frequency of the adapting stimulus. Recovery time increases with the duration of the inspection (adaptation) or time to reach saturation (Blakemore, Muncey and Ridley 1973; Rose and Evans 1983; Magnussen and Greenlee 1985; Georgeson and Georgeson 1987). Both the magnitude and recovery time of contrast adaptation are also affected by the methods of how contrast thresholds are measured and whether the eye is closed or opened after adaptation.

1.5.4 The Origin of Contrast Adaptation

1.5.4.1 Cortical Neurons

For many years, contrast adaptation was thought to have its origin at the visual cortex alone since the cortical neurons respond to elongated stimulus of a specific orientation and spatial frequency (see 1.5.3) and often show inter-ocular transfer (Blakemore and Campbell 1969; Maffei, Fiorentini and Bisti 1973). Several physiological studies have shown that neurons in the cat's (Maffei, Fiorentini and Bisti 1973; Albrecht, Farrar and Hamilton 1984; Ohzawa, Sclar and Freeman 1985) and monkey's striate cortices (Sclar, Lennie and DePriest 1989) adapt to prolonged stimulation in a way generally consistent with expectations from psychophysical experiments, in that during prolonged high contrast stimulation, the responses of most cells exponentially decayed from a transient peak response to a sustained plateau response. For example, Maffei, Fiorentini and Bisti (1973) reported that for 1 min of adaptation, the recovery time varied from 20 s to about 2 min in some simple cells.

In another study, intracellular recording and current injections of the dLGN and visual cortical neurons found that adaptation to high contrast was followed by a prolonged period of reduced responsiveness to a low-contrast stimulus for about 5 to 80 s (Sanchez-Vives, Nowak and McCormick 2000). Compared with psychophysical estimates of human contrast adaptation, the time courses and magnitudes were similar in neurophysiologic studies (Figure 1.7) (Albrecht, Farrar and Hamilton 1984). Therefore, the response of cortical neurons to the prolonged presentation of a high contrast stimulus progressively decreases (adapts) with a time constant of seconds which correlates well with the psychophysical response of high contrast adaptation in human subjects. This effect is found to be more obvious in cortical simple cells as both the decay and recovery times are shorter in complex than in simple cells (Maffei, Fiorentini and Bisti 1973; Albrecht, Farrar and Hamilton 1984).

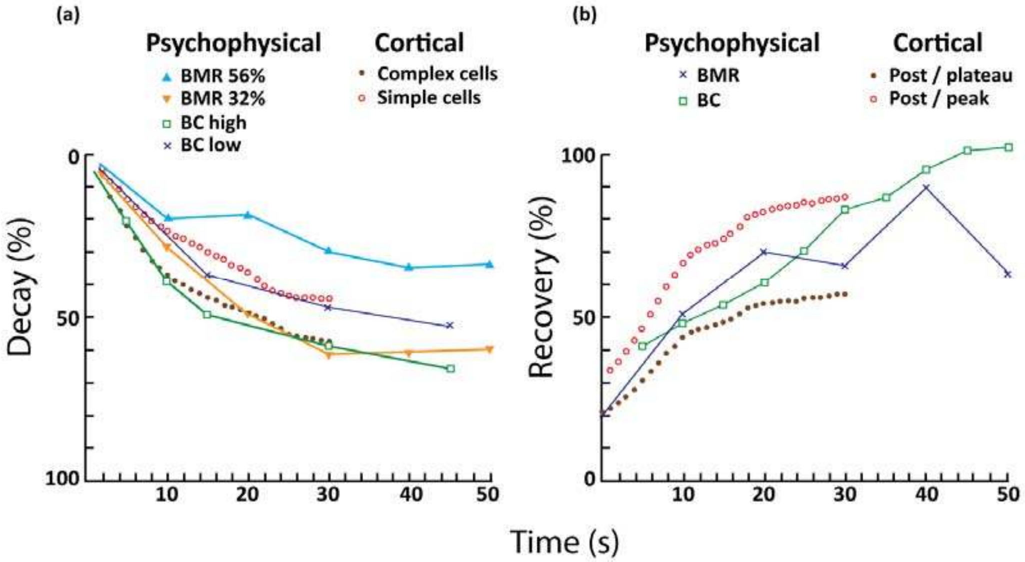


Figure 1.7 Comparison of several psychophysical estimates of contrast adaptation during adaptation (a) and recovery (b) with the neuro-physiological estimates of cortical cell contrast adaptation.

In (a), Albrecht et al (1984) plotted 4 psychophysical estimates of adaptation induction: two of these show the decay of contrast sensitivity produced by adaptation to different contrast levels, with two contrast at 32% (BMR 32%) and 56% (BMR 56%) obtained from Figure 1, Blakemore, Muncey & Ridley 1973) and the other two with 1.25 (BC high) and 0.75 (BC low) log unit above thresholds of a subject (Figure 3, Blakemore & Campbell 1969). They included two estimates of cortical cell adaptation and plotted the decay in the averaged normalized responses of the total population of simple cells (n = 64) and complex cells (n = 80) from their own experiments.

In (b), the same authors plotted the psychophysical estimates of recovery in contrast sensitivity BMR (Figure 3, Blakemore, Muncey & Ridley 1973) and BC (Figure 2, Blakemore & Campbell 1969); the neuro-physiological estimates of recovery were taken from the averaged normalized responses of the total population of cells (both simple and complex) during the post-adaptation interval; these post-adaptation responses were expressed as a percentage of (a) the peak response of the pre-adapt interval or (b) the plateau response of the pre-adapt interval. Adapted from Albrecht et al (1984).

Note the psychophysical and neuro-physiological estimates of both the adaptation and recovery are quite similar.

1.5.4.2 Retinal Neurons

Recent work has described contrast adaptation in the retina of salamander (Smirnakis, Berry, Warland et al. 1997; Kim and Rieke 2001), rabbit (Brown and Masland 2001; Baccus and Meister 2002), and macaque (Chander and Chichilnisky 2001). The slow contrast adaptation takes place over many seconds and is similar to the contrast adaptation recorded in the cortical neurons that correlates with the psychophysical studies.

There are two forms of contrast-adaptation in the retina: the faster process termed "contrast gain control" that occurs with an extremely short timescale of about 100 ms, and the slower process termed "contrast adaptation" that occurs over a longer timescale of 1 – 10 s (Baccus and Meister 2002) or more than 10 s (Smirnakis, Berry, Warland et al. 1997; Chander and Chichilnisky 2001; Kim and Rieke 2001). The fast form of contrast adaptation was inferred from differences in retinal ganglion cell response amplitude and kinetics with low and high contrast stimuli (Shapley and Victor 1978; Shapley and Victor 1981; Victor 1987; Benardete, Kaplan and Knight 1992). The function of contrast gain control is discussed in 1.5.6.

The slow contrast adaptation begins in the bipolar cells within the retina using either patch recording (intracellular recording of a slice of retinal preparation of tiger salamanders) (Kim and Rieke 2001) or receptive field stimulation and extracellular recording of rabbit retina (Brown and Masland 2001). Besides the bipolar cells, other cells such as some amacrine cells (Baccus and Meister 2002) and ganglion cells (Chander and Chichilnisky 2001; Kim and Rieke 2001; Baccus and Meister 2002; Solomon, Peirce, Dhruv et al. 2004) also show contrast adaptation, suggesting that slow contrast adaptation occurs at multiple sites within the retinal circuit (Brown and Masland 2001; Rieke 2001; Baccus and Meister 2002). Recording the action potentials of bipolar cells using high contrast checkerboard stimuli, Brown and Masland (2001) found that rate of adaptation is slower for larger stimuli than for smaller ones. In addition, slow contrast adaptation has been shown to affect the sensitivity of ON and OFF retinal ganglion cells differently (Chander and Chichilnisky 2001; Kim and Rieke 2001). These findings could be due to the retina containing different types of retinal neurons, which are tuned to different aspects of the visual scene (Brown and Masland 2001).

The slow contrast adaptation was potent in all magnocellular (M) cells but essentially absent in parvocellular (P) cells (Solomon, Peirce, Dhruv et al. 2004). Sminarkis et al, (1997) found that contrast adaptation in the retinal cells are spatially sensitive. Solomon et al (2004) found that adaptation recorded from the M cells was broadly tuned for spatial frequency and lacked orientation selectivity. A supporting claim on contrast adaptation occurring in the human retinal neurons came from a recent study which found that contrast adaptation could be induced monocularly, disputing that it occurs at "binocular sites" in the cortex (Ohlendorf and Schaeffel 2009).

In summary, both retina and striate cortex show contrast adaptation effects. Fast gain control (timescale of about 100 ms) is followed by the slow adaptation (timescale of 1 – 10 s) in the visual system. Contrast adaptation recorded from the M cells is broadly tuned for spatial frequency and lacks orientation selectivity whereas the contrast adaptation recorded from both simple and complex cells of the visual cortex displays orientation and spatial frequency selectivity which correlates well with the contrast adaptation in psychophysical studies using sine wave grating stimuli.

1.5.5 Mechanism of Contrast Adaptation

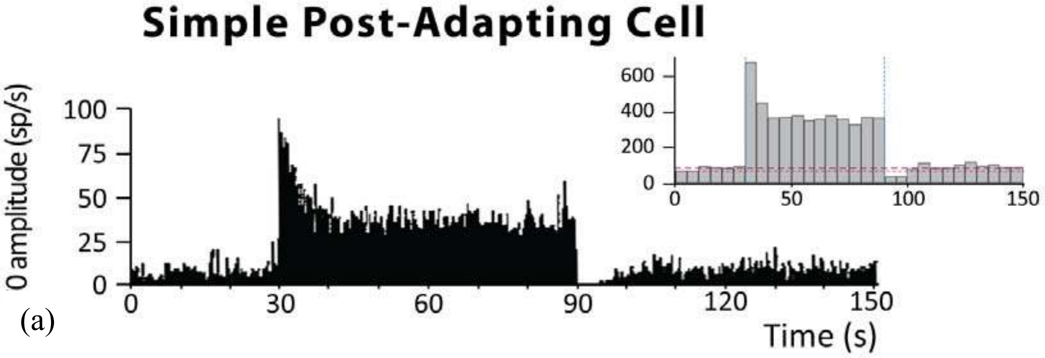
The mechanism of contrast adaptation is not understood. Several mechanisms have been proposed to explain contrast adaptation phenomena. One of the most common ideas in the literature concerns "visual fatigue" (Maffei, Fiorentini and Bisti 1973; Barlow, Macleod and Meeteren 1976; Georgeson and Harris 1984) or "neural fatigue" (Goldstein 2007) i.e. the visual system is "desensitized" as a function of its own activity. The mechanism of contrast adaptation has also been described as desensitization of a particular population of orientation sensitive neurons (Blakemore, Muncey and Ridley 1973) with specific spatial bandwidth or depression of activity in these neurons (Blakemore and Campbell 1969).

Some researchers have suggested that adaptation represents a deleterious result of processes such as ionic depletion, transmitter exhaustion or "fatigue" with no functional advantages (Barlow, Macleod and Meeteren 1976). Any test contrast presented after adaptation behaved as if one-third of the adapting contrast was subtracted from it, hence, conforming fairly closely to a simple subtractive process (Georgeson and Georgeson 1987). The subtractive process is equivalent to decreasing all input contrasts by a constant amount that is proportional to the adapting contrast over a wide range of adapting and test contrasts when adapting and test spatial frequencies are equal (Georgeson and Georgeson 1987).

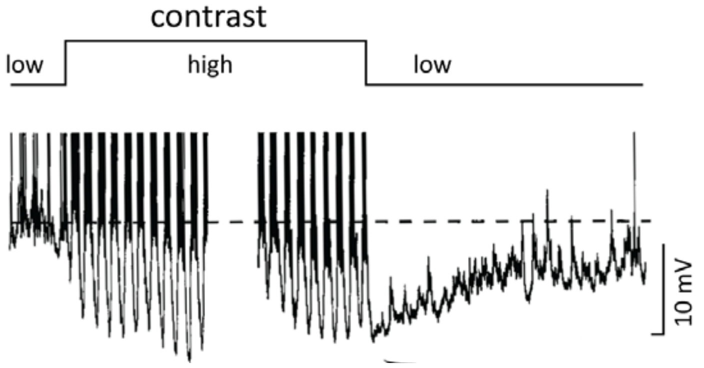
Some researchers, however, believe that the fatigue theory is not likely because firstly, high contrast is easier to discriminate following adaptation (Greenlee and Heitger 1988) and therefore it is unlikely that fatigue can lead to an improvement in performance in high contrast (see also 1.5.6). Secondly, adaptation does not occur following 30 ms or less of pattern adaptation; fatigue should affect the results of the short duration tests as well as long duration tests (Wilson and Humanski 1993). Thirdly, contrast adaptation is not affected by suppressing cell activity by the application of the inhibitory transmitter - GABA in the close vicinity to the cell (Vidyasagar 1990). Vidyasagar suggested that adaptation is not caused by the excitatory or inhibitory activity of the cell itself, and that adaptation could be the expression of reduced activity in a stimulus specific co-operative network whose effect on each individual cell is largely mediated through excitatory connections (Vidyasagar 1990).

Some scientists proposed that adaptation is a result of prolonged inhibition driven by other excited channels of the cortical cells (Dealy and Tolhurst 1974; Ohzawa, Sclar and Freeman 1985). Dealy and Tolhurst (1974) showed that a channel can be adapted by stimuli which probably do not excite it. In this case, a channel is inhibited by some units other than itself; this indicates that it could be adapted even when inactive. The mechanism on the prolonged inhibition at the synapses of the cortical cells is questionable as blockade of GABA (Vidyasagar 1990) or GABA receptors (McLean and Palmer 1996) does not block the firing rate reduction that follows adaptation to a high contrast visual stimulus.

The other mechanism put forward is the decrease in tonic synaptic excitation which leads to hyperpolarization of the membrane potential (Carandini and Ferster 1997; Sanchez-Vives, Nowak and McCormack 2000; Sanchez-Vives, Nowak and McCormick 2000). Visual cortex cells and dLGN neurons have been observed to exhibit a reduction in firing rate (extracellular recording) during prolonged presentation of high contrast visual stimuli (Sanchez-Vives, Nowak and McCormick 2000). This reduction was followed by a prolonged (5-80 s) period of reduced responsiveness to low-contrast stimuli called post-adaptation suppression (Figure 1.8a), an effect associated and positively correlated with a hyperpolarization of the membrane potential (by intracellular recording) and an increase in apparent membrane conductance (Figure 1.8b) (Sanchez-Vives, Nowak and McCormick 2000). The increase in membrane conductance is due to the activation of Ca^{2+} and Na^{+}-dependent K^{+} conductances (Carandini 2000; Sanchez-Vives, Nowak and McCormack 2000; Sanchez-Vives, Nowak and McCormick 2000). In other words, adaptation to high contrast leads to a hyperpolarization of the membrane potential (an intrinsic cell property) that contributes to the post-adaptation suppression of activity. However, not all cells recorded showed contrast adaptation as shown in Figure 1.8.



(a)



(b)

Figure 1.8 (a) Contrast adaptation and adaptation effects in a cortical simple cell. The adaptation protocol consisted of a pre-adaptation period of 30 s of low-contrast sinusoidal stimuli followed by an adaptation period of 30-60 s of a high-contrast stimulus. The post-adaptation period consisted of 60-120 s of a low-contrast stimulus. The peristimulus time histograms exhibited a decrease in action potential discharge rate during the adaptation period (adaptation) followed by a decreased responsiveness during the post-adaptation period (post-adaptation suppression). The insert is a non-normalized peristimulus time histograms with a bin width of 5 s.

Figure 1.8 (b) An example of membrane potential responses (raw traces) to the adaptation protocol. Intracellular recording from a cortical simple cell during the presentation of low (10%)-, high (60%)-, low (10%)-contrast grating sequence. A substantial portion of the response to the high contrast stimulus has been removed for illustrative purposes. Note the large (average of -11.9 mV) hyperpolarization of the membrane potential during the presentation of the high-contrast stimulus and the persistence of this hyperpolarization as an after-hyperpolarization following the transition back to the low-contrast stimulus.

Both figures are adapted from Sanchez-Vives et al (2000).

Through their experiments, Sanchez-Vives and co-workers argued that the fatigue model need not imply metabolic exhaustion. Instead, it could be defined as a form of self inhibition determined by the activities of the cell (Sanchez-Vives, Nowak and McCormick 2000). In terms of magnitude of adaptation measured, dLGN cells showed the least while complex cells showed the strongest adaptation. But, in terms of time course of firing decay, the adaptation time constant was significantly faster in simple and complex cells compared to dLGN cells (Sanchez-Vives, Nowak and McCormick 2000).

Similar gradual hyperpolarizations were also observed in the contrast adaptation of the retinal ganglion cells (Baccus and Meister 2002; Manookin and Demb 2006) and LGN neurons (Sanchez-Vives, Nowak and McCormack 2000; Sanchez-Vives, Nowak and McCormick 2000). However, unlike in cortical cells where the hyperpolarization is driven by an intrinsic cellular property (Sanchez-Vives, Nowak and McCormick 2000), this adaptation arises from reduced glutamate release from presynaptic (non-spiking) bipolar cells of the retina (Manookin and Demb 2006).

Whether contrast adaptation is due to "neural fatigue", decrease in the activity of presynaptic neurons, synaptic facilitation of inhibitory neurons, network interactions or plasticity of excitatory synapses, the phase of reduced sensitivity to low contrast stimuli displayed by the neurons following contrast adaptation remain a fact. The mechanism may occur at the cellular or neural level or even involve network interaction between the retina and the visual cortex as reviewed above. The reduced retinal signal that occur due to contrast adaptation could be an indication of reduced retinal activity which simulates a retinal error signal involved in the aetiology of myopia (see 1.5.8) (Diether, Wallman and Schaeffel 1997).

1.5.6 Function of Contrast Adaptation

As discussed in 1.5.4.2, there are two forms of contrast-adaptation in the retina: the faster process termed "contrast gain control" that occurs with an extremely short timescale of about 100 ms, and the slower process termed "contrast adaptation" that occurs over a longer timescale of 1 – 10 s or more than 10 s. Contrast gain control is thought to affect the moment-to-moment response of the retina (Victor 1987). It is a process that reduces the gain and advances the phase of ganglion cell responses as stimulus contrast is raised (Shapley and Victor 1978). This is because an individual retinal neuron is limited in the range over which it can respond. The neuron activity could reach saturation point by overly strong stimulation. Hence, the contrast gain control magnifies the retina's sensitivity when the contrast is low, and sharpens the retina's temporal response to make it more selective for objects with high contrast (Shapley 1997). Therefore, its potential benefit is to expand the dynamic range of the adapted ganglion cells in retinal processing of visual signals, so as to maintain a high level of differential sensitivity over the large range of contrast levels experienced when different scenes are viewed (Shapley 1997).

The above explanation on the function of contrast gain control was based on the models of light/dark adaptation of automatic gain control whose purpose is to maintain the average power of the retinal signal's response constant despite fluctuations in the mean luminance of the visual world (Abbonizio, Langley and Clifford 2002). This form of an adaptive model is consistent with the observation that the reduction in the absolute magnitude of a neuron's response after stimulation may nevertheless enhance differential sensitivity (Rushton 1965).

Many of the contrast gain control studies involved investigating the responses of simple and complex cells of cats or macaques monkeys (Albrecht, Farrar and Hamilton 1984; Ohzawa, Sclar and Freeman 1985; Sclar, Lennie and DePriest 1989). Some simple cells showed adaptive sensitivity shifts [Figure 1.9 (a), (b)] after adaptation to a high contrast pattern but some do not [Figure 1.9 (c)]. In adapted cells compared to an un-adapted state, their operation ranges shifted to higher contrasts [Figure 1.9 (a), (b)]. The contrast response curve maintained its form when shifted along a logarithmic contrast axis. In this way, the units of which have a limited dynamic response range, seems to try to retain a high differential sensitivity (Määttänen and Koenderink 1991) by reducing the absolute magnitude of the neuron's response after stimulation.

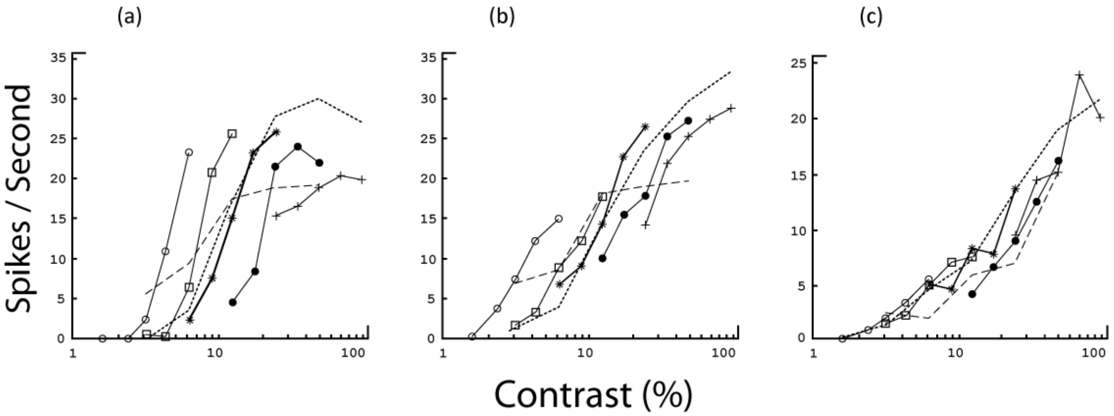


Figure 1.9 Contrast-response functions of simple cells (a), (b) and (c). Each graph is arranged to show varying degrees of adaptation observed in cortical cells, from substantial adaptation in (a) to minimal in (c).
The response amplitudes indicated as spikes/sec, are plotted as functions of stimulus contrast. These contrast-response functions were obtained at 5 different contrast-adaptation levels (from left to right, 3.1, 6.25, 12.5, 25 and 50% contrast of adapting stimuli respectively). Dashed curves represent steady-state contrast-response functions. Dotted curves were obtained by randomly interleaving a wide range of contrasts (1.56 – 100%) in a single run (Ohzawa, Sclar and Freeman (1985).

Therefore, if the human visual system makes use of a contrast gain control mechanism, and if the contrast transfer function shifts in the same way as the contrast-response functions of individual cortical cells, we would expect the contrast discrimination sensitivity to change during contrast adaptation, and to improve particularly at the adapting contrast level. However, psychophysical investigations of contrast discrimination after adaptation have yielded contradictory results (Määttänen and Koenderink 1991).

Barlow et al (1976) tried to find improvement in discrimination sensitivity using a stationary grating of 6 cpd as a stimulus. They did not find any improvement in the contrast discrimination sensitivity after adaptation, either with a spatial or with a temporal discrimination method. Legge (1981) studied contrast discrimination using various experimental conditions which included different states of contrast adaptation. He found no consistent change in the contrast discrimination sensitivity in both of his experimental conditions with either the continuous presence of the background grating or with background grating present only during the stimulus presentation. Määttänen and Koenderink (1991) found contrast detection thresholds were elevated and contrast discrimination thresholds remain unchanged after contrast adaptation (Määttänen and Koenderink 1991). The findings of these experiments failed to demonstrate any improvement in contrast discrimination after contrast adaptation.

The only positive evidence for contrast gain control in human psychophysical experiments is the study of Greenlee and Heitger (1988). In their experiments, two sets of gratings were presented. The contrast of one of the test gratings was fixed at a defined background level, known as the background contrast. The contrast of the second test grating was incremented and subjects were asked to state which set of the gratings had higher contrast (Greenlee and Heitger 1988). Their observers required more incremental contrast for background contrast levels between 0.1 and 0.4 following adaptation but for contrast level above 0.5, they required less incremental contrast following adaptation to discriminate which of two gratings was incremented in contrast. Greenlee and Heitger recognized that the contrast response function of the human visual system shows a saturation characteristic like what others have found (Barlow, Macleod and Meeteren 1976; Legge 1981) and in addition that the shift of the response function toward higher contrast level indicated the dynamic characteristic of the response function after adaptation.

Abbonizio and co-workers repeated some of the experiments of Greenlee and Heitger (1988) and Määttänen and Koenderink (1991) and concluded that contrast discrimination may be enhanced after adaptation, but these effects can vary markedly across subjects and test conditions. Enhancements in contrast discrimination were significant when adapting and testing at low levels of contrast, but just significant at higher levels of contrasts (Greenlee and Heitger's used a high background contrast of more than 0.5 and therefore their result showed enhanced contrast discrimination after adaptation) (Abbonizio, Langley and Clifford 2002). In addition, binocular viewing conditions (Greenlee and Heitger 1988) enhance contrast discrimination compared to monocular viewing conditions (Määttänen and Koenderink 1991; Abbonizio, Langley and Clifford 2002).

Määttänen and Koederink (1991) proposed that adaptation to a suprathreshold contrast would presumably result in an elevation of the contrast detection threshold because the response to adaptation at the lowest contrast decreases. Threshold elevation and the reduction of subjective contrast after adaptation are well-known phenomena which have been discussed as an important effect of contrast adaptation (1.5.1). The adaptation effect could also be explained as response compression (Albrecht, Farrar and Hamilton 1984), i.e. by an overall reduction of the response level due to a diminished signal-generating capacity of the system. Such a process would impair also the overall contrast discrimination sensitivity (Määttänen and Koenderink 1991).

In summary, although the physiological studies (in cats and monkeys) show that there could be potential benefit in contrast adaptation in expanding the dynamic range of the adapted retinal ganglion cells (Shapley and Victor 1978), LGN neurons (Kaplan, Purpura and Shapley 1987) and simple and complex cells of visual cortex (Albrecht, Farrar and Hamilton 1984; Ohzawa, Sclar and Freeman 1985; Sclar, Lennie and DePriest 1989) in processing visual signals, psychophysical studies showed conflicting results on this benefit in human subjects. Moreover, there was no reduction in apparent contrast when testing at contrasts higher than the adapting contrast, suggesting that contrast adaptation is not simply a shift of the contrast response function to higher contrast levels (Heinrich and Bach 2002b). A plausible hypothesis is that the mechanism for contrast adaptation is available at every stage of the visual pathway, perhaps even in every synapse (Baccus and Meister 2004). The multiple forms of contrast adaptation may tune to different aspects of the visual scene, suggesting the diversity in the functional roles of contrast adaptation and scientists are still far from understanding each type of contrast adaptation.

1.5.7 Contrast Adaptation in Humans

The retinal and cortical contrast adaptations in human were simultaneously measured using pattern electroretinogram (PERG) and cortical visual evoked potentials (VEPs)

(Heinrich and Bach 2001; Heinrich and Bach 2002b; Heinrich and Bach 2002a). Henrich and Bach (2002a) used sinusoidal gratings of 98% contrast with spatial frequencies of 0.5 and 5.0 cpd, phase reversing at 17 reversals/s to avoid local luminance adaptation. The results obtained are shown in Table 1.2. They proposed that the existence of both adaptable and non-adaptable mechanisms allows the retina to discern between overall low contrast and defocus in emmetropization control (Heinrich and Bach 2002a).

Table 1.2 Responses of PERG and VEP obtained in the experiments of Heinrich and Bach, 2002b.

Adapting Frequency	**Test Frequency**	**Responses Measured**	
		PERG (retina)	VEP (visual cortex)
5	5	Reduced amplitude (-22%) and latency time (-0.95 ms)	Reduced amplitude (-58%)
5	0.5	Increased latency time (+1.35 ms)	Increased amplitude (+26%)
0.5	5	No change in amplitude; increased latency (+0.65 ms)	No change in amplitude
0.5	0.5	No adaptation	No adaptation

Contrast adaptations are qualitatively different in the retina (PERG) and the cortex (VEP) (Heinrich and Bach 2002b). In the retina, adaptation to high contrast reduces the amplitude by about 20%, regardless of the temporal frequency of the test and adapting patterns. Cortical contrast adaptation displayed a pronounced interaction of adapting and test frequency, hence explaining the paradoxical effect of amplitude increase when the adapting and test frequencies are different (Table 1.2). The temporal frequency of the adapting and test patterns is also suggested to have an effect on cortical contrast adaptation (Heinrich and Bach 2002b).

When contrast adaptation was assessed using multifocal electroretinogram (mfERG), there was no significant changes in response to adaptation of a vertical grating at 5 cpd to the amplitude of the mfERG waveform, but an increase in the implicit time (delay in response) was reported (Chen, Brown and Schmid 2006). This finding is in contrast with the reduced amplitude findings of Heinrich and Bach (Heinrich and Bach 2002a). The difference in findings were attributed to inter- and intra-subject variability (Chen, Brown and Schmid 2006).

As discussed in 1.5.6, contrast adaptation in human may not simply be a shift of the contrast response function to higher contrast levels (Heinrich and Bach 2002b). However, another study reported that contrast response functions in V1, V2 and V3 shift to approximately center on the adapting contrast using event-related fMRI (functional magnetic resonance imaging) and a data-driven analysis approach (Gardner, Sun, Waggoner et al. 2005). Their results demonstrate contrast gain changes in the human cortex roughly serve to center contrast response functions on the adaptation contrast, thus allowing neurons with limited dynamic range to represent the much larger range of contrasts present in the visual world. With the conflicting findings on the function of contrast adaptation in human, it is uncertain if the effect is beneficial to the visual system, or is there any underlying changes which may act against the anatomical changes in the eye due to the increase in contrast thresholds after adaptation.

1.5.8 Contrast Adaptation, Blur Adaptation and Accommodation

Axial elongation can be induced by restricting spatial frequency content and lowering image contrast in animal models. The finding that chicks become more sensitive to low contrast after the removal of diffusers (worn for 1.5 days - Figure 1.10) led to speculation that selective contrast adaptation to the altered spatial frequency spectrum of the environment could relate to a retinal error signal involved in the etiology of myopia (Diether, Wallman and Schaeffel 1997).

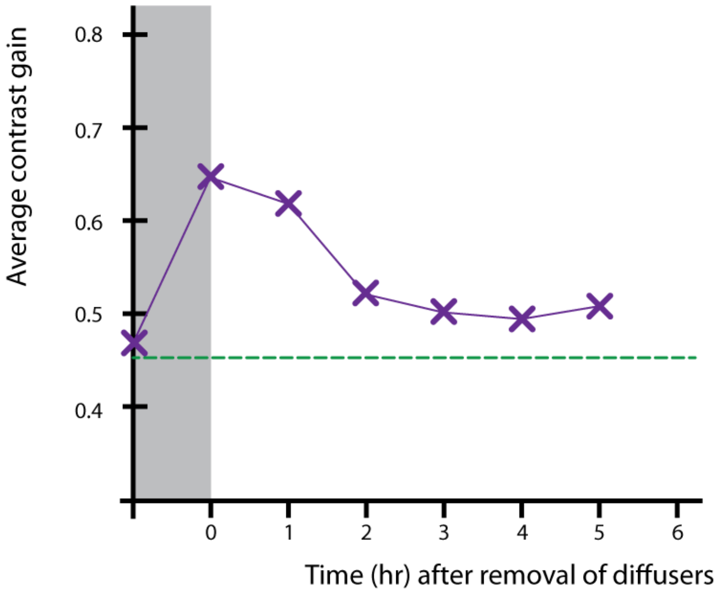


Figure 1.10 Decay of average contrast adaptation of 4 different chicks
Chicks showed improved sensitivity to low contrast after the removal of diffusers worn for 1.5 days (emphasized by the grey background). The dashed lines show the baseline contrast sensitivity. The increased sensitivity took a few more hours to dissipate before contrast sensitivity was returned to baseline. Adapted from Diether and Schaeffel (1999).

Contrast adaptation was referred to as an increase in contrast sensitivity after the removal of the frosted occluder (Diether, Wallman and Schaeffel 1997; Diether and Schaeffel 1999; Diether, Gekeler and Schaeffel 2001). Diether, Gekeler and Schaeffel (2001) suggested that frosted diffusers cause adaptation changes in contrast sensitivity, and when removed, improve contrast sensitivity at a low spatial frequency of 0.5 cpd. They found that drugs that suppress myopia such as atropine and reserpine have effects on contrast adaptation, so myopia development could be inhibited by suppressing contrast adaptation (Diether and Schaeffel 1999). They suggested that lags of accommodation of children during prolonged reading (Gwiazda, Thorn, Bauer et al. 1993b; Goss and Jackson 1996) may trigger contrast adaptation and thus contrast adaptation becomes a possible candidate for a retinal error signal for myopia development (Diether and Schaeffel 1999).

Another visual adaptation that is potentially important in myopia development is blur adaptation. Blur adaptation changes the visual sensitivity to blur. Emmetropic subjects showed initial reduced visual acuity when they wore + 1 D spectacle lenses, but their visual acuity improved after persistent defocus for 30 min (Mon-Williams, Tresilian, Strang et al. 1998). A decrease in sensitivity to mid range spatial frequencies (5 – 25 cpd) occurs following exposure to optical defocus, with the low and high frequencies remaining unaffected. This shift was thought to represent "neural compensation" to the blur.

Similarly when blur adaptation was performed on 22 myopes, significant improvements in letter and grating acuities were found after 3 hr of sustained blur without any changes in the refractive errors (Rosenfield, Hong and George 2004). George and Rosenfield (2004) observed significant increases in Landolt C acuity and grating acuity following blur adaptation in both emmetropes and myopes, with greater changes in the latter for the myopes.

Cufflin, Mankowska and Mallen (2007) measured proximal and distal blur thresholds (depth-of-focus limits) on 8 emmetropes, 8 EOM and 8 LOM under cycloplegia, following a 30 min period of +1.0 D blur. Adaptation to blur increased blur thresholds. The distal blur thresholds increased significantly between refractive groups with greatest increase in EOMs. The blur discrimination increased significantly after blur adaptation but did not show any difference in refractive group.

Differences in the effects of blur adaptation on the ability to detect blur could alter accommodation accuracy in myopes. There have been conflicting results between studies investigating the influence of blur adaptation upon accommodation responses. Two studies failed to observe any effect of adaptation to defocus (George and Rosenfield 2002; Cufflin, Hazel and Mallen 2007), either for emmetropes or myopes. However, Vera Diaz, Gwiazda and Thorn et al (2004) observed that Gaussian blur (diffuse image blur, and not myopic or hyperopic defocus) increased accommodation response in myopes, but not in emmetropes. Cufflin, Hazel and Mallen (2007) suggested that the participants in Vera Diaz et al were accommodating to the target before blur was added, whereas in their study, accommodation responses subsequent to a period of blur adaptation were examined. In essence, the study by Vera-Diaz et al tested the accommodative response to degraded stimuli in myopes and emmetropes at one stimulus level and showed that myopes immediately react to defocus in a different manner than emmetropes. The increase in accommodation response in Vera-Diaz et al's study could represent an attempt by the accommodation system to restore image contrast (Cufflin, Hazel and Mallen 2007).

In summary, adaptation to blur as defocus improves visual resolution with some evidence that myopes exhibit greater improvements than emmetropes. Adaptation to blur changes the visual system's sensitivity to blur particularly for early onset myopes, but there is limited evidence that the adaptation changes accommodation response.

1.5.9 Contrast Adaptation and Eye Growth

For an adaptation process to have an effect on eye growth, the slow contrast adaptation process which integrates signals on a slower time-scale would be a more likely candidate to influence axial elongation than the fast contrast adaptation. The firing rate of the slow process changes abruptly in response to changes in the stimulus contrast level and then settles to a new level over tens of seconds in the retina of salamander, rabbit (Smirnakis, Berry, Warland et al. 1997) and monkey (Chander and Chichilnisky 2001). The slow contrast adaptation also explains the type and degree of contrast adaptation observed in human psychophysical studies (Blakemore and Campbell 1969; Blakemore, Muncey and Ridley 1973; Georgeson and Harris 1984; Greenlee and Magnussen 1988; Greenlee and Heitger 1988; Greenlee, Georgeson, Magnussen et al. 1991; Greenlee, Georgeson, Magnussen et al. 1992). This slow contrast adaptation process that was observed in the human psychophysical studies may be involved in myopia associated with reading.

Contrast adaptation has been postulated as a potential error signal for emmetropization as the adaptation process alters the sensitivity of the visual system with defocused stimuli (Diether and Schaeffel 1997; Diether, Wallman and Schaeffel 1997; Diether and Schaeffel 1999). The discovery of its location in the retina is important for theories linking contrast adaptation to myopia development since visual control of eye growth is largely based on retinal image processing (Winawer and Wallman 2002; Wallman and Winawer 2004). Moreover, with the multiple forms (1.5.4), the visual stimuli for contrast adaptation may not be confined to grating stimuli alone. Any form of high contrast stimuli may induce a certain form of contrast adaptation as well. For example, reading high contrast text may also induce a certain form of contrast adaptation in the retina, since reading requires intense viewing of the reading text for a prolonged duration.

As reviewed in 1.5.1, contrast threshold was reported to be elevated at spatial frequencies from 1.45 to 6 cpd after reading single-spaced text on a VDU (Lunn and Banks 1986; Magnussen, Dyrnes, Greenlee et al. 1992). The authors of one of the studies suggested that the reduction in sensitivity could account for objective optometric measures of disturbed accommodation as well as some subjective symptoms of fatigue in VDU viewing (Lunn and Banks 1986). In addition, when reading time was increased from 10 min to 1 hr, it was observed that the longer duration adds only a little to the magnitude of contrast threshold elevation but prolongs the effect considerably on the recovery time (Magnussen, Dyrnes, Greenlee et al. 1992). The authors concluded that contrast adaptation develops more rapidly in repeated sessions if the recovery is not complete between sessions. Therefore, reading could induce contrast adaptation and alters the contrast sensitivity of the visual system. As there is a reduction in contrast sensitivity during and following reading, the retinal image perceived may be degraded to the similar extent as a degraded image caused by translucent diffusers in producing myopia in animal studies (Sivak, Barrie and Weerheim 1989; Bartmann and Schaeffel 1994).

Besides the loss of contrast sensitivity, another study observed that the brief threshold elevation after prolonged near work is associated with VDU-induced transient myopia (Jaschinski-Kruza 1984). Near work induced transient myopia (NITM) refers to the small, transient, pseudomyopic shift in the far point of the eye after a period of sustained near work. It is a form of accommodative adaptation where accommodation induced during near work is not dissipated immediately. Several studies have reported NITM to be greater in LOMs and EOMs than in emmetropes [reviewed in (Chen, Schmid and Brown 2003)]. It has also been reported that progressive myopes were more susceptible to NITM than were stable myopes (Vera-Diaz, Strang and Winn 2002; Vasudevan and Ciuffreda 2008). Thus, NITM is one of many possible environmentally based, myopigenic near work contributory factors (Ciuffreda and Vasudevan 2010).

Therefore contrast adaptation in itself may result in chronic retinal defocus in prolonged reading or it may be linked to the adaptation of other visual functions such as accommodation and play an important role in myopia development. There are no data on contrast adaptation in reading hard copy of text in children. As children are starting to read at a younger age and the age of myopic children is becoming younger (Saw, Tong, Chua et al. 2005), we suspect that the adaptation process in contrast and accommodation may play a role in disrupting the emmetropization process and be involved in the aetiology of myopia development.

1.6 Accommodative Adaptation

Besides contrast adaptation, the other visual adaptation that occurs during reading which has been linked to myopia is accommodative adaptation. Many studies have been performed during the last decade on accommodative adaptation, but its role in myopia development is still debated. The following sections review the different aspects of accommodation and their possible roles in myopia development.

1.6.1 Accommodation

Accommodation is a prominent feature of near work. When an object is located at distances further than 6 m, light rays that reach the eye from a point object are essentially parallel and the rays are brought into focus on the retina of an emmetrope. Ignoring higher order and chromatic aberrations, the eye is said to have relaxed accommodation. If the object is moved closer to the eye, the light that enters the eye would focus behind the retina. To bring the image into focus, the eye accommodates to increase its focusing power. During accommodation, the lens surfaces increase in curvature and the lens increases in central thickness - these changes have the effect of increasing the optical power of the lens. Drugs that block accommodation, such as atropine, can be used to prevent myopia progression in children (Wallman and Winawer 2004); although it remains unclear whether this inhibition occurs through a retinal or scleral or accommodative mechanism.

1.6.2 Accommodation and Near Work

During reading, the accommodation response is activated and this mechanism may play an important role in myopia development. There have been several aspects of accommodation that have been linked to myopia development : (1) amplitude of accommodation, (2) tonic accommodation, (3) accommodation stimulus response, (4) accommodative adaptation and near work-induced transient myopia (Rosenfield 1998; Chen, Schmid and Brown 2003).

1.6.3 Amplitude of Accommodation

Amplitude of accommodation reflects the maximum accommodative response, and has been defined as the dioptric distance between the far-point and the near-point conjugate with the retina when accommodation is fully exerted (Rosenfield 1998). Previous studies failed to report consistent findings in amplitude of accommodation for myopes and emmetropes. Maddock et al (1981), McBrien and Millodot (1986a) and Fledelius (1981) reported higher amplitudes of accommodation in myopes than emmetropes, while Fong (1997) reported lower amplitudes in myopes, and Fisher et al. (1987) and Mantyjarvi (Mantyjarvi 1987) did not find a difference between the two refractive groups. The lack of consistency in findings makes amplitude of accommodation an unlikely causative factor for myopia development. Also, highly hyperopic children have to accommodate much more than myopic children and yet highly hyperopic children do not tend to become myopic (Wildsoet and Wallman 1995).

1.6.4 Tonic Accommodation

In the absence of an adequate visual stimulus, accommodation adopts an intermediate position of approximately 0.5 to 1.0 D or higher. This position is believed to reflect the level of tonic innervation to the ciliary muscle and has been termed tonic accommodation (Rosenfield, Ciuffreda, Hung et al. 1993). Some studies (Suzumura 1979; Gawron 1981; Simonelli 1983) have reported that myopic subjects had higher dioptric tonic accommodation values, while others have reported (Maddock, Millodot, Leat et al. 1981; Ramsdale 1985) lower levels of tonic accommodation in myopes than emmetropes. Other studies (Gilmartin, Hogan and Thompson 1984; Whitefoot and Charman 1992) did not demonstrate any significant correlation between tonic accommodation and refractive error (Rosenfield 1998). When myopia was classified based on age of onset, some studies observed lower dioptric values of tonic accommodation in late onset myopes (LOM). In a longitudinal study, Adams and McBrien (1993) found that the "became myopic group" showed reduced tonic accommodation. Two longitudinal studies in children have also suggested lower tonic accommodation as a consequence of myopia rather than a predictor of later myopia development (Yap, Garner, Kinnear et al. 1999; Zadnik, Mutti, Kim et al. 1999). Therefore, these studies concluded that tonic accommodation cannot be used as a predictor for future myopia development.

This leaves two plausible aspects of accommodation that are considered to be involved in myopia development. One is the accommodation error that occurs during reading, and the second is the accommodation hysteresis that occurs following reading, i.e. the accommodation takes time to relax for distance viewing after prolonged near tasks (Ebenholtz 1983; Ebenholtz and Zander 1987; Ehrlich 1987).

1.6.5 Accommodative Responses and Errors

Myopes tend to have reduced accommodative responses at near distances (McBrien and Millodot 1986b; Gwiazda, Thorn, Bauer et al. 1993b; Abbott, Schmid and Strang 1998), thus resulting in higher accommodation error than in emmetropes. McBrien and Millodot (1986) found that LOM accommodated less for near targets compared to early-onset myopes (EOM), followed by emmetropes and hyperopes. Gwiazda, Thorn, Bauer et al (1993b) measured the accommodative stimulus response curves under monocular viewing conditions in emmetropic and EOM children (myopia onset before 15 yr old) aged between 5 and 17 yr and found that EOM children had significantly larger lags of accommodation at near than emmetropic children, particularly as accommodation demand increases. Abbot, Schmid and Strang replicated the study of Gwiazda et al in young adults and found that accommodative responses of emmetropes, EOM and LOM, did not significantly differ, but that the responses of progressing myopes differed from those of stable myopes and emmetropes. A similar study with Asian young adults (Yeo, Kang and Tang 2006) found that progressing myopes showed higher accommodative lags for higher accommodation demands than the non-progressing myopes and emmetropes. In the studies described above, accommodative lags are highest when the accommodation demand is created using minus lenses, i.e. for minus lens induced accommodation. The magnitudes of typical accommodative errors found in myopes for minus lens induced accommodation are shown in Table 1.3.

Table 1.3 Accommodative errors in myopes using negative lenses to induce accommodation (Yeo et al, 2006 – all Asian population).

Study	**Age Range (yr)**	***Refractive Group***	***Accommodation (D)***				
***Abbott et al (1998)**	**13-31**	***Accommodative Stimulus***	***0.25***	***1.20***	***2.20***	***3.20***	***4.00***
		AE for EM (n = 10)	+0.55	+0.30	+0.10	-0.20	0
		AE for SM (n = 10)	+0.85	+0.35	+0.15	-0.10	-0.10
		AE for PM (n = 12)	+0.55	+0.20	-0.10	-0.60	-0.65
***Gwiazda et al (1993)**	**5-17**	***Accommodative Stimulus***	***0.0***	***1.0***	***2.0***	***3.0***	***3.5***
		AE for Child EM (n = 48)	+0.05	-0.50	-0.80	-1.45	-1.60
		AE for Child M (n = 16)	+0.05	-0.80	-1.45	-2.25	-2.85
Yeo et al (2006	**16-23**	***Accommodative Stimulus***	***0.25***	***1.23***	***2.19***	***3.12***	***4.03***
		AE for EM (n = 17)	-0.26	-1.10	-1.45	-1.76	-2.69
		AE for NM (n = 22)	-0.41	-1.10	-1.39	-2.09	-3.21
		AE for PM (n = 11)	-0.81	-1.16	-1.69	-2.42	-3.51

***Values estimated from Abbott et al (1998) in a mainly Caucasian population**

AE – Accommodative Error
EM – Emmetropes
PM – Progressing Myopes
NM – Non-progressing Myopes
+ indicate accommodative leads

SM – Stable Myopes
M – Myopes
PM – Progressing Myopes
- indicate accommodative lags

In the case where the accommodation response is less than the demand, hyperopic defocus occurs which could trigger the emmetropization process and compensatory myopia. The hyperopic defocus increases in tandem with the increase in lag of accommodation at near. This could lead to an adaptation response that is detrimental to the quality of the retinal image and hence results in myopia development and progression.

Hung and Ciuffreda (2000) believed that refractive error and the absolute value of the accommodative error or retinal defocus are involved in the long-term feedback loop in which they interact and modulate each other. They believe that it is the property related to the magnitude of the retinal defocus itself (not plus or minus lag of accommodation) that governs the appropriate rate of axial length growth relative to normal (Hung and Ciuffreda 2000).

In recent years, accommodation stimulus-response curves were found to be affected by pupil size, binocular fixation and higher order aberration levels (Buehren and Collins 2006). Accommodation errors are reduced in binocular compared with monocular viewing conditions because of the significant constriction of the pupil during binocular viewing. This is due to the reduced effects of spherical aberration and higher-order aberrations within the smaller pupils (Buehren and Collins 2006). Even though pupil size affects the measures of accommodative accuracy, it is still advisable to analyze the accommodation response based on natural pupil data because it takes into account the full optical information to estimate retinal image quality (Buehren and Collins 2006). The authors explained that the accuracy of representation of the retinal image should determine the most appropriate description of the eye's optics rather than using accommodation leads and lags to estimate the visual performance at different accommodation levels.

1.6.6 Accommodative Adaptation or NITM

A period of sustained near work induces a small amount of accommodative adaptation (Ebenholtz 1983; Jaschinski-Kruza 1984; Ehrlich 1987; Gwiazda, Bauer, Thorn et al. 1995; Wolffsohn, Gilmartin, Li et al. 2003). These studies examine the accommodative adaptation under the open-loop condition which is typically achieved by making the pre- and post-task measurements in total darkness (Figure 1.11a).

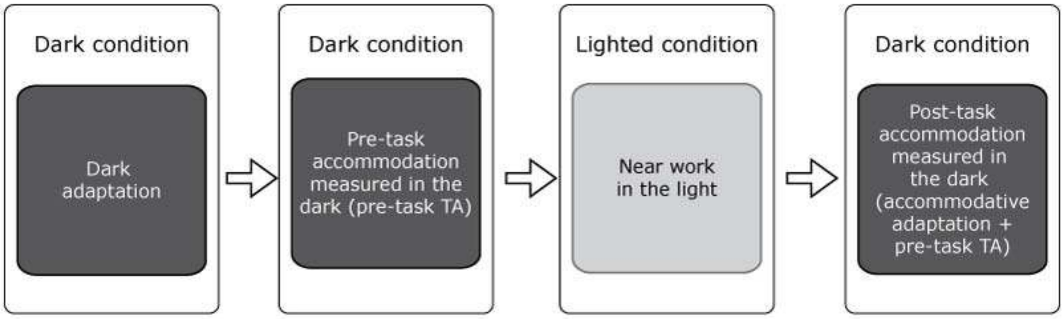


Figure 1.11a Experimental sequences for assessing open-loop accommodative adaptation
TA: Tonic accommodation

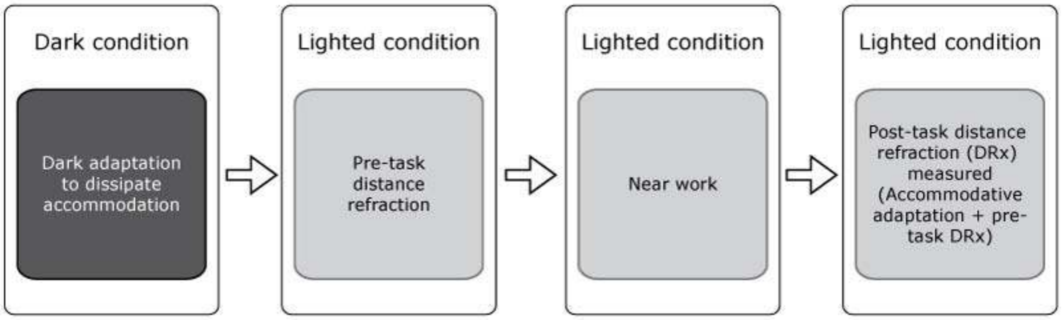


Figure 1.11b Experimental sequences for assessing closed-loop accommodative adaptation
DRx: Distance refraction

For studies that examined adaptation under closed-loop viewing conditions, the near work shift (accommodative adaptation) is known as near work-induced transient myopia or NITM (Ebenholtz 1983; Ehrlich 1987; Ciuffreda and Ordonez 1995; Gwiazda, Bauer, Thorn et al. 1995; Ong and Ciuffreda 1995). The general experimental paradigm used in the assessment of near work induced transient myopia is outlined in Figure 1.11b. The initial dark adaptation allows all the residual accommodation to be dissipated and all the pre-task, near task and post-task measurements are obtained in lighted conditions.

1.6.6.1 Accommodative Adaptation – Open-loop

In the open-loop condition, accommodative adaptation or accommodative hysteresis has been used to describe the near work induced shift in accommodation and tonic accommodation (TA) is the reference point against which accommodative adaptation is measured (Rosenfield, Ciuffreda, Hung et al. 1993; Rosenfield, Ciuffreda, Hung et al. 1994). Immediately following the removal of a sustained accommodative stimulus, the output of the fast blur-driven accommodative response (FBAR) will dissipate rapidly, whereas the slow blur-driven accommodative response (SBAR) will exhibit a lower rate of decay (Rosenfield 1998). While the pre-task measurement may reflect baseline tonic accommodation, the accommodative output measured immediately following task completion will be a composite response including both tonic accommodation and the sustained output of SBAR (Rosenfield 1998).

Ebenholtz (1983) suggested that the slow decay of 'post-task tonic accommodation' following a period of near fixation may play a role in the aetiology of axial myopia. Several studies have examined accommodative adaptation in different refractive groups (Table 1.4) (Fisher, Ciuffreda and Levine 1987; McBrien and Millodot 1987; Rosenfield and Gilmartin 1988; Rosenfield and Gilmartin 1989; Gilmartin and Bullimore 1991). Most of these studies have demonstrated a higher magnitude of accommodative adaptation in myopes than in emmetropes, and myopes exhibited a slower rate of decay than emmetropes (Rosenfield and Gilmartin 1988; Gilmartin and Bullimore 1991). The proposed mechanism was a deficit in the sympathetic input in LOM which may be responsible for the slow regression of adaptation effects in myopes and is thought to predispose an individual to myopia development for further myopia progression (McBrien and Millodot 1988; Gilmartin and Bullimore 1991).

1.6.6.2 Accommodative Adaptation – Closed-loop or NITM

In the closed-loop accommodative adaptation, pre- and post-task measurements of accommodation were performed while subjects viewed a distant target, typically a visual acuity chart, thus allowing normal blur-feedback mechanisms to operate (Rosenfield 1998). The transient increase in post-task response observed immediately following completion of the near-vision task will be the combined response of the far point of accommodation plus the residual output of the SBAR. The accommodative adaptation observed under closed-loop conditions is smaller than that recorded in the open-loop situation due to the effect of blur driven accommodation which is allowed to operate in the closed-loop condition (Rosenfield 1998). The shift of myopia under closed-loop condition represents the accommodative adaptation observed under the naturalistic conditions with blur-feedback present. The magnitude and regression time of NITM of some studies are presented in Table 1.5. This will be discussed further in 1.6.8.

1.6.7 Accommodative Adaptation and Myopia Development

There are 2 different mechanisms that have been suggested in linking accommodative adaptation to the development of myopia. The first mechanism is linked to accommodative accuracy and the second mechanism to retinal image defocus.

1.6.7.1 Accommodative Adaptation and Accommodation Accuracy

As reviewed in 1.6.5, hyperopic defocus increases in tandem with accommodative lag during near work, which may trigger axial elongation to grow the eye plane to coincide with the image plane. When accommodative adaptation and responses were measured after a sustained 10 min near work task at a viewing distance of 33 cm, the adaptor group (defined as having adaptation more than 0.3 D) was found to have significantly less in accommodative lag compared to the non-adaptor group. The measured accommodative lag in the adaptor and non-adaptor groups were 0.06 D and 0.14 D respectively (Rosenfield 1998).

In another study with only 1 subject, it was reported that accommodative adaptation resulted from the increased output of SBAR decreasing the lag of accommodation

(Schor, Kotulak and Tsuetaki 1986). Here, accommodative adaptation seems to reduce accommodative lag or reduce hyperopic defocus, but increase accommodative accuracy and therefore suggest its importance in preventing myopia development. These two studies discussed above assessed accommodative adaptation using open-loop conditions. However, subsequent studies using closed-loop conditions seem to favour the second mechanism that link accommodative adaptation to retinal defocus, rather than accommodative accuracy because myopes show higher magnitude and longer decay time in NITM compared to emmetropes, and progressing myopes show higher magnitude and longer decay time in NITM than stable myopes and emmetropes (Ong and Ciuffreda 1995; Ciuffreda and Wallis 1998; Vera-Diaz, Strang and Winn 2002; Wolffsohn, Gilmartin, Li et al. 2003).

1.6.7.2 NITM and Retinal Defocus

Myopes are reported to have enhanced susceptibility to NITM (Ciuffreda and Wallis 1998). Ciuffreda and Vasudevan (2005) proposed that the non-decay NITM acts like an addition of a low-powered plus lens (about 0.25 to 0.50 D on average), that creates a myopic defocus (when viewing distant objects), which could be myopigenic in humans (Ciuffreda and Vasudevan 2008). In animal studies, myopic defocus produces a compensatory eye growth which results in hyperopia in chicks (Schaeffel, Glasser and Howland 1988; Irving, Sivak and Callender 1992), tree shrews and monkeys (Smith and Hung 1999). However other animal such as cats generally produced axial myopia, irrespective of whether positive or negative lenses were used [reviewed in (Wildsoet 1997)]. In humans, imposing retinal defocus with under-correction (Chung, Mohidin and O'Leary 2002; Alder and Millodot 2006) has been associated with further myopia progression. Therefore, it has been suggested that the slight myopic shift immediately after near work that produce transient periods of retinal defocus may be a precursor to axial elongation (Ong and Ciuffreda 1995; Vera-Diaz, Strang and Winn 2000; Wolffsohn, Gilmartin, Li et al. 2003; Ciuffreda and Vasudevan 2008). Therefore, the current research suggest that in the presence of artificially imposed retinal defocus, by means of either positive or negative lenses, normal eye growth can be altered and this imply that there are mechanisms in place which detect and compensate for the effect of induced retinal defocus [for reviews see (Goss and Wickham 1995; Wildsoet 1997)].

Far viewing has been demonstrated to reduce myopic progression in children (Rose, Morgan, Ip et al. 2008) and has been described as being protective in nature (Onal, Toker, Akingol et al. 2007). The authors hypothesized that the increased light intensity of outdoor environment constrict the pupils and result in a greater depth of field and less image blur. It is also likely that distance viewing helps to dissipate more quickly the saturation effect of NITM (Ciuffreda and Vasudevan 2008) than persistent near work. Therefore, as we believe that the retinal defocus associated with accommodative inaccuracy is a precursor for myopia, the transient myopia may also provide substantial retinal defocus and promote myopia development in susceptible individuals if the cycle were repeated many times (Ong, Ciuffreda and Rosenfield 1995). Ciuffreda and Vasudevan (2010) reported recently that it is likely that the myopigenic effect is related to the interaction between central foveal myopic defocus (~ 0.25 D due to NITM) versus the near retinal periphery which has a hyperopic defocus (~ 0.75 D) based on blur perception, near work and the retinal periphery.

Table 1.4 Findings of Studies Investigating Accommodative Adaptation as a Function of Refractive Error under Open-loop Conditions

Study (yr)	N	Age (yr)	Refractive error criteria	Instrument	Testing conditions	Accommodation adaptation (AA) (D) Regression time only if applicable
(Mc Brien and Millodot 1988)	47	18-27	11 H (> + 0.75 D) 16 E (- 0.25 D to + 0.75 D) 10 EOM (> - 0.25 & < 1.00 cyl) 10 LOM (> - 0.25 & < 1.00 cyl)	Infrared optometer	Counting exercise at 0.2 m, 0.37 M for 15 min Contact lens correction	LOM have greater AA LOM (~ 0.38 D) > E (~ 0.10 D) > EOM (~ 0.12 D) ~ H (~ - 0.25 D) Regression time: LOM (> 15 min)
Gilmartin and Bullimore, 1991)	30	19-25	15 E (0 to +0.50 D) 15 LOM (-0.50 to -2.25 D)	Infrared optometer	Perform arithmetic task at 1, 3 and 5 D stimulus distances for 10 min. Contact lens correction	LOM have greater AA at 1 D task distance No significant difference at 3 and 5 D task distances. LOM (0.15 D) > E (0.00D) Regression time: LOM longer than E LOM (78 to > 90 s); E (31 to 78 s)
(Woung et al 1993)	51	19-38	18 E (- 0.25 to + 0.75) 18 EOM (> - 0.50 & < 1.00 cyl) 15 LOM (> - 0.50 & < 1.00 cyl)	Infrared optometer	Internal asterisk-shaped target at 4 D above far point for 2 min No refractive correction	LOM have greater AA LOM (1.19D ± 0.24D) > E (0.66 D ± 0.14D) > EOM (0.27D ± 0.09D)
(Gwiazda et al 1995)	87	6.5 – 16.5	12 H (+ 1.00 to + 4.12) 57 E (- 0.25 to + 0.75) 18 EOM (- 0.25 to -7.00)	Infrared optometer	Video game at 4 D for 15 min Spectacle correction	EOM have AA EOM (1.15D) > E (0.68D) > H (0.24D)
(Woung et al 1998)	34	7-12	15 E (- 0.25 to - 0.75) 19 EOM (- 1.25 to – 5.25)	Infrared optometer	Internal asterisk at 8 D for 2 min No refractive correction	No significant differences in AA EOM (0.50D ± 0.61D) > E (0.39D ± 0.37D)
Hazel, Strang and Vera-Diaz, 2003	30	18-26	10 E (0 to + 0.25 D) 20 M (-0.75 to -5.75)	Infrared optometer	0.3 logMAR with contrast 90% and luminance 55 cd/m^2 Monocular at 25 cm for 10 min	M > E in AA (~ 0.70 D in M and ~ 0.60 D in E) (Regression time M (> 120 s) > E (~ 40 s)

Table 1.5 Findings of Studies Investigating NITM under Closed-loop Conditions

Study (yr)	No of Subjects	Age (yr)	Instrument	Near task paradigm	Target/Task details	Post-task monitoring period	Post-task decay time	NITM results (D)
(Ehrlich 1987)	15	18-30	Dioptron II Infrared optometer	Binocular 20 cm for 2 hr	6/9 number table / number search	1 hr	Decay incomplete after 1 hr	Mean NITM of 0.29 D
(Rosenfield and Ciuffreda 1994)	12	21-25	Infrared optometer	Monocular 20 cm for 10 min	Matrix of numbers (N6)/adding	90 s	Decay time constant of 17 s	Mean NITM of 0.23 D
(Fisher, Ciuffreda and Levine 1987)	48 12 HM 12 LM 12 E 12 H	21-35	Hartinger Optometer	Monocular Near point for 10 min	6/6 letters / maintaining clarity	20 min	NA	Mean NITM of 0.20 D; no difference in NITM and its rate of decay between refractive error groups
(Ciuffreda, Colburn and Wallis 1996)	12 E	21-28	Infrared optometer	Binocular 20 cm for 0.25, 0.5, 1, 2, 4, 8 min	Matrix of numbers / adding	100 s	Decay time constant of ≤ 40 s	Mean NITM of 0.30 – 0.60 D (after a 4min task)
(Ong, Ciuffreda and Rosenfield 1996)	16 LOM	21-31	Infrared optometer	Binocular 40 cm for 10 min	Matrix of numbers / adding	NA	Decay time constant of 51 s	Mean NITM of 0.21 D
(Ciuffreda and Wallis 1998)	44 9 H 11 E 13 EOM 11 LOM	21-30	Infrared optometer	Binocular 20 cm for 10 min	6/9 Snellen letters / maintaining clarity	120 s	Decay time constant of EOM (35 s) LOM (63 s)	Myopes most susceptible to near work aftereffects LOM (0.36) > EOM (0.34) > E (0.09) > H (0.01)
(Ciuffreda and Lee 2002)	16 4 H 4 E 4 EOM 4 LOM	17-31 (mean 24)	Infrared optometer	Binocular Habitual working distance for 4 hr	Newspaper, lecture transcripts, novels	20 min	Decay time < 8 min	Mean NITM, EOM (0.13 D) > LOM (0.12 D) > E (0.09 D) > H (0.44 D hyperopic shift)

(Vera-Diaz, Strang and Winn 2002)	41 14 E 16 SM 13 PM	18-27	Infrared optometer	Binocular 20 cm for 10 min	6/9 Snellen letters / maintaining clarity	120 s	Decay time constant of PM (>120 s) SM (42 s) E (35 s)	PMs are most susceptible to near work aftereffects PM (0.33 ± 0.04) > SM (0.17 ± 0.03) > E (0.16 ± 0.03)
(Hazel, Strang and Vera-Diaz 2003)	30 10 E 20 M	Mean age 22±2.7	Infrared optometer	Monocular 25 cm for 10 min	0.3 logMAR with contrast 90% ; target maintaining clarity	120 s	Decay time 30s (M) 20 s (E)	M (> 0.26 D) E (< 0.20 D)
(Wolffsohn, Gilmartin, Li et al. 2003)	45 10 E 35 M	6-12 Median 7.5	Infrared optometer	Monocular 20 cm and 40 cm for 5 min	Letters at 0.00 logMAR, maintaining clarity	120 s	Decay time M (> 120 s) E (25 s)	M (0.37 D to 0.5 D) E (0.10 D to 0.2 D)
(Vasudevan and Ciuffreda 2008)	44 15 LOM	21-34 Mean 23.7	Infrared optometer	Monocular 35 to 40 cm for 2 hr	Optometry lecture notes, maintaining clarity	120 s	Decay time LOM (60 s) EOM (87 s) E (50 s)	LOM (0.20 ± 0.03) EOM (0.29 ± 0.03) E (0.15 ± 0.02)

LOM – late onset myopes
EOM – early onset myopes
E – emmetropes
M - myopes

1.6.8 Magnitude and Regression Time of NITM

Tables 1.4 and 1.5 show magnitude of accommodative adaptation measured under open and closed-loop conditions respectively. Accommodative adaptations measured under closed-loop conditions are generally smaller in magnitude than that of open-loop conditions (1.6.6). Refractive error groups show differences in susceptibility to accommodative adaptation (Table 1.4). Myopic shifts in distance refraction of 0.15 D to 0.6 D in magnitude have been reported for NITM (Tables 1.5), whereas post-task myopic shifts in accommodation measured under open-loop conditions range from 0.15 D to 1.19 D (Table 1.4). In open-loop condition, LOM exhibit significantly greater myopic shifts of accommodation after sustained near work, followed by a slower decay to pre-task tonic accommodation compared to EOM, emmetropes and hyperopes. In closed-loop condition, either LOM or progressing myopes showed higher NITM than the other refractive groups (Table 1.5). In one study, when myopia was categorized under LOM and EOM, there was no significant different between myopes and emmetropes. The significant difference in NITM between myopes and emmetropes was found when myopia was categorized under progressing and stable myopes (Vera-Diaz, Strang and Winn 2002) with progressing myopes presenting with higher magnitude of NITM than both the stable myopes and emmetropes.

The time taken for regression to the pre-task tonic accommodation level is also used to assess the degree of adaptation generated by close work (Chen, Schmid and Brown 2003). The time course of dissipation from adapted levels to pre-task values varies in the range of several seconds (Baker, Brown and Carney 1983; Gilmartin and Bullimore 1987) to a few minutes (Fisher, Ciuffreda and Levine 1987; McBrien and Millodot 1988; Gwiazda, Bauer, Thorn et al. 1995), to even a few hours, measured in open-loop condition (Ebenholtz 1983).

Myopic subjects showed significantly more prolonged open-loop regressions than closed-loop regressions compared to emmetropes as they appear to be more affected by the measurement conditions than the emmetropes (Hazel, Strang and Vera-Diaz 2003).

In closed-loop, the accommodation level of the myopes dropped to baseline very quickly (within 20 sec post task) as compared to the regression time of about 120 s post task (Hazel, Strang and Vera-Diaz 2003) in open-loop. The differences may be due to:

1) Lack of sympathetic inhibition in prolonged near work results in higher accommodation shift in certain individuals. Therefore, sympathetic response may be one of the signals that can influence the regression profile.
2) Presence of blur feedback in closed-loop conditions may help to improve the speed of the accommodation regression back to the pre-task levels.

NITM is thought to be a function of task duration. A five-minute rest period was sufficient to enable the NITM (induced by brief near work) to decay fully, but full decay was not found for continuous tasks (Ong and Ciuffreda 1995). The decay time depends on task duration more than accommodative demand and the initial magnitude of NITM (Ong and Ciuffreda 1995). Tasks of extended duration (> 40 min) generally resulted in more prolonged aftereffects (minutes) (Ong and Ciuffreda 1995). However, in another of Ciuffreda's studies, the magnitude and regression time did not correlate with the duration of near work. With a four-hour reading task (Ciuffreda and Lee 2002), NITM magnitude was not higher than that obtained in shorter duration in the study of Ciuffreda and Wallis (1998) (see Table 1.4), and regression time was also shorter than what has been reported in open-loop condition (Ebenholtz 1983). However, one should be careful in interpreting the results obtained in the study of Ciuffreda and Lee as it was not easy to quantify the duration of near work when subjects were allowed to eat, drink and use the restrooms at their leisure during the 4-hr of near work.

For the closed-loop measurement of NITM, because of the small magnitude of the change, the target still falls within the eye's depth of focus, so individuals remain asymptomatic and blur-free. When NITM was measured in patients who reported blur for 3 s after 15 min of near-work, it could go up to as high as 1.4 D (Ciuffreda and Ordonez 1995). Similarly, the decay component showed a variable and abnormally long decay of 200 s after post-task.

In a recent study, Vasudevan and Ciuffreda (2008) compared NITM magnitude and regression after 1-hr and 2-hr of near work and found that NITM magnitude was additive in both EOM and LOM but not in emmetropes. When the myopic group was categorized into stable and progressing myopes, there was a significant increase in NITM after the second hour in progressing myopes only. For regression time, however, while the second hour reading increased the regression time significantly within each refractive group, the decay duration of EOM was longer than the emmetropes after the second hour, which approached significance ($P = 0.06$). Hence, they agreed with the speculation of Ong and Ciuffreda (1995) that repeated cycles of near-far-near work over an extended period (days or months), in which residual NITM persisted after brief distance viewing, would result in a small but significant transient myopia shift, and, may play a role in the aetiology of permanent myopia.

Ciuffreda and Wallis (1998) reported decay time constants of 35 and 63 s for their EOM and LOM respectively. However, the general observation in Table 1.5 seems to indicate that progressing myopes show a longer regression time (> 120 s) compared to stable myopes (42 s) and emmetropes (25 s to 35 s) (Vera-Diaz, Strang and Winn 2000; Wolffsohn, Gilmartin, Li et al. 2003). The after effect of NITM was also found to be more sustained in children (Ciuffreda and Thunyalukul 1999) in comparison with the adults. Differences in sympathetic innervation and/or sensitivity to blur are possible mechanisms to explain these results (Ciuffreda and Thunyalukul 1999).

1.6.9 Aetiology of NITM

The etiology of NITM remains unclear. It is thought to have innervational and/or neuropharmacological origin and be related to an inability to relax accommodation rapidly and fully to the baseline far point (Ong and Ciuffreda 1995). The neuropharmacological origin may involve the autonomic nervous system where presence of a sympathetic inhibitory dysfunction would result in the increased activation of accommodation through the parasympathetic system, which would result in an increased myopic shift because of its heightened excitatory action (Vasudevan and Ciuffreda 2008).

The introduction of highly precise non-contact, partial coherence interferometric methods for assessing axial length has also revealed that small, transient changes in eye length accompany accommodation. An increase of axial length of magnitude about 5 to 48 µm (up to 6 D stimulus) associated with accommodation have been reported (Drexler, Findl, Schmetterer et al. 1998; Mallen, Kashyap and Hampson 2006; Read, Collins, Woodman et al. 2010). However, conflicting results were obtained on the changes of axial length during accommodation between emmetropic and myopic young adults. Drexler et al (1998) reported a greater change in axial length with accommodation in emmetropes compared with myopes; Mallen et al (2006) reported a significantly greater eye elongation in their myopic subjects compared with their emmetropic subjects and Read et al (2010) found no significant change in magnitude of eye elongation in their myopic and emmetropic subjects. The difference in findings could be due to how the axial length changes were measured and the degree of myopia of the participants (Read, Collins, Woodman et al. 2010).

In another study, axial elongation was observed following a prolonged near task of 30 min at 5 D of accommodation in a group of young adults (Woodman, Read, Collins et al. 2010). This elongation persists for a short period of time after near work but returned to baseline level after 10 min. Both EOM and progressing myopes showed significantly greater increase in axial length than emmetropes. The difference could be due to the reduced ocular rigidity associated with myopia which allows for greater transmission of ciliary muscle force to the choroid and sclera (Mallen, Kashyap and Hampson 2006), as the sclera is more extensible in myopes. There is also a possibility that the eye length effect could be a result of changes in the choroidal thickness, as observed in chicks (Nickla, Wildsoet and Wallman 1998) and human studies (Chakraborty, Read and Collins 2011).

The magnitude of change in eye length is observed to increase for larger accommodation demands (Read, Collins, Woodman et al. 2010). This imply that larger amounts of near work, performed at closer working distances, might potentially be expected to lead to prolonged short-term eye length changes of greater magnitude that could potentially predispose a patient to greater amounts of eye elongation in the longer term (Read, Collins, Woodman et al. 2010). This transient axial elongation in myopes could account for the increased NITM observed in myopes.

Another possible aetiology of NITM is the corneal power. Myopes exhibited greater corneal power and spherical aberration (Vasudevan, Ciuffreda and Wang 2007) than emmetropes before reading (at baseline). This difference increases following prolonged reading. Forces from the upper lid during the down gaze in reading are thought to compress the cornea locally which induces transient changes in superior corneal topography and transient changes in corneal aberrations (Buehren, Collins and Carney 2005). Due to the lid forces, the superior corneal thickness was increased in myopes more than emmetropes following reading (Vasudevan, Ciuffreda and Wang 2007) as myopes are observed to have a narrower lid aperture during reading (Buehren, Collins and Carney 2005). This could also induce a higher transient myopia in myopic than emmetropic individuals.

1.6.10 Other Factors Affecting NITM

Besides the method of measurements (open- versus closed-loop conditions) and duration of near task, other factors investigated were cognitive demand (Rosenfield and Ciuffreda 1994) and letter size and contrast of the near task on NITM (Schmid, Hilmer, Lawrence et al. 2005).

Rosenfield and Ciuffreda (1994) investigated the effect on NITM of near tasks which involved low, moderate or high cognitive demand and found no significant differences between the three cognitive levels. They thus proposed that the degree of NITM elicited is related to the within-task accommodative response rather than to variations in cognitive demand during the course of the task. Schmid, Hilmer, Lawrence et al (2005) studied the effects of two letter variables, size and contrast, on accommodation accuracy during a near task and on NITM and its subsequent decay. There was a significant effect of letter size but not of contrast on accommodation accuracy, but differences were small and not clinically relevant. NITM was greater and decay longer for larger letters than for smaller letters, but the differences in NITM and its decay between myopes and emmetropes were of similar magnitude for all six combinations of letter size and contrast. Schmid, Hilmer, Lawrence et al (2005) concluded that variations in letter size and contrast of reading material could not be the cause of greater accommodation inaccuracy and greater near work-induced adaptation that would exacerbate myopia development in young adults.

1.7 Issues to be Addressed

Based on review of the literature, there may be an important role for visual adaptation to play in myopia development. Adaptation to contrast and accommodation could potentially be mechanisms necessary for temporal averaging of retinal image defocus which give rise to retinal error signals for the control of eye growth.

Form deprivation experiments indicate that emmetropization has both spatial frequency and contrast requirements. Considering animal models, excessive axial elongation can be induced by restricting the spatial frequency content and lowering image contrast, with diffusers placed over the eye (Wiesel and Raviola 1977; Wallman, Gottlieb, Rajaram et al. 1987). Furthermore, the more frosted the diffusers are, the greater the amount of myopia developed (Bartmann and Schaeffel 1994), indicating that the visual system can quantify these features over time (Schaeffel and Diether 1999). The visual system is thought to analyse the spatial frequency content and/or image contrast and that this can provide information on the plane of focus. As the position of the image plane fluctuates continuously with accommodative status and viewing distances, the control of eye growth can only occur by an averaging procedure with a long time constant (Diether and Schaeffel 1999).

Since myopia development has been consistently associated with prolonged near work, it is reasonable to assume that adaptation effects occur during prolonged reading. Therefore, a reduction of image contrast occurring under extended periods of defocus through prolonged reading which results in contrast or accommodative adaptation processes (when accommodation is inaccurate) may have caused myopia development. While contrast adaptation has been suggested as a possible reason reading is associated with myopia, there has been no research investigating this theory. In this thesis, both contrast and accommodative adaptations induced by reading will be investigated.

Reading involves prolonged viewing of high contrast text with characteristic orientation and spatial frequency (Majaj, Pelli, Kurshan et al. 2002). We propose that reading may cause contrast and spatial adaptation to occur, especially when the reading task involves long continuous near viewing of essentially unchanging material and the page occludes all distant objects (Wallman and Winawer 2004). Moreover, this human activity requires hours of fixation at a particular distance. The adaptation to the high contrast printed text may suppress the visual strength of certain spatial frequency of targets during this prolonged viewing, thus reducing the retinal sensitivity to these spatial frequencies which could be similar to that created by rows of letters and spaces between rows (essentially a horizontal grating) and the stroke frequency of the letters themselves (Majaj, Pelli, Kurshan et al. 2002). The reduced retinal sensitivity may lead to reduced retinal activity that mimics the lowered retinal activity that occurs when defocus is present and thus promotes axial elongation. The young age at which reading begins is important because of the plasticity of the neural system. Reading duration also plays an important role as prolonged reading would lead to a longer period of reduced retinal activity and persistent retinal signal error would interfere with normal emmetropization process.

In the first 2 experiments of this thesis, contrast adaptations induced after reading and viewing of a classic target of sine wave gratings were explored. The term: “text induced contrast adaptation” has been used to describe the contrast adaptation effect because of its similarity with the known phenomenon of contrast adaptation that occurs after viewing a high contrast sine wave grating (Blakemore and Campbell 1969; Georgeson and Harris 1984). Myopes may have a retina that is more sensitive to the effects of adaptation and/or show greater adaptation to reading materials due to their greater blur (Thorn, Corwin and Comerford 1986; George and Rosenfield 2004; Rosenfield, Hong and George 2004) and accommodative adaptations [review in (Chen, Schmid and Brown 2003)]. In this thesis, the difference in the degree of contrast adaptation that occurs in response to gratings (as a measure of classic contrast adaptation phenomena) and/or text in myopes and non-myopes will be determined.

Myopes have been showed to present with reduced accommodation at near which leads to a higher lag of accommodation (McBrien and Millodot 1986b; Gwiazda, Thorn, Bauer et al. 1993b; Yeo, Kang and Tang 2006). As a result, the effect of the reduced retinal sensitivity in contrast adaptation and hyperopic defocus occur when reading may augment the total effects of near work on eye growth in children. In addition, the accommodative adaptation will be investigated under closed-loop condition. The transient myopia induced by accommodative adaptation after near work, creates a myopic defocus which may linger on without fully dissipating. This could also enhance the adverse effects of near work on eye growth in children as discussed in 1.6.7.2.

Therefore, the objectives of this research are to:

1. Investigate the effect of reading on the contrast sensitivity function of a group of Singaporean children. Contrast sensitivity function before and after reading was studied in myopic and emmetropic children in Singapore. We hypothesize that a greater adaptation effect would be observed in the myopic children.

2. Investigate the effect of reading Chinese and English text on contrast adaptation. Chinese text appears more complicated than English text, and prevalence of myopia is higher among Chinese children. We hypothesize that Chinese text would induce a greater contrast adaptation effect than English text.

3. Investigate the effect of reading Chinese and English text on accommodative adaptation. For similar reasons stated in 2, this research aimed to determine if accommodative adaptation was greater following a period spent reading Chinese versus English text. Furthermore, the effect of accommodative adaptation when reading distances change will be investigated for a group of Singaporean children.

The subsequent chapters in this thesis consist of the following: Chapter 2 comprises a detailed description of the equipment and methodology used in the experiments. Chapter 3 describes Experiment 1 in which contrast adaptation between emmetropic and myopic children was investigated. Chapter 4 describes Experiment 2 in which the effect of reading English and Chinese text on contrast adaptation was studied. Chapter 5 describes Experiment 3 in which the effect of reading English and Chinese text on accommodative adaptation was investigated. Chapter 6 consists of an overall discussion of near adaptation on myopia development and the final conclusion.

CHAPTER 2

DETAILED EXPERIMENTAL METHODOLOGY

There are three major experiments conducted in the research work reported in this thesis. Experiments 1 and 2 used similar apparatus for the study of contrast adaptation in children and young adults respectively. Experiment 3 used a different set of apparatus to investigate accommodative adaptation in children. Details of the apparatus and methodologies are described here.

2.1 Recruitment of Subjects

Primary school children from age 7 to 12 yr of age were invited to participate in the research experiments. Subjects were recruited from the Singapore Polytechnic Optometry Centre and the satellite clinic at West Coast Optometry Centre. Some subjects were children of the Polytechnic staff and relatives of the Polytechnic students. In addition, invitation letters were sent out to the principals of four primary schools located near the vicinity of Singapore Polytechnic. Only one primary school principal was willing to distribute the invitation letters to the children of her school. For the other schools, the children were recruited by the author of this thesis, meeting both the parents and children at the school gate before and after the school hours to explain the studies to them.

It was intended that the primary school children recruited performed three adaptation tasks: reading English, reading Chinese and viewing horizontal gratings, for 1.5 days duration. However, the tediousness of the experiment put some of the children off. As a result, getting them to return for subsequent sessions was a challenge. Some parents were also not willing to bring the children in for the second time. Eventually, the approach had to be changed such that the children subjects would adapt for English and gratings only. Children were used in Experiment 1 and young adults were used in Experiment 2 for both the contrast adaptation experiments. This arrangement also allowed the author to recruit child subjects from other races, such as the Malays and Indians to participate in the study since the children were not required to read Chinese text in Experiment 1.

Recruitment for young adult subjects in Experiment 2 was mainly done within Singapore Polytechnic since it has a large pool of young adult students. Most of these subjects were optometry students and their friends who were studying in Singapore Polytechnic. They were in the age range 16 to 23 yr. Only those who could read and understand Chinese were recruited.

Recruitment for children subjects for Experiment 3 was easier than that in Experiment 1 because the duration for each child to go through two adaptation tasks with two different reading distances was about three hours versus the whole day in Experiment 1. The requirement was also that the child must be able to read Chinese text. Therefore, children recruited for this Experiment were mainly Chinese dominated. A total of 15 children participated in both Experiments 1 and 3.

2.2 Preliminary Examination

All the children and young adult participants undertook a series of preliminary tests to ensure that they met the inclusion criteria of (i) at least 6/6 monocular visual acuity using a Snellen chart and monocular contrast sensitivity better than 1.65 on the Pelli-Robson chart for either eye; (ii) cylinder ≤ 0.75 DC (for either eye), myopia ≤ 6.00 D, hyperopia ≤ 0.75 D and anisometropia ≤ 1.00 DS, (iii) absence of any ocular disease including strabismus.

Preliminary examination was performed in a standard optometric room with room luminance 50 cd/m^2 at the wall next to the projected screen. Visual acuity was measured using a Snellen chart, which was projected with a luminance of 130 cd/m^2. The cover test was performed to rule out strabismus. Subjective refraction was performed with a trial frame. Retinoscopy was performed first to obtain an estimation of the refractive error. Plus spherical lenses were always added first before minus spherical lenses to check for the best sphere before Jackson Crossed-cylinder was performed to measure the astigmatism of the eyes. Binocular balancing using the monocular fogging balance technique was used to balance the accommodation of the two eyes. The final refractive errors were based on the technique of maximum plus for best acuity (Elliott 2003).

Ocular health was screened using a slit lamp biomicroscope, Topcon SL-D2 and a Keeler direct ophthalmoscope. Axial length was measured with the Carl Zeiss IOLMaster which uses a non-contact technique. The IOLMaster measured 4 readings with ± 0.02 mm precision. Contrast sensitivity was screened using a Pelli-Robson chart. The chart was illuminated from a bright distant source, so as to ensure even illumination. Its luminance was 65 cd/m^2. Contrast sensitivity measured using this chart has been found to be repeatable to within ± 0.15 log units (Elliott, Sanderson and Conkey 1990).

The preliminary examination for Experiment 3 was somewhat similar to the preliminary procedures in Experiments 1 and 2, except that amplitude of accommodation was performed instead of the Pelli-Robson contrast sensitivity. The monocular amplitude of accommodation was measured with an aperture rule with a fixation target of N5, at a luminance of 95 cd/m^2. The amplitude of accommodation obtained must be at their age norm, calculated from the Duane-Hoffstetter formula for minimum amplitude (15.0 – 0.25 x age). A total of 4 children were rejected due to low amplitudes.

2.3 Contrast Threshold Measurement Apparatus (used in Experiments 1 and 2)

Contrast thresholds were measured using the Metropsis Psychophysical Vision Testing (MPVT, Cambridge Research System). The Metropsis vision testing suite is able to perform visual function tests such as contrast sensitivity function, Cambridge colour test and macular pigment optical density with precise measurements. The module purchased for Experiments 1 and 2 consists of the contrast sensitivity function measurement. The test requires no programming or specialist computer skills, but is sufficiently flexible for most research requirements. The technology of the Metropsis vision testing is the same as the high-end visual stimulator systems produced by Cambridge Research Institute. All the tests use the supplied DVP-14 digital video processor. This incorporates dynamic range enhancement technology with the Bits++ system, which delivers true 14 bit video for each colour and provides the fidelity to accurately reproduce any visual stimulus. The supplied calibration device ensures that luminance and chromaticity is precisely controlled from one use to another. For optimum performance, the Metropsis vision tester was calibrated every week on Monday morning. The CRT monitor was switched on an hour before any measurements were taken to ensure consistent characterization of contrast and colours.

The test stimulus was presented on a high definition 53 cm View Sonic Professional Series P225f CRT monitor. The angular size of the monitor was approximately 17° x 22° at a test distance of 1 m, and a mean luminance of 50 cd/m^2 was set for contrast sensitivity measurement. The frame rate was set at 100 Hz or more to remove any perceived flicker and that the screen resolution is 1024 x 768. Generally there is a compromise between frame rate and screen resolution. The CRT monitor was used because LCD monitors often do not support a high enough line scan rate to maintain large screen resolutions at high refresh rates (http://www.crsltd.com/research-topics/displaytech/index.html). The higher the line scan rate, the better the vertical resolution. In the CRT monitor for contrast measurement, the line scan rate was set to 80 kHz. The clock rate of the monitor determines the maximum number of pixels that can be output. The greater the number of pixels, the better the horizontal resolution.

Besides the low scan rate in LCD monitors, the other advantage of using a CRT over a LCD monitor is that the CRT has a wider range of grayscale resolution that can display low contrast stimuli. Most of the LCD monitors digitize the incoming video voltages with a resolution of only 6- or 8–bit as compared to the higher 14-bit video generated by

CRT as mentioned above. Furthermore, the optical filtering properties of LCD monitors have a strong angular dependence, so a slight off-axis viewing may affect the contrast perceived by the observer (Brainard, Pelli and Robson 2002).

The CB6 button box (Figure 2.1) was used by the subjects to indicate their response. For the 2-interval forced choice protocol, if the grating was seen on the first beep tone, button "A" was pushed and if it was seen on the second beep tone, button "C" was pushed. It communicates with the visual stimulus generation device via an infra red link.

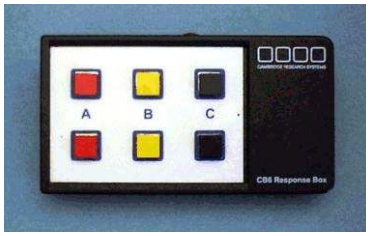


Figure 2.1 The response box

The contrast sensitivity function test measures a range of spatial frequencies. The MPVT comes with a test protocol wizard which allows researchers to define all test parameters sequentially, define specific stages in the protocol set up and changes in stimulus or spatial frequency options. The protocol wizard allows the researchers to define the type, size and orientation of the stimulus to be presented during contrast sensitivity test and the psychophysical procedure used to control the test and calculate the end results. The test protocol and all the other parameters for Experiments 1 and 2 are specified in Table 2.1.

2.3.1 Psychophysical Procedure

Three standard test protocols based on the Linear Staircase, Logarithmic Staircase and Quest adaptive procedures were provided. The Logarithmic Staircase was chosen for Experiments 1 and 2 because log unit of contrast was the preferred option for quantifying contrast sensitivity function in most studies (1 db = 0.1 log unit). In the Logarithmic Staircase procedure, it is necessary to have a starting estimate of where the contrast threshold lies. The initial stimulus contrast is then set either above the estimated threshold, to perform a descending staircase, or below the estimated threshold, to perform an ascending staircase. The program presents a stimulus at the initial contrast, and then based on the subject's response it presents the next stimulus at either an increased or decreased contrast, gradually converging on the threshold, until predefined termination criteria are met (Figure 2.2).

Table 2.1 Settings used in Experiments 1 and 2

Protocol	**Setting Level 1**	**Setting Level 2**
Psychophysics test method	2 interval forced choice	
Adaptive procedure	Logarithmic staircase Properties	
	Initial contrast	20%
	Termination criterion	12 reversals
	Threshold determination	8 reversals
	Number of positive confirmation	1
	No of negative confirmation	1
	Initial step size	1.5 dB
	Positive step size	0.2 dB
	Negative step size	0.6 dB
Show a motivational trial every	10 trials	
Mean luminance	50 cd/m^2	
Fixation target	Cross, 0.2 degrees, black	
Gabor or grating	Gabor	1 deg per standard deviation
	orientation	180 deg
	Spatial phase	180 deg
Spatial offset of the stimulus from the fixation target	Location	0 deg
Stimulus presentation time	800 ms	
Specify spatial frequency (cpd)	0.5, 1.2, 2.7, 4.4, 6.2	

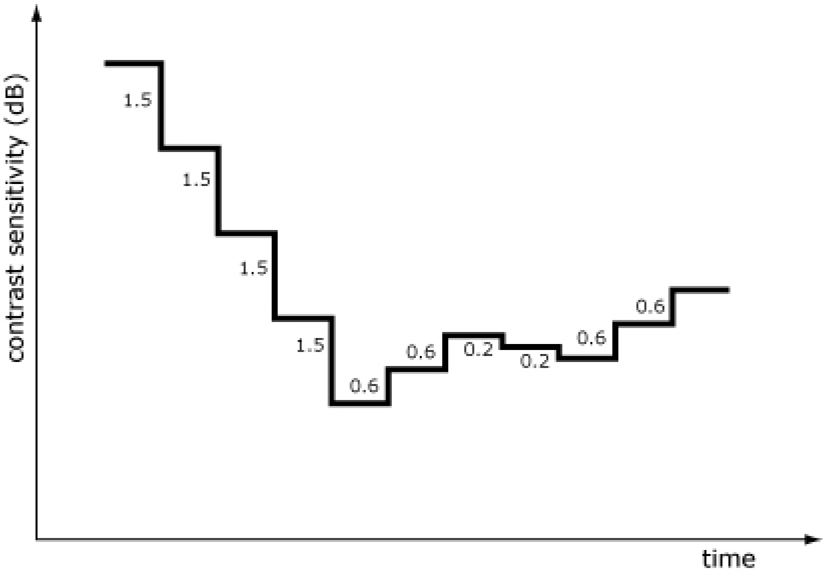


Figure 2.2 The algorithm of the logarithm staircase testing procedure.
At the beginning of the test, when a correct response was obtained, contrast was reduced by 1.5 dB step until the first mistake was made. Contrast was increased by 0.6 dB step until the subject sees the target. Subsequently, contrast was reduced by steps of 0.2 dB until a mistake was made. The steps of 0.6 dB increment and 0.2 dB decrement continue until contrast thresholds were obtained. A single threshold determination consists of 12 reversals; the average of the last 8 closest reversals determined the threshold value.

2.3.2 Initial Contrast

Initial contrast defines the contrast at which all stimuli will first be displayed. This can be tuned for each test frequency in the protocol wizard. In Experiments 1 and 2, the initial contrast was set at 20%. It is important that the initial contrast is not set too high, otherwise the contrast test will take an unnecessarily long time to work its way to threshold.

2.3.3 Termination Criteria and Threshold Determination

The test will end after a certain number of reversals. The number of reversals for threshold determination is usually set lower than the total number of reversals required for termination: the first few reversals are not used in the calculation, as they probably occurred before the procedure had settled properly around the sensitivity threshold. The result of the test, the contrast threshold determination, is calculated as the average contrast over a specified number of reversals. Motivational trials are presented randomly in each of the test spatial frequencies at a contrast 10% above the current contrast for that spatial frequency, but they are not used when computing final threshold.

2.3.4 Initial Step Size, Positive Step Size, Negative Step Size

The initial step size is designed to bring the stimulus contrast close to the subject's sensitivity threshold within a few stimulus presentations. These relatively large contrast steps will continue until the first reversal occurs, at which point smaller positive (or negative) contrast modifications will take place depending on the subject's correct (or incorrect) responses (Figure 2.2).

2.3.5 Fixation Target

The fixation target is a small mark in the center of the screen, on which the subject fixated gaze during the test. The protocol wizard allows the researchers to specify the type, shape, size, colour and the location of the fixation targets. In the 2- alternate forced choice test, one stimulus will appear on the left of the fixation target, and the other would appear on the right. In the 2-interval forced choice test the stimuli will always appear centered on the fixation target. The 2-interval forced choice fixation was used in the experiments because contrast sensitivity was measured from the central foveal region. This is to allow comparison of future studies on measuring contrast sensitivity at the peripheral retinal region using the same testing protocol. The peripheral retinal locations have been indicated as possible locations which cause axial elongation (Smith, Kee, Ramamirtham et al. 2005). The length of time for which the stimulus will appear in milliseconds can also be set by the protocol wizard. In Experiments 1 and 2, the stimulus presentation time was set at 800 ms as recommended by the manufacturer (Table 2.1).

2.3.6 Test Stimulus Pattern - Gabor Stimuli

In contrast adaptation experiments, Gabor stimuli were selected because Gabor functions have traditionally been used as a realistic model of the receptive field structure of simple cells of V1 (Marcelja 1980). The Gabor model uses Gaussian-windowed sinusoidal gratings, so that the contrast fades away from the centre and hence does not have sharp edges (Figure 2.3). Edges produce spatial frequency effects, which mean that they can affect the contrast threshold. Therefore, Gabor gratings are the stimulus pattern of choice (Smyth, Willmore, Baker et al. 2003). The Gabor used in the Metropsis Contrast test is radially symmetrical, with equal standard deviations. The full width of a Gabor at half of maximum amplitude is 2.35 standard deviations. Although the extent of a Gaussian is infinite, its amplitude asymptotes toward zero within a few standard deviations and the Metropsis software ensures the Gabor patch is large enough to represent the complete envelope to a resolution of better than 1 least significant bit. In the experiments, the Gabor size was set at 1 deg per standard deviation, which means that the full width of the Gabor at half of maximum amplitude was 2.35 deg.

Previous studies found that maximum contrast adaptation occurs at test orientations similar to that of the adapting stimulus (Greenlee and Heitger 1988; Heinrich and Bach 2002b). In the case of reading material, the eyes move from left to right to read and therefore the adapting gratings were orientated in the horizontal direction. The Gabor stimulus with sine wave gratings was also oriented in horizontal direction (Figure 2.3). The test spatial frequency was either started with 0.5 cpd followed by the other spatial frequencies in ascending order or 6.2 cpd followed by the other spatial frequencies in descending order. The choice of which order went first was randomized for each subject.

Figure 2.3 Picture of a Gabor patch displayed on the test screen. The stimulus would appear on either the first or the second beep tone.

2.3.7 Spatial Frequencies

The contrast sensitivity test is usually performed for a range of spatial frequencies, in order to plot contrast sensitivity as a function of spatial frequency. Spatial frequency is specified in cycles per degree (cpd) subtended at the eye. During the preliminary trials of contrast testing in children in Experiment 1, it was found that the children's attention and concentration were better with shorter test runs. To allow for more frequent, short breaks the protocol was modified to testing the contrast threshold of each spatial frequency separately.

Contrast threshold was measured for horizontal sine-wave gratings of 0.5, 1.2, 2.7, 4.4 and 6.2 cpd in Experiments 1 and 2. These spatial frequencies were chosen as they cover the range of frequencies of the adapting tasks. Moreover, 2.7 and 4.4 cpd are close to the most sensitive spatial frequency perceived by a human eye (see 1.3). Spatial frequencies 1.2 and 6.2 cpd were chosen based on the row frequency and stroke frequency, respectively, of the text (see 2.4). In animal studies, the mid spatial frequency range is thought to be the most important for the retinal image processor controlling eye growth (Schmid and Wildsoet 1997a; Schaeffel, Weiss and Seidel 1999). Contrast of high spatial frequencies declines rapidly even with little defocus, leaving a narrow operating range of a defocus detector (Diether and Schaeffel 1999). Probably for this reason, lower spatial frequency analysis is more powerful since it provides a larger operating range (Diether and Schaeffel 1999). It was on these bases that the above spatial frequencies were chosen for use in the current study.

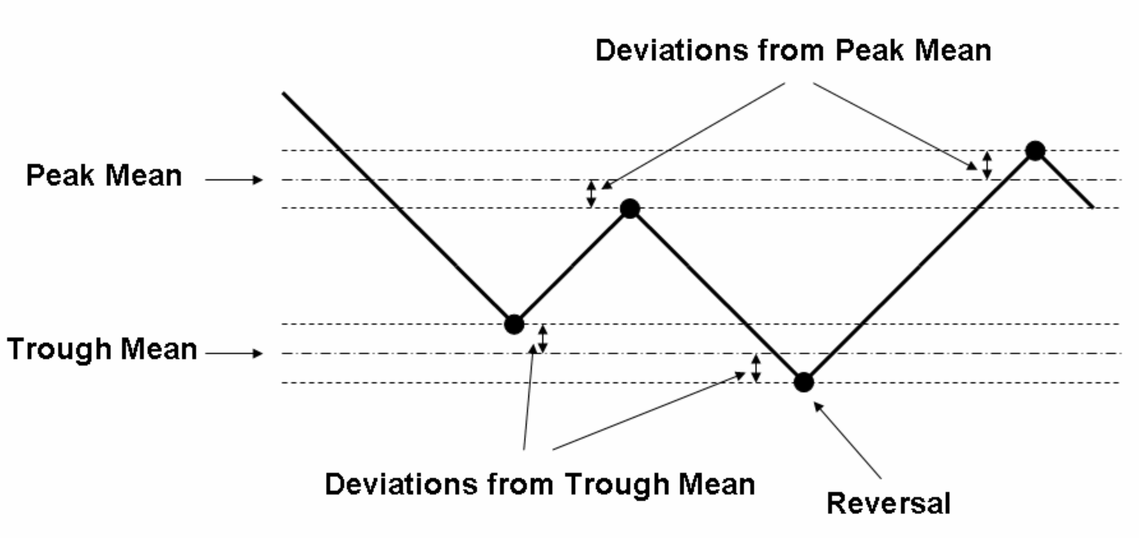


Figure 2.4 Contrast thresholds are calculated as the mid-point between the peak and trough means. The deviations of the peak reversals from their peak mean and deviations from the trough reversals were squared and averaged to obtain the peak variance and trough variance respectively. Both variances are then square rooted and averaged to generate the threshold standard deviation.

At the end of the test, Metropsis calculates the contrast threshold and its standard deviation for each test spatial frequency. Threshold and standard deviation are calculated using the contrasts at the reversal points in the staircase procedure. Metropsis calculates separate mean contrasts for peaks and troughs. Contrast threshold is calculated as the mid-point between the peak and trough means. Metropsis then calculates the deviations of the peak reversals from their peak mean and uses the average square of these deviations to calculate a peak variance (Figure 2.4). These calculations are then repeated for the trough reversals to calculate a trough variance. Both variances are then square rooted and averaged to generate the threshold standard deviation. The threshold standard deviations are used as a guide to determine the variability of the measured contrast threshold in each test run. In Experiments 1 and 2, when the standard deviation was more than 1.50 %, the data were excluded. When that happened, the measurement was repeated after the subject had rested.

2.4 Adaptation Tasks

Three definitions have been used for measuring the contrast of test targets: the Weber fraction definition of contrast, the rms contrast and the Michelson formula (Pelli 1990). The Weber fraction definition of contrast was used to measure the local contrast of a single target of uniform luminance seen against a uniform background:

$$C = \frac{\Delta L}{L}$$

where ΔL is the increment or decrement in the target luminance from the uniform background luminance L. One usually assumes a large background with a small test target, in which case the average luminance will be close to the background luminance. If there are many targets, or if there is a repetitive target as in the case of a grating stimulus, these assumptions do not hold (Pelli 1990). Therefore the Weber fraction was not appropriate in categorizing the contrast of the sinusoidal test targets used in the MPVT, but it can be used for calculating the contrast of the printed reading tasks.

Another way to define contrast in an image is to measure the root-mean-square (rms) contrast (Pelli 1990). This formula is used to compare the contrast of two different images. The rms is defined as

$$rms = \left\{ \frac{1}{n-1} \sum_{i=1}^{n} (x_i - x)^2 \right\}^{1/2}$$

where x_i is a normalized gray-level value such that $0 \le x_i \le 1$ and x is the mean normalized gray level:

$$x = \frac{1}{n}\sum_{i=1}^{n} x_i$$

The rms contrast does not depend on spatial frequency content of the image or the spatial distribution of contrast in the image, and, it is not suitable for defining the contrast of sinusoidal gratings.

The Michelson formula is used for measuring the contrast of a periodic pattern such as a sinusoidal grating (Pelli 1990), and was the most appropriate formula in measuring the test targets used in the experiments. In this thesis, three adaptation tasks were used. One of them was a sinusoidal grating at 6.2 cpd and two other adaptation tasks were English text and Chinese text. In Experiment 1, only English text and grating were used as adaptation tasks. In Experiment 2, English text, Chinese text and grating were used as adaptation tasks.

Both the English and Chinese tasks consisted of high contrast (92%) texts, calculated using the Michelson contrast formula

$$C = \frac{L_{max} - L_{min}}{L_{max} + L_{min}}$$

where L_{max} is the maximum luminance of the white paper background and L_{min} is the luminance of the black print on the letter. The luminances were measured using a Minolta Luminance Meter LS-100. When the Weber fraction was used, the contrast of the text was calculated to be 96%.

For the English task, the printed reading material was children's stories of size 12 points Times New Roman font, with a line spacing of 17.5 points on A4 landscape paper. This was based on the local newspaper “The Straits Times”, which is the most widely read English paper in Singapore. Two of the five spatial frequencies, 1.2 and 6.2 cpd need special mention here. To determine the spatial frequency that best described the lines of text, the text was assumed to form the black bars of the grating and the spaces in between formed the white bar of the grating. For a distance of 40 cm, the spatial frequency of the related grating was 1.2 cpd (Figure 2.5). So, 1.2 cpd was the row frequency of the text used.

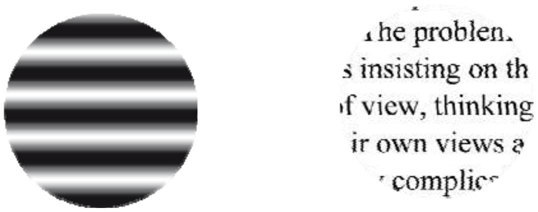
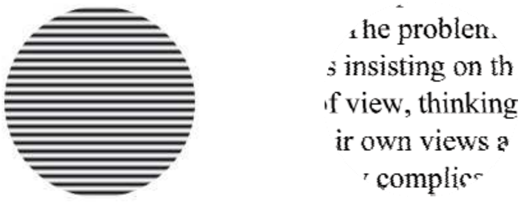


Figure 2.5 Diagrammatic representation of row frequency
The lines of letters correspond to the black bars and the spaces between the rows of text correspond to the white bars. This forms the row frequency of 1.2 cpd at 40 cm.

The spatial frequency of the English letters was calculated based on the stroke frequency, which, as was suggested by Majaj et al (2002), is an excellent predictor of the centre frequency for identifying letters. First, a horizontal line was drawn across the letters of a word and the number of vertical strokes of the letters that crossed the horizontal line was counted. Stroke frequency was obtained by averaging the number of strokes crossing the horizontal midline for all the letters, divided by the average letter width in degrees. The first 2 rows of words, on the first page of the adapting text stimuli were measured. The stroke frequencies for English and Chinese text were found to be 6.04 and 6.21 cpd respectively. Both the stroke frequencies were taken into consideration when setting the test frequency that represents the stroke frequency of the texts. As the MPVT was not able to generate 6.0 cpd due to its internal calibration, spatial frequency 6.2 cpd was used as a compromised stroke frequency of both the texts (a small part of the text is shown in Figure 2.6b).

The second adaptation task consisted of a high contrast horizontal sine-wave grating (92%) with a spatial frequency of 6.2 cpd (at a viewing distance of 40 cm) printed onto a white A4 landscape paper (a small part of it is shown in Figure 2.6a). During adaptation, the subject was required to stare at the fixation point placed at the centre of the page. The grating was made similar to the stroke frequency because previous studies (Lunn and Banks 1986; Magnussen, Dyrnes, Greenlee et al. 1992) used the row frequency on VDU, so no one has investigated the stroke frequency on contrast adaptation before.



a b

Figure 2.6 The Adapting stimuli used in this experiment (a) Sine wave grating at 6.2 cpd (b). Lines of English text

For Chinese text, the simplified version of the Chinese characters was used as this version is used widely in Singapore and China. The row frequency for Chinese text was fixed at 1.2 cpd, so that it was similar to the row frequency in English text (Figure 2.7). This sets the font size of the Chinese text to be SimSun 10.5 with a spacing of 17 points. This font size was also found to be similar to the font size used in one of the popular Chinese newspaper widely read by the Singaporean teenagers, “My Paper”. Contrast of the reading materials was set at 92%.

Figure 2.7 Diagrammatic representation of row frequency.
The lines of letters correspond to the black bars and the spaces between the rows of text correspond to the white bars.

The stroke frequency was also calculated using the method proposed by Majaj et al (2002) as described above. The Chinese text had a stroke frequency of 6.21 strokes/degree. This was not very different from the English text. Due to the logographic character, the width of each Chinese character was bigger than each letter in English text, even though the font size was smaller than the English text (SimSun 10.5 versus Times New Roman 12). As the stroke frequencies of the English and Chinese texts were calculated to be 6.04 and 6.21 respectively, the grating adaptation task of 6.2 cpd was created (Figure 2.8). The sequence of the 3 adaptation tasks was randomized for each subject in Experiment 2.

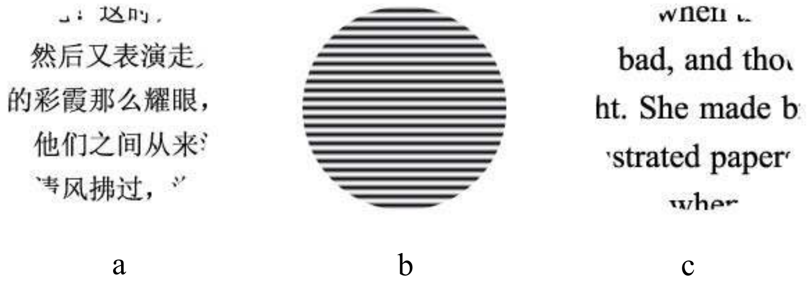


Figure 2.8 Diagrammatic representation of stroke frequency of adapting stimuli (a) Lines of Chinese text (b) Sine wave grating at 6.2 cpd (c) Lines of English text

The sequence of which adaptation task was to be performed first was randomized among the subjects. In Experiment 1, the children were instructed to choose 2 pieces of folded papers, one containing “E” which signified the English task and the other containing “G” which signified the grating task. The chosen letter would be the task to be performed first. In Experiment 2, each task was assigned a number, for e.g. English as 1, Chinese as 2 and grating as 3. The sequence of randomization process consisted of the following: 1,2,3 or 1,3,2 or 2,1,3 or 2,3,1 or 3,1,2 or 3,2,1. The first subject recruited was assigned to perform based on the sequence of 1,2,3 and the second subject was assigned to the sequence of 1,3,2 etc. This randomization process ensured that all the adaptation tasks had equal chances of being the first or the last task.

2.5 Contrast Sensitivity Testing Procedure

Room illumination of 45 cd/m^2 was measured from the wall just behind the MPVT using the Minolta Luminance Meter LS-100. Local luminance was adjusted beside the adaptation stimuli (reading text or horizontal sine wave gratings) to ensure that the adaptation task was similar to the illumination of the computer screen (~ 50cd/m^2).

The adapting stimuli and the computer screen of the contrast testing equipment were placed 90 deg to each other and at 40 cm and 1 m, respectively, from the subject (see Figures 2.9 and 2.10). The angular subtense for adapting stimuli was 35 deg horizontal and 27 deg vertically. Chin rests were used for both the measurements and the adaptation tasks, to ensure that constant viewing distances and head orientations were maintained at all times. The adaptation task was placed on a reading stand on a table of adjustable height. Each subject's height in a sitting position was adjusted so that the adaptation task and the contrast testing screen were at his/her eye level.

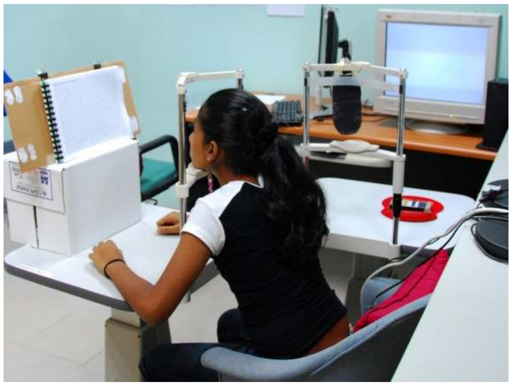


Figure 2.9 A subject was reading the text placed 40 cm away. The test screen displayed by the computer was placed perpendicularly from the text at 1 m distance

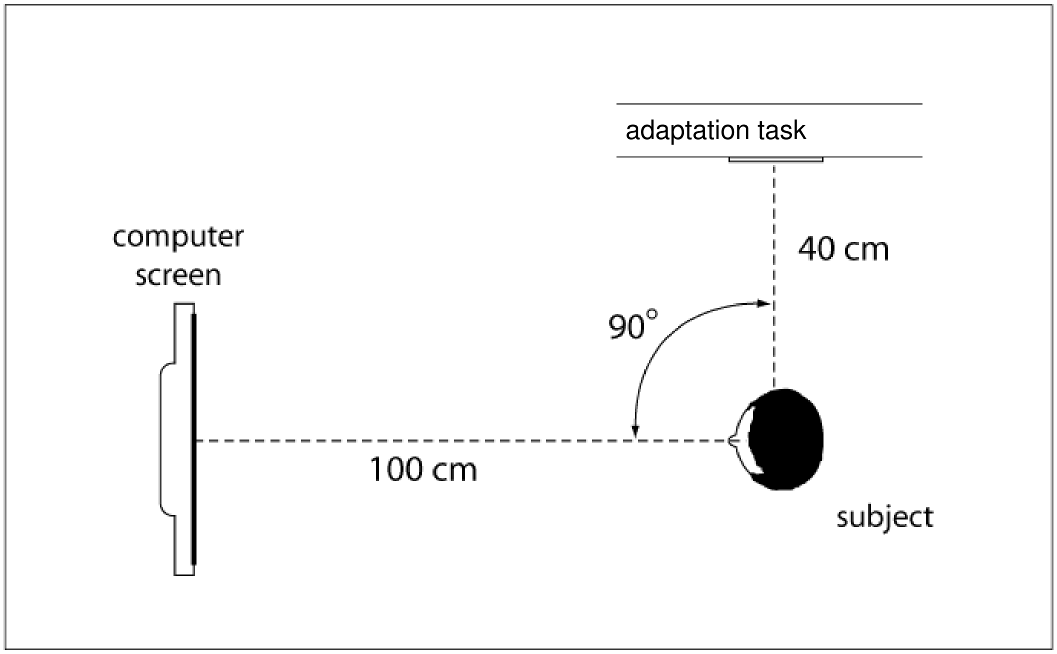


Figure 2.10 Schematic diagram of the experimental design. The adaptation task was placed 90º to the test stimuli. The participant adapted to the task for 1 min, then turned his or her head to the computer screen for the contrast threshold measurement which lasted 30 s. This procedure was repeated until three threshold values were obtained for each spatial frequency.

Subjects were able to revolve, so they could quickly change fixation from the adapting to test stimuli. Subjects viewed the adaptation tasks binocularly. An occluder aligned with the left eye was attached to the chin rest so that contrast threshold was measured monocularly. Refractive errors (based on subjective refraction) of subjects were corrected using a trial frame and lenses. This is important as incorrect optical correction, i.e. defocus is known to affect the contrast sensitivity function (Woods, Strang and Atchison 2000). As the degree of myopia of the subjects were below -6.00 D, the correcting lenses either due to spectacle magnification (Collins and Carney 1990) or optical distortion (Liou and Chiu 2001) would not have much effect on their contrast sensitivity function.

Since there were five spatial frequencies 0.5, 1.2, 2.7, 4.4 and 6.2 cpd to be tested, the participant was instructed to pick one out of two folded papers presented. If the participant picked the folded paper that contained 6.2, then the 6.2 cpd spatial frequency would be tested first, followed by the other frequencies in descending order. If he picked a folded paper that contained 0.5, then the 0.5 cpd spatial frequency would be tested first, followed by the other frequencies in ascending order.

Once the first spatial frequency to be tested was determined, baseline contrast thresholds for the spatial frequency either following an ascending or descending order were measured before the adaptation tasks were performed. Prior to the baseline measures, subjects were not allowed to perform any near work. Three trials were conducted for each spatial frequency. Contrast threshold at each spatial frequency was obtained by averaging the values of the three trials. As there could be a learning effect on the use of the MPVT, the first few trials were not included in the data analysis. They served as practice runs for the subjects to familiarize with the test. A lack of familiarity with the response button box or the test itself may cause early errors and lead to inaccurate results (Metropsis Help Manual). Moreover, learning can have an effect on reducing the contrast needed for detection (Bao, Yang, Rios et al. 2010).

To provide an indication of the within session repeatability of the contrast sensitivity testing, we calculated the coefficient of variation (within subject standard deviation divided by the mean), for each spatial frequency tested, for the population of children and young adults. Table 2.2 shows the average coefficient of variation (COV) for baseline contrast sensitivity measurements. The values of COV show that the CSF measures were consistent.

Table 2.2 Coefficient of variation (COV) of baseline contrast sensitivity (CS) measures

	Spatial Frequency				
	0.5	1.2	2.7	4.4	6.2
COV of Baseline CS in Children (%)	13.23	12.71	13.21	13.82	13.16
COV of Baseline CS in Adults (%)	11.51	12.10	12.76	12.51	12.68

After the baseline measurements, subjects commenced the first adaptation task, which was either reading English stories or staring at the fixation dot in the middle of a high contrast horizontal grating of 6.2 cpd for 5 min. Subjects then turned 90 deg to view the test stimuli and contrast thresholds were measured for 30 s. Subjects were told to turn back to the adaptation task to top-up the effect of adaptation for 1 min, and then turned back to the test stimuli for measurement for 30 s. Subjects turned back and forth between the adaptation task (1 min) and test stimuli (30 s) until the run was completed and the threshold contrast determined. The decision to test for 30 s and adapt for 1 min periods was based on the research of Blackmore & Campbell (1969), who reported that the adaptation effect reaches a plateau after viewing for about 1 min and declines 30 to 40 s after the adapting stimulus is removed. The adapt-test-readapt paradigm should ensure stable levels of contrast sensitivity as it balances exactly the amount of recovery that occurs during testing (Rose and Evans 1983). Moreover, too long an adaptation task, say, up to 30 min as proposed by Magnussen and Greenlee (1985) would produce fatigue which would affect the accuracy of contrast adaptation effect.

The adaptation stimulus was placed at 40 cm (2.5 D accommodative demand) and the test stimulus was placed at 1 m (1 D accommodative demand), which means that subjects needed to make a small adjustment in their accommodation in order to shift from viewing the adaptation and test stimuli. Previous research has shown that the time constants of accommodation response time to change from 1 D amplitude to 2.5 D amplitude is about 0.4 s (Kasthurirangan, Vilupuru and Glasser 2003). The latency of accommodation from stimulation was about 0.4 s for accommodation and 0.3 s for dis-accommodation (Kasthurirangan and Glasser 2006). With less than 1 s of accommodation response time, it is unlikely that delays in focusing between the adaptation and test stimuli adversely influenced the results of the post adaptation contrast sensitivity testing, given that the whole period of testing was 30 s. Furthermore no subject reported any symptoms of blur during the tasks.

It took approximately 7 min to complete a run to obtain a contrast threshold during and after adaptation. Therefore, approximately 20 min was required for completing the task at one spatial frequency as 3 runs were obtained for each spatial frequency. Therefore a total of 15 contrast thresholds were obtained for 5 spatial frequencies for each adaptation task. As the experiment on reading and adaptation was long, some children were reminded regularly to concentrate on the near task given to them. This was especially true of grating adaptation task, as staring at the grating was not an interesting task to the children. So, the children were constantly reminded to look at the centre fixation of the grating throughout in the experiment.

In between the tests, if a child was observed to show loss of attention or signs of fatigue, the test would stop anytime after a complete run, as it has been proposed that diminished attention can reduce contrast sensitivity in both children and adults (Bradley and Freeman 1982). During such breaks, the child would visit the washroom, or have some snacks and drinks or walk at the corridor outside the building for 3 to 5 times to relax their eyes. To determine if fatigue affected the measurements, a subset of children had baseline contrast sensitivity measures performed before and after the completion of all the adaptation tasks. In addition, for each measurement of the contrast threshold, there was a standard deviation generated by the MPVT to present the variability of that particular measurement. When a standard deviation of > 1.5 % was obtained, the measurement was repeated after the child was given a break. This served as a guideline for accepting the contrast threshold measurements for both Experiments 1 and 2. It occurred more often in children of 7 to 8 years old than those older than 10 years old.

2.6 Comparison of Baseline Contrast Sensitivity Readings Made Before and After Adaptation in Children

A comparison of baseline contrast sensitivity measures before and after adaptation was made for 10 children randomly selected from the test group. They were 5 myopes (mean SE ± SD: -2.60 D ± 0.60 D) and 5 emmetropes (mean SE ± SD: -0.05 D ± 0.11 D). The first set of the baseline tests were performed before any adaptation tasks and the second set of baseline tests were performed at least 10 min after the completion of contrast adaptation tasks and measurements. Since the reading time for each run was about 7 min, a resting duration of 10 min or longer was used to allow contrast adaptation to dissipate before the next test was performed. A longer resting time was used for a previous longer duration of adaptation. This was based on the reports of some studies that adaptation and recovery times are similar (Rose and Evans 1983; Magnussen and Greenlee 1985; Georgeson and Georgeson 1987). Analysis of variance using general linear models was performed to compare both sets of the data.

There was no statistically significant difference between the two sets of baseline measures ($F_{1,73} = 0.00$, $P = 0.954$) (see Figure 2.11); contrast sensitivity for the two trials for each test spatial frequency were similar. There was also no significant difference between emmetropes and myopes ($F_{1,7} = 0.02$, $P = 0.883$) (Figure 2.12). These results showed even after the long testing on adaptation, the children were still able to perform as reliably as before the adaptation tasks. Moreover, the standard deviation generated in each trial did not show any evidence of variability in the standard deviations at the end of the testing, thus fatigue did not confound the results.

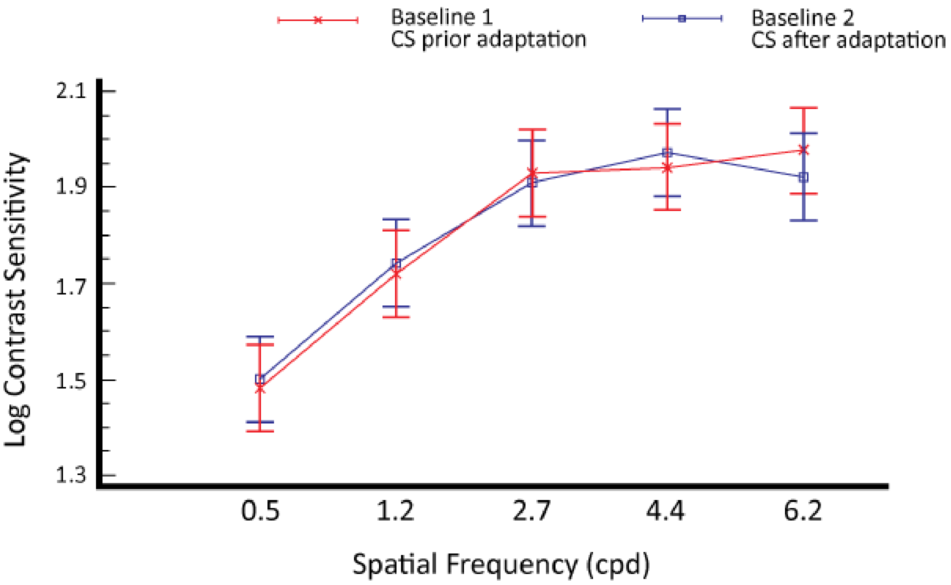


Figure 2.11 There was no statistical significant difference between the two sets of baseline measures. Error bars show the 95% confidence intervals.

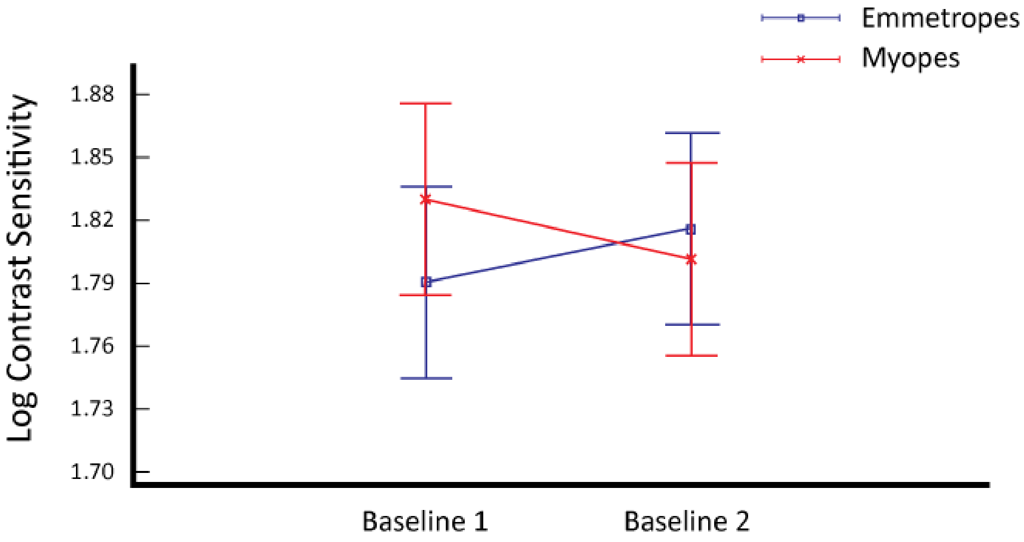


Figure 2.12 There was no statistical difference between emmetropes and myopes at these baselines, averaged across all tested spatial frequencies. Error bars show the 95% confidence intervals.

2.7 Data Analysis – Experiments 1 and 2

Contrast threshold measured in % before and after adaptation was performed 3 times for each spatial frequency. Each measurement was converted to log contrast sensitivity and then averaged. Analysis of variance using general linear models was performed to analyze the data. This model provides analysis of variance for one dependent variable caused by one or more factors. Contrast adaptation effect, which is defined as the difference in log contrast sensitivity of adaptation task and the baseline, was the dependent variable. The independent variables were refractive error group nested in subjects, spatial frequencies and adaptation tasks. The general linear models analyzed the data for the 5 spatial frequencies and the 2 tasks (reading English text and viewing horizontal gratings) in 2 refractive error groups with subject factor randomized. The randomized subject factor recognized subjects in the study as a random sample that may be obtained from a larger population, so that the goal of the study is to make a statement regarding the larger population. Analysis of variance using general linear models was also performed for Experiment 2 to analyze the 3 adaptation tasks of reading English text, reading Chinese text and viewing horizontal gratings in 2 refractive error groups at 5 spatial frequencies, with subject factor randomized.

2.8 Issues of Contrast Sensitivity Testing in Children

The most challenging part of measuring contrast sensitivity in children was to keep the children attentive to the task. Each run had to be short so that they were encouraged to move on to the next stage. They were shown how much they had achieved half way through the experiment and were given rewards such as sweets and snacks during the small break sessions between the tests. On completion of the experiment, each of them received S$50 as reimbursement for transportation and compensation for their time in spending a whole day in the experiment.

One of the good ways to capture their attention was to let them read the English stories. They loved the stories in the English text presented to them. When it came to the grating target, it was a challenge to keep them awake by reminding them to look at the centre of fixation all the time. To overcome this, all the children were informed that they had to sleep well the night before the test.

Most children were able to learn the test with 10 to 20 min coaching, explaining, and demonstrating, and another 20 min practising. However, there were 2 children where the practice session took 3 hr and the children were still not able to perform the test and were therefore excluded from the study.

Parents were advised to leave their child behind from 8.30 am to 5.30 pm on the day of the test. They signed the informed-consent form when bringing the child in first thing in the morning, left for work and picked up the child after work. This worked well for working parents. For some, they were advised to go shopping or run errands and not to disturb the child during the testing procedures. Lunch was provided for the children.

2.9 Contact Lens Correction for Accommodation Measures

In Experiment 3, all subjects were corrected with soft contact lenses, including the emmetropes and those with no or very low corrections. This was to ensure consistency in refractive correction and to allow only the ocular refraction to be considered in the calculation of ocular accommodation. Contact lens correction avoids the situation that occurs with spectacle lenses in which the accommodation demand and magnification vary as the magnitude of correction changes (Rosenfield 1998). Contact lenses also helped to eliminate reflection off the lens surface that would pose a problem in taking the autorefractor reading if spectacles or trial lenses were worn during the measurement. Logi Enhanced View soft disposable contact lenses were used for the study. The parameters for the contact lens were base curve 8.6 mm, diameter 14.0 mm, DK 19.5, water content 55%. The lenses were manufactured using the materials hydroxyethyl methacrylate (HEMA), glycerol methacrylate (GMA) and methacrylic acid (MAA). The powers of the spherical contact lenses ranged from +0.75 D to -6.00 D, with 0.25 D steps increment (lenslogic.com/clear.php).

2.10 Open-field Refraction Measures

The main apparatus used in Experiment 3 was an open-field auto refractor, WAM-5500 (Grand Seiko Co. Ltd). This was used in a static mode to measure the refractive state of the eye objectively. The open-field autorefractor is a binocular open-field autorefractor and keratometer that permits dynamic recording of refraction and pupil size by connection to an external PC via an RS-232 port. This allows for filing of data by high speed measurement as the data output was entered automatically to Excel spreadsheets.

Refraction can be obtained at different viewing distances and therefore accommodation responses can be determined. This type of autorefractor has wide application in myopia and accommodation research. The Shin-Nippon autorefractor, SRW-5000 (similar technical principle as the WAM-5500) has been reported to have good accuracy when compared to subjective refraction and good repeatability in adults (Mallen, Wolffsohn, Gilmartin et al. 2001) and children (Chat and Edwards 2001). Another recent study on the validity and reliability found that refractive error determined by the WAM-5500 was similar to subjective refraction (difference -0.01 ± 0.38 D) (Sheppard and Davies 2010). The instrument was accurate and reliable over a wide range of refractive errors from -6.38 D to +4.88 D (Sheppard and Davies 2010).

Refractive error is calculated in two stages, as has been described previously (Mallen, Wolffsohn, Gilmartin et al. 2001). A ring target of infra-red light is brought into rough focus by rapid movement of a lens on a motorized track after being reflected from the retina. The toroidal refractive prescription is calculated by digital analysis of the image in multiple meridians. The refractions measured by the instrument are in the range of ± 22 D sphere and ± 10 D cylinder in increments of 0.01, 0.12 or 0.25 D for power and 1 deg for cylinder axis.

Additional features necessary for accommodation studies include a system to alter the vergence demand of near targets and the ability to measure refraction through small pupils due to the pupillary constriction that accompanies accommodative effort (Wolffsohn, O'Donnell, Charman et al. 2004; Win-Hall, Ostrin, Kasthurirangan et al. 2007). The autorefractor is able to measure through pupils of 2.3 mm or larger in diameter (Win-Hall, Ostrin, Kasthurirangan et al. 2007). In the measurement of refraction for the accommodation study, off-axis viewing often results in large amounts of cylinder registered in the measurements. A large amount of cylinder is not possible since astigmatism greater than 0.50 D was excluded, so if this occurs, the measurement was repeated.

2.11 Accommodation Testing Procedure

When the subjects were looking straight ahead at 4 m, an internally-illuminated distance visual acuity chart, LIGHTHOUSE modified ETDRS (Early Treatment Diabetic

Retinopathy Study) chart, (Lighthouse International, USA) was used as a fixation target (Figure 2.13). Subjects were asked to fixate the middle letter of 0.2 logMAR (equivalent to 6/9). The mean luminance of the chart was approximately 110 cd/m^2, as measured by the Minolta Luminance Meter LS-100.

Reading materials were projected from a tablet PC, HP Pavilion TX 1000 with a screen luminance of 90 cd/m^2 and maximum contrast. The turntable screen of the tablet PC was measured at 26 cm x 16 cm. The tablet PC was placed in front of the auto refractor (see Figure 2.14). When the subjects were looking at the distance target, the screen would be closed (Figure 2.13), but when subjects were to perform the reading task at near, the screen was quickly raised (Figure 2.14). After reading, the screen was immediately closed so that subject could fixate at the distance target (Figure 2.13).

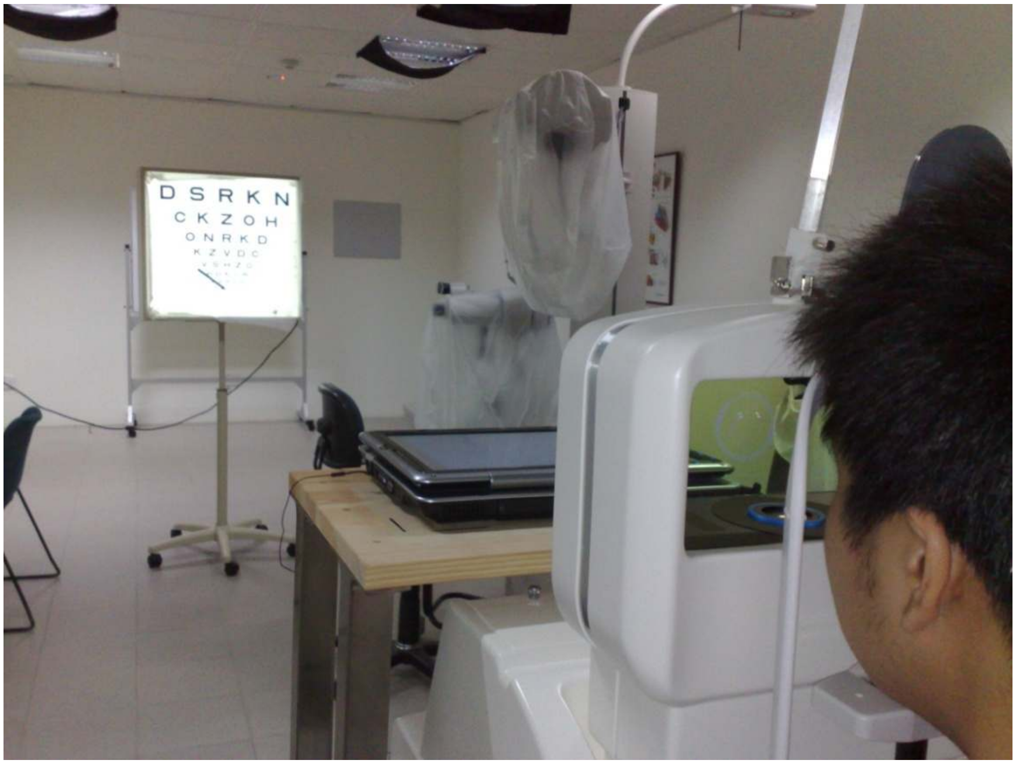


Figure 2.13 Measurement of refraction before and after adaptation when subject is fixating a distant target, through the open-viewed autorefractor.

Figure 2.14 A subject reading from the computer screen (adaptation).

2.12 Measures of Reading Distance in Children

A study was conducted on 20 children (mean age 10.2 ± 1.3 yr) to determine their reading distances for both English and Chinese story books of appropriate age difficulty. A previous study recommend that the near vision testing distance of 25 cm should be used for children aged 6 to 11 years (Rosenfield, Wong and Solan 2001). However, there was no standard reading distance for reading Chinese text reported in the literature. A range of near tasks distances was used to determine NITM, including 20 cm (Ciuffreda and Wallis 1998; Ciuffreda and Lee 2002; Wolffsohn, Gilmartin, Li et al. 2003), 25 cm (Vera-Diaz, Strang and Winn 2002; Hazel, Strang and Vera-Diaz 2003; Schmid, Hilmer, Lawrence et al. 2005) and 40 cm (Wolffsohn, Gilmartin, Li et al. 2003; Vasudevan, Ciuffreda and Gilmartin 2009). In addition, this study would also determine if reading distance was different for the two texts commonly read by Singaporean children.

The study was carried out at a national library in the Western part of Singapore, the Jurong East Regional Library. The children were given a page of an English story to read aloud. They were told to hold the reading material at their normal reading distance. The font size of the English text was Times New Roman 12 points. The reading distance was measured after 5 min of reading. The child was then handed a Chinese story and the reading distance was also determined for the Chinese text after 5 min. The font size of the Chinese text was SimSun 10.5, which is commonly used in story books and newspaper print. The sequence of which type of text the child read first was randomized. The average reading distances of the 20 subjects were obtained for each text (see Table 2.3). The reading distance determined here was used as the reading distance for the accommodative adaptation study.

The average reading distances for English and Chinese text were 34.4 ± 5.5 cm and 33.2 ± 5.7 cm respectively. Based on this, a reading distance of 33 cm was used in the later experiments reported in this thesis. In addition, measures with this reading distance were compared to those at 25 cm as some studies have used a 25 cm reading distance in accommodation studies involving children (Gwiazda, Thorn, Bauer et al. 1993b; Vera-Diaz, Strang and Winn 2000; Vera-Diaz, Strang and Winn 2002).

Table 2.3 Reading distances obtained from the pilot study

S/N	Age	Gender	Reading distance with Chinese	Reading distance with English
1	9	F	36	34.5
2	11	F	33	33
3	10	M	37	32
4	9	F	24	28
5	8	F	30	32
6	11	F	30	33
7	12	M	36	37
8	10	F	39	42
9	9	M	33	40
10	9	F	38	37
11	11	M	41	40
12	11	M	36	38
13	10	F	37.5	36.5
14	10	F	31.5	33.5
15	8	F	21	21.5
16	10	M	35	34.5
17	9	M	37	42
18	12	F	24	23
19	12	M	38.2	38
20	12	M	26	32.3
Average			**34.4 ± 5.5**	**33.2 ± 5.7**

2.13 Reading Tasks used During Accommodation Experiment

All subjects performed four near tasks with high contrast; these tasks were administered in random order between the different text types. The four near tasks were reading English texts of Times New Roman font of point 12 for 10 min at 33 cm and 25 cm and reading SimSun Chinese font of 10.5 point for 10 min at 33 and 25 cm. Reading materials were projected from a tablet PC, HP Pavilion TX 1000 with a screen luminance of 90 cd/m^2 and maximum contrast. The luminances were measured using a Minolta Luminance Meter LS-100.

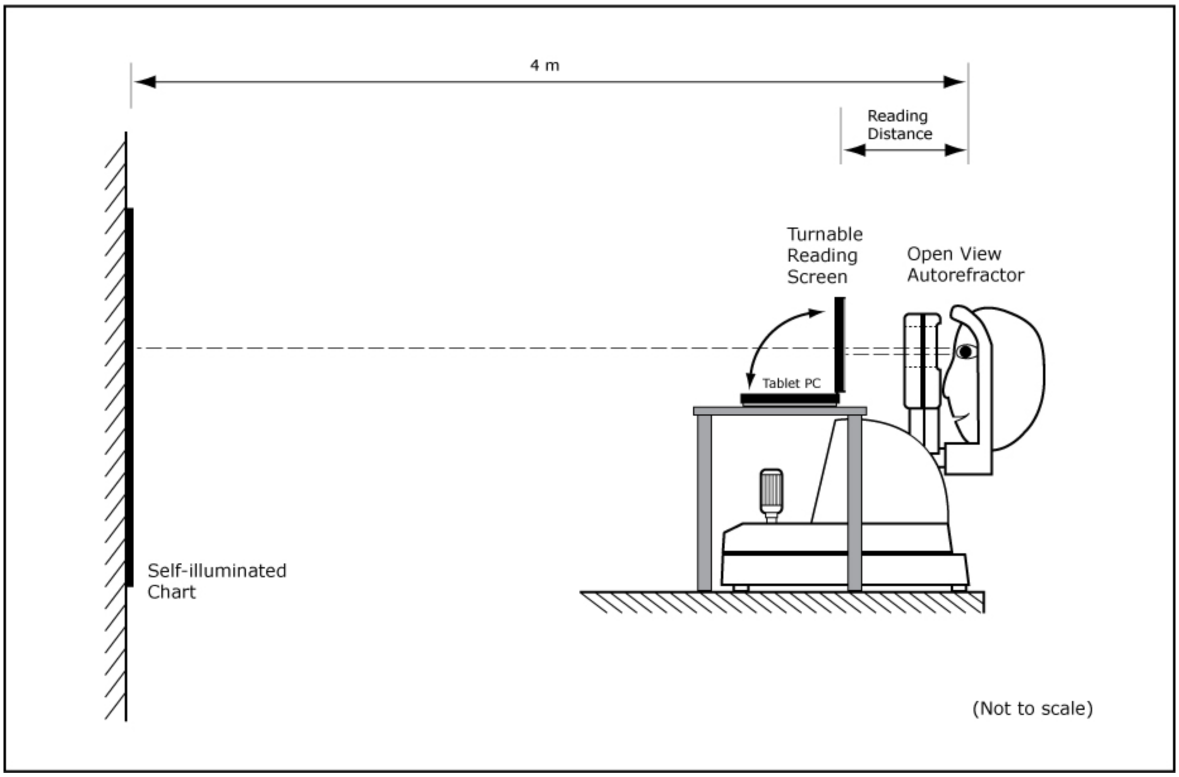


Figure 2.15 Schematic diagram of the experimental set up for measuring accommodative adaptation

The reading materials subtend an angular equivalent of 0.7 log MAR at 33 cm to 0.8 log MAR at 25 cm. The screen of the tablet PC was 26 cm by 16 cm. The size of the reading material was not changed according to distance of viewing so as to allow us to investigate the effect of change of reading distance on NITM. The near tasks were performed binocularly. Reading distance of 33 cm and 25 cm were adjusted by moving the tablet PC away or towards the subjects (Figure 2.15).

2.14 Accommodation Error and NITM Standard Testing Procedure

The autorefractor was aligned with the tested eye of the subject. Even though subjects were looking ahead and reading with both eyes opened, monocular readings were obtained from the tested eye, which was the right eye; if the right eye failed the screening criteria, the left eye was used. The autorefractor measured the refraction of the subjects before, during and after reading. When the subjects were looking straight ahead at 4 m at the internally-illuminated ETDRS distance visual acuity chart, they were asked to fixate at the middle letter of 0.2 logMAR of the ETDRS chart.

Subjects spent 5 min in darkness to open the accommodation loop (Chen, Schmid and Brown 2005). Following this period, 30 refractive error measures were taken immediately when the room illumination was switched on (pre-task closed-loop accommodation value). Once 30 readings were obtained in 1 min, the screen of the tablet was raised along the midline of the fixating eye at 33 cm (3.00 D), measured from the ocular plane of the subject to the screen. The target consisted of short paragraphs of stories either in English or Chinese text in high contrast. Each subject was asked to read the passage out softly to ensure that he/she continued to keep the text clear at all times, with chin firmly placed at the chin rest. The screen of the tablet PC covered nearly the entire view of the subject with angular subtence 38 deg horizontally and 26 deg vertically at 33 cm and 46 deg horizontally and 33 deg vertically at 25 cm. When refractive error readings were taken at intervals of 2 min during the near task, subjects were asked to fixate a word that was pre-determined on the passage in which the subject's near focus was best aligned with the auto-refractor. Ten monocular accommodation responses were measured at each interval of 2 min, so a total of 40 accommodative responses were obtained for the entire 10-min reading period. The 10 min reading time was chosen as 15 min was deemed too long as it induces fatigue effects (Rosenfield 1998).

Following the completion of the 10 min near reading task, the screen of the tablet was quickly closed, so that subjects were instructed to view at the same pre-task distance target. Accommodation measurements were taken every 2 s over a 3 min period with 90 measurements in total. Subjects took a visual break (toilet breaks, water breaks or watching TV at a distance of 4 m) longer than 10 min before the commencement of the second near task at 33 cm. A 10-min or more resting period was used as several studies found the dissipation times between 17 to 63 s for persistent near work of 10 min duration (Rosenfield and Ciuffreda 1994; Ciuffreda and Wallis 1998; Hazel, Strang and

Vera-Diaz 2003). The experiments were conducted four times for each subject with reading English and Chinese texts at both reading distances of 33 cm and at 25 cm. For each near task, the pre-task, on task and post-task refractions were measured.

2.15 Data Analysis – Experiment 3

The measured refractions were converted to accommodation responses using the formulae (Mutti, Jones, Moeschberger et al. 2000) below:

Accommodation response (AR) = $$AR = \frac{1}{\dfrac{1}{\dfrac{1}{\dfrac{1}{RawAR_{cornea}} + DLE} + LENS} - DLE} - RX_{cornea}$$

where AR is the corrected accommodation response, RX_{cornea} is the refractive error at the corneal plane (as correction), *DLE* is the vertex distance in meters, *LENS* is the signed dioptric power of the lens in front of the eye and $RawAR_{cornea}$ is the spherical equivalent of the instrument reading calibrated for the corneal plane.

Since the eyes were corrected with contact lenses and DLE is approximately zero, the above equation is reduced to:
AR = $RawAR_{cornea} + LENS - Rx_{cornea}$

As the refractive error of the cornea was corrected by contact lenses, accommodative response is equal to the $Raw\ AR_{cornea}$

Individual post-task data (mean spherical equivalent) were normalized to each individual's pre-task closed-loop accommodation value (post-task value – pre-task value). Data for each subject were then divided into 6-s bin intervals. Previous studies used 10-s bin intervals for post-task accommodation measurement. Since myopes showed a significantly faster closed-loop regression than open-loop regression (Hazel, Strang and Vera-Diaz 2003), a shorter 6-s bin intervals was used in this experiment to prevent loss of data through a longer bin interval (90 measures reduced to more manageable 30). The accommodative responses during task were obtained by the average of 10 readings of the accommodation responses measured at 2nd, 4th, 6th and 8th min. The accommodative accuracy was calculated by subtracting the accommodative stimulus from the averaged accommodative response. The values of both NITM and accommodative accuracy are independent of the distance of 4 m since each value was obtained from the differences of two measures.

The accommodative responses for the 2 refractive groups at initial post task at 6-s bin intervals for the first 24 s post-task were compared using the Statgraphic analysis of variance, general linear models. The regression pattern of NITM and accommodative accuracy of the two refractive groups were investigated. The NITM induced by Chinese and English text at different reading distances were compared.

2.16 Measurement Issues

There were two children who were afraid of having contact lenses placed on the eye, so they decided to withdraw from the study. The participating subjects were able to follow the instructions to continue reading or looking straight ahead. The children went through a complete test cycle to ensure that they were able to perform the test. The most challenging part of this experiment was to continue to remind the children to fixate at the distant target for 3 min post task while taking the refraction measurement. A strap was used to secure the head of the children who moved the head constantly during the experiment. In some cases when too many errors appeared on the data screen due to intermittent loss of attention, the measurements were repeated. In such cases, more readings were quickly taken to compensate for the lost data.

CHAPTER 3

NEAR WORK INDUCED CONTRAST ADAPTATION IN MYOPIC AND EMMETROPIC CHILDREN

Abstract

Purpose: Contrast adaptation has been postulated as a potential error signal for emmetropization. This research aims to determine whether reading causes contrast adaptation in children and, if so, to determine whether myopes exhibit greater contrast adaptation than emmetropes.

Methods: Baseline contrast sensitivity was determined in 34 emmetropic and 34 spectacle corrected myopic children for 0.5, 1.2, 2.7, 4.4 and 6.2 cpd horizontal sine wave gratings. The effects of near tasks on contrast sensitivity were determined during periods looking at a horizontal grating and during periods spent reading lines of English text. The grating was 6.2 cpd and the text comprised 1.2 cpd row frequency and 6 cpd stroke frequency. Both stimuli were printed landscape on A4 paper and viewed at 40 cm distance.

Results: Both emmetropic and myopic groups showed reduced contrast sensitivity during both near tasks. The adaptation induced by viewing the grating (mean ± SD: 0.15 ± 0.16 log unit, range: 0.07 to 0.27 log unit) was significantly greater than the adaptation induced by reading text (0.11 ± 0.16 log unit, 0.08 to 0.16 log unit)($F_{1,594} = 10.7$; $P = 0.001$). Myopic children (0.15 ± 0.16 log unit) showed significantly greater adaptation across the two tasks than emmetropic children (0.10 ± 0.16 log unit)($F_{1,66} = 7.30$; $P = 0.009$). The greatest differences in the magnitude of the contrast adaptation effect of emmetropic and myopic children occurred at 4.4 cpd (mean: 0.11 log unit).

Conclusion: Both grating and reading tasks induced contrast adaptation; viewing horizontal gratings induced greater adaptation than reading, and myopes exhibited

greater adaptation than emmetropes. Contrast adaptation is associated with myopia - our research does not show if this is consequential or causal.

3.1 Introduction

The increased prevalence of myopia amongst young children in East Asian countries such as Japan (Matsumura and Hirai 1999), Hong Kong (Fan, Lam, Lam et al. 2004), Taiwan (Lin, Shih, Hsiao et al. 2001) and Singapore (Saw, Tong, Chua et al. 2005) indicates an early impact of environmental factors on refractive development (Morgan and Rose 2005). A highly competitive education system and long periods spent performing near work are the environmental factors reported to be most strongly linked to myopia development in these countries (Saw, Wu, Seet et al. 2001; Saw, Chua, Hong et al. 2002a). The near work myopia association has been found in many studies (Rosenfield and Gilmartin 1998a; Tan, Saw, Lam et al. 2000; Saw, Chua, Hong et al. 2002a), however, how near work causes and/or exacerbates myopia development generally and particularly in children is poorly understood [reviewed in (Rosenfield and Gilmartin 1998)]. In addition, the biological link for how a near visual task like reading stimulates the axial elongation that causes myopia in children is unknown.

There is increasing evidence that the eye growth process is guided by a visual feedback system involving the quality of the visual signal (reviewed in Wildsoet 1997, Wallman and Winawer 2004). A good quality visual signal, which is made up of a variety of spatial frequencies and contrast information above-threshold (Bartmann and Schaeffel 1994; Schmid and Wildsoet 1997a; Schmid, Brinkworth, Wallace et al. 2006) is critical for normal visual development, and eyes that experience poor retinal images (deficient in spatial frequency and contrast content) show excessive growth and develop myopia (Schaeffel, Glasser and Howland 1988; Bartmann and Schaeffel 1994; Schmid and Wildsoet 1997a; Wildsoet and Schmid 2000; Wallman and Winawer 2004). Reading typically involves looking at a high contrast text (Wallman and Winawer 2004) at near for a prolonged period of time. The prolonged reading activity may be deficient in spatial frequency and contrast content and this would be exacerbated by contrast and spatial adaptations (Blakemore and Campbell 1969; Wallman and Winawer 2004). Contrast adaptation is a mechanism that enhances or decreases contrast sensitivity, depending on the input contrast and mean luminance of the visual scene: if contrast is high, sensitivity is reduced and if it is low, sensitivity is enhanced (Ohlendorf and Schaeffel 2009).

Extensive psychophysical studies describe contrast adaptation as the decrease in contrast sensitivity that occurs in response to prolonged viewing of high contrast gratings (Blakemore and Campbell 1969; Blakemore, Nachmias and Sutton 1970; Blakemore, Muncey and Ridley 1973). Adaptation is stronger for a higher contrast than a lower contrast adapting pattern (Blakemore and Campbell 1969; Blakemore, Muncey and Ridley 1973) and is measureable when the adapting grating has the same spatial frequency and orientation as the test grating (Pantle and Sekuler 1968; Blakemore and Campbell 1969). Although it was originally suggested that the effect of adaptation to contrast saturates after as little as 40 s (Blakemore and Campbell 1969), Magnussen and Greenlee demonstrated that for an adapting contrast of 0.6, thresholds continue to rise for up to 30-60 min of adaptation for different subjects (Magnussen and Greenlee 1985). As adaptation time increases, recovery time also increases, with the growth and decay functions of the aftereffects having approximately the same slope, thus indicating that adaptation and recovery are symmetric processes (Rose and Evans 1983; Magnussen and Greenlee 1985; Georgeson and Georgeson 1987).

Reading is an activity that requires intense viewing of the reading text for several minutes to hours. The text, being high contrast, could serve as a stimulus for adaptation (Chen, Brown and Schmid 2006). Based on the known characteristics of contrast adaptation, it is predicted that contrast adaptation to text should reduce the retinal sensitivity to spatial frequencies similar to that created by the row frequency or stroke frequency of the letters themselves. Alternatively, there could be a general reduction of contrast sensitivity measurable at the peak of the contrast sensitivity function (a spatial frequency of ~ 4 cpd). If this phenomenon is associated with myopia production, then the reduction in retinal sensitivity may be greater in myopes than emmetropes. Therefore, we hypothesize that myopic children will exhibit greater contrast adaptation effect than emmetropic children.

The aim of this study was to determine if reading causes contrast adaptation in children and to determine if myopes exhibit greater contrast adaptation effects than emmetropes. Whether the relative magnitude of contrast adaptation differed for gratings (the classic stimuli used to measure contrast adaptation) and reading material (i.e. text) was also assessed.

3.2 Materials and Methods

Contrast sensitivity was measured in emmetropic and myopic children under 3 conditions. Baseline contrast thresholds were determined using standard contrast sensitivity measurement for gratings of 0.5, 1.2, 2.7, 4.4 and 6.2 cpd. The effect of near tasks on contrast thresholds were determined by measuring contrast sensitivity testing following periods spent looking at horizontal gratings, and following periods spent reading lines of English text. Contrast sensitivity measured after performing the near tasks was compared to the baseline measures and the difference was used as a measure of contrast adaptation.

3.2.1 Participants

Sixty-eight children aged 7 to 12 yr (mean age of 10.3 ± 1.4 yr) from Chinese, Malay and Indian descent were recruited. The children were classified as emmetropic (SE +0.75 to -0.25 D) or myopic (SE $\geq$ 0.50 D of myopia) based on the mean spherical subjective refraction value. There were 34 emmetropes (mean SE ± SD: +0.03 ± 0.13 D) and 34 myopes (mean SE ± SD: -2.73 ± 1.18 D). A summary of the characteristics of the children in terms of race, age and gender for each refractive error group are presented in Table 3.1.

Table 3.1 Summary of the Children's Fundamental Biographic Characteristics

		Number of Children		
		Emmetropes	Myopes	Total Number
Age (yr)	7 to 8	8	3	11
	9 to 10	9	9	18
	11 to 12	17	22	39
Ethnicity	Chinese	17	19	36
	Malay	7	10	17
	Indian	10	5	15
Gender	Male	17	14	31
	Female	17	20	37

Inclusion criteria for the subjects were (i) at least 6/6 monocular visual acuity using a Snellen chart and monocular contrast sensitivity better than 1.65 on the Pelli-Robson chart for each eye; (ii) cylinder ≤ 0.75 DC (for each eye), myopia ≤ 6.00 D, hyperopia ≤ 0.75 D and anisometropia ≤ 1.00 DS and (iii) absence of any ocular disease including strabismus. Parents completed a questionnaire on behalf of their children. Questions included past and present ocular history and details of ocular health. The rate of myopia progression was determined based on optometric records, and when those were not available (n = 28 cases) an estimate was made by comparing the current spectacle prescription to the subjective refraction and reported age of spectacles. All myopic subjects were full-time wearers of their prescription. The myopes in this study were all progressing myopes, according to the specification that myopia had increased by at least 0.50 D per year for the past 2 consecutive years (McBrien and Adams 1997). In Singapore, stable myopes are not common in this age range and cannot be recruited in high numbers. Contrast sensitivity testing was performed on the right eye unless this eye had just failed to meet the inclusion criteria and the left eye met the criteria. This occurred in 6 subjects. Four right eyes had astigmatism > 0.75 D and two right eyes had a Pelli-Robson score of 1.60.

Subjects were recruited from the Singapore Polytechnic Optometry Centre in Singapore Polytechnic and its satellite clinic in the West Coast Community Centre. Letters of invitation were also given out to parents of 4 primary schools located in the vicinity of the two centres. All experiments were conducted with ethics approval in accordance with the "National Statement on Ethical Conduct in Human Research" published by the National Health and Medical Research Council of Australia. Approval was obtained from both Singapore Eye Research Institute Institutional Review Board and the Queensland University Technology (Ref 4251H), University Human Research Ethics committee. Written, informed consent was obtained from both the child and a parent or guardian prior to participation. The purpose of the study and details of the tests were explained to the children and their parents and any questions answered. Testing was carried out at the Vision Science Centre at Singapore Polytechnic.

3.2.2 Preliminary Tests

All children undertook a series of preliminary tests to ensure that they met the inclusion criteria. Subjective refraction was performed to measure refractive errors using the technique of maximum plus for best visual acuity (Elliott 2003). The subjects were screened for ocular disease using slit lamp biomicroscopy and direct ophthalmoscopy. Contrast sensitivity was assessed using a Pelli-Robson chart and monocular visual acuity was measured using a Snellen projector chart.

3.2.3 Contrast Sensitivity Testing

Contrast thresholds were measured using the Metropsis Psychophysical Vision Testing (MPVT). Test stimuli were presented on a high definition 53 cm View Sonic Professional Series P225f CRT monitor. The angular size of the monitor was approximately 17° x 22° at a test distance of 1 m, and a mean luminance of 50 cd/m^2 was set for contrast sensitivity measurement. The protocol used in the contrast threshold measurement was 2-interval forced choice (IFC) Logarithmic Staircase procedure. The threshold measured using this method was defined as the limit of contrast (%). For each test run, threshold and standard deviation were calculated using the contrasts at the reversal points in the staircase procedure (see 2.3 for details).

3.2.4 Adaptation Tasks

Two adaptation tasks were used: English text and sine-wave gratings of 6.2 cpd (Figure 2.6). The reading task consisted of a high contrast (92%) hard copy print out of children's stories written in English in 12 points Times New Roman font, with a line spacing of 17.5 points on A4 landscape paper. The row and stroke frequencies of the text were 1.2 cpd and 6.04 cpd respectively (see 2.4). Since the test equipment was not able to generate 6.0 cpd due to its internal calibration procedure; 6.2 cpd was the closest achievable and thus this spatial frequency was used for testing. The angular subtences for adapting stimuli were 35 deg horizontal and 27 deg vertically and the testing Gabor size was set at 2.35 deg (full width and half maximum) at 1 m distance.

3.2.5 Testing Procedure

The adapting stimuli and the computer screen of the contrast testing equipment were placed 90 deg to each other and at 40 cm and 1 m, respectively, from the subject (see Figures 2.9 and 2.10). Subjects were corrected using a trial frame and ophthalmic lenses. All the subjects went through an initial practice session to become familiar with the test. These trial runs were not included in the analysis of the data. Baseline contrast thresholds of spatial frequencies at 0.5, 1.2, 2.7, 4.4 and 6.2 cpd were measured before adaptation. The contrast threshold of these spatial frequencies were tested either in ascending (commencing at 0.5 cpd) or descending (commencing at 6.2 cpd) order; this was randomized and all the repeat runs followed the same order in the adaptation tasks. Three trials were performed for each spatial frequency and averaged.

Contrast sensitivity measurement for the two adapting conditions was randomized. Subjects viewed the adaptation tasks binocularly for 5 min initially. During adaptation for English text, they were instructed to read the English stories in silence. For the grating, they were instructed to stare at the fixation dot in the middle. The adapt-test-readapt paradigm (adapt 1 min, test 30 s and readapt 1 min) which was described in 2.5, should ensure stable levels of contrast sensitivity as it balances exactly the amount of recovery that occurs during testing (Rose and Evans 1983). Figure 3.1 shows the flow chart which outlines the contrast adaptation experimental procedures. With the subjects adapting at 40 cm and tested at 1 m, the accommodation responses change from 2.5 D to 1 D and vice versa between the 2 distances. For reasons suggested in 2.5, it is unlikely that delays in focusing between the adaptation and test stimuli adversely influenced the results of the post adaptation contrast sensitivity testing. Moreover, none of the subjects reported blur during the experiment.

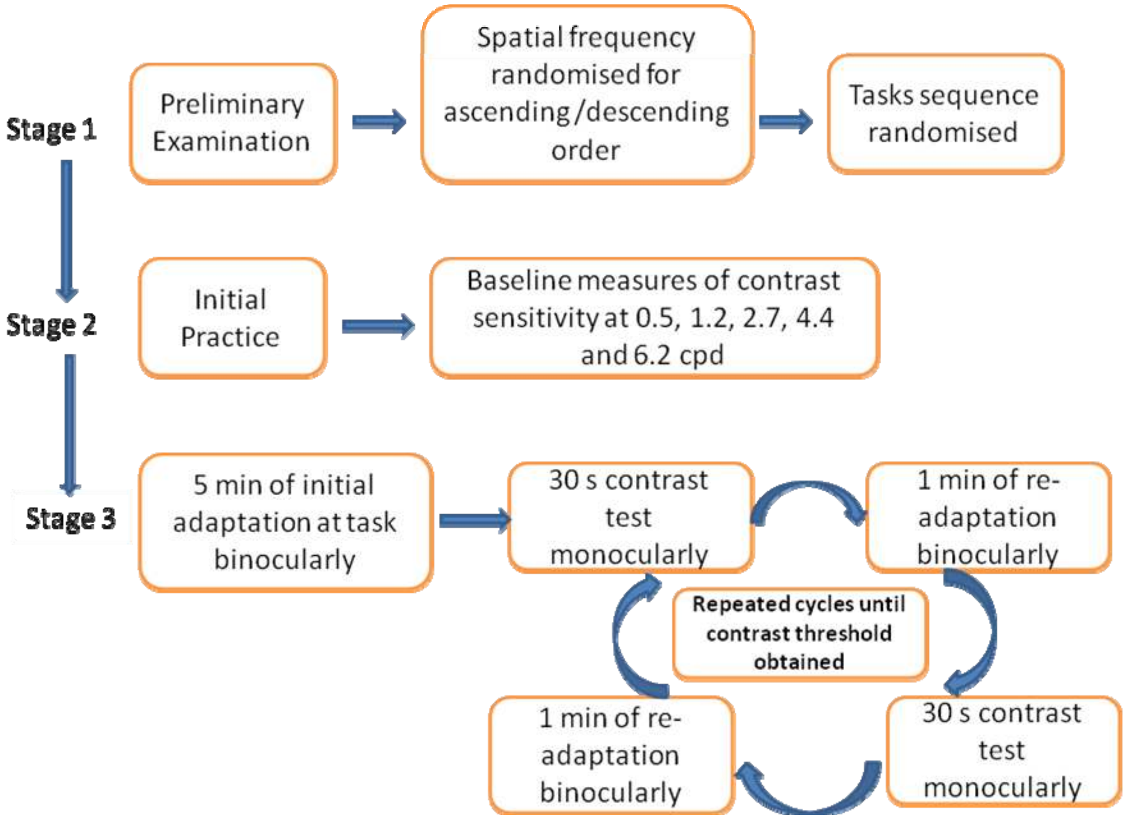


Figure 3.1 Flow chart of the contrast adaptation experimental procedures

With the 2-IFC protocol, subjects were instructed to respond by pressing an “A” button if the stimulus was seen in the first time interval (designated by the first beep tone) and the “C” button if the stimulus was seen in the second time interval (designated by the second beep tone). If subjects could not tell in which time interval the grating target was located, they were instructed to guess. All the measurements were made on the same day since both parents and children did not like the idea of multiple visits. In between each adaptation task, the children were given a lunch break and in each task, they were given short breaks for each spatial frequency.

As described in 2.6, fatigue did not affect the measurements. The children were able to perform the test reliably even though all the measurements were made on the same day. Moreover, for each measurement of the contrast threshold, there was a standard deviation generated by the MPVT to present the variability of that particular measurement. When a standard deviation of > 1.5 % was obtained, the measurement was repeated after the child was given a break. Hence, the issue of fatigue did not confound the results.

3.2.6 Data Analysis

Contrast thresholds measured in % were converted to log contrast sensitivity for all measurements. Analysis of variance using the general linear models was used to analyze the data. Contrast adaptation effect, which was defined as the difference in log contrast sensitivity of adaptation task and the baseline, was the dependent variable. The independent variables were refractive error group nested in subjects, spatial frequencies and adaptation tasks. General linear models were analyzed at 5 spatial frequencies and the 2 tasks of reading English text and viewing horizontal gratings in 2 refractive error groups, with subject factor randomized, so that the results can be generalized to the larger population. For two-level comparison, Fisher’s Least Significant Difference (LSD) intervals were used for comparison of significant findings. Post-hoc analysis was performed using the Bonferroni 95% confidence interval to reduce the type 1 error rate due to stepwise multiple comparison.

3.3 Results

3.3.1 Baseline Contrast Sensitivity

Contrast sensitivity was measured at 0.5, 1.2, 2.7, 4.4 and 6.2 cpd. The peak contrast sensitivity at baseline was 2.007 ± 0.181 log units at 2.7 cpd, and the lowest was 1.514 ± 0.149 log units at 0.5 cpd across all subjects. The baseline contrast sensitivity (before reading) was not affected by ethnic background ($F_{2,65} = 1.26$, $P = 0.291$), gender ($F_{1,66} = 0.02$, $P = 0.884$) or refractive error group ($F_{1,66} = 0.05$, $P = 0.829$), but was significantly affected by the age of the children ($F_{5,62} = 5.90$, $P < 0.001$). Post-hoc Bonferroni test showed greater contrast sensitivity in older children of 11 and 12 yr than younger children of 7 and 8 yr (Figure 3.2). The mean age for myopic children (10.6 ± 1.2 yr) was slightly greater than the mean age of emmetropic children (10.0 ± 1.6 yr).

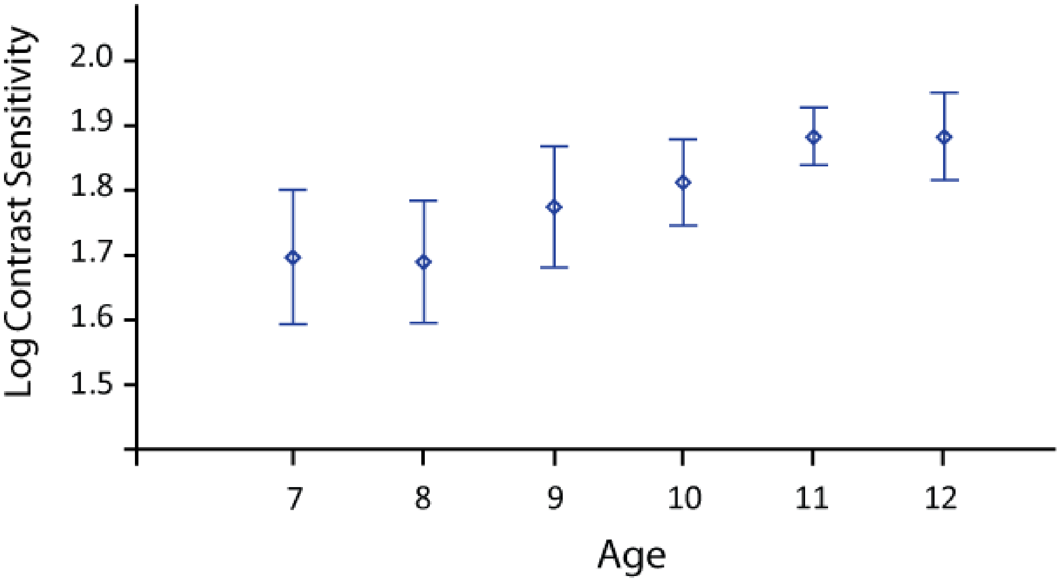


Figure 3.2 Baseline log CS and age of subjects in Experiment 1. Significant differences in log contrast sensitivity was observed between the 7 and 8 year-old groups and the 11 and 12 year-old groups. Error bars show Bonferroni corrected 95% confidence intervals.

Figure 3.3 shows the baseline log contrast sensitivity of the children between the current study and that of other studies. The children in our study showed lower baseline log contrast sensitivity than those reported in similar age groups in some studies (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997; Ellemberg, Lewis, Liu et al. 1999; Adams and Courage 2002) but comparable contrast sensitivity to those measured in other studies (Mantyjarvi, Autere, Silvennoinen et al. 1989; Scharre, Cotter, Block et al. 1990). The difference in contrast sensitivity of these studies will be further discussed in 3.4.5.

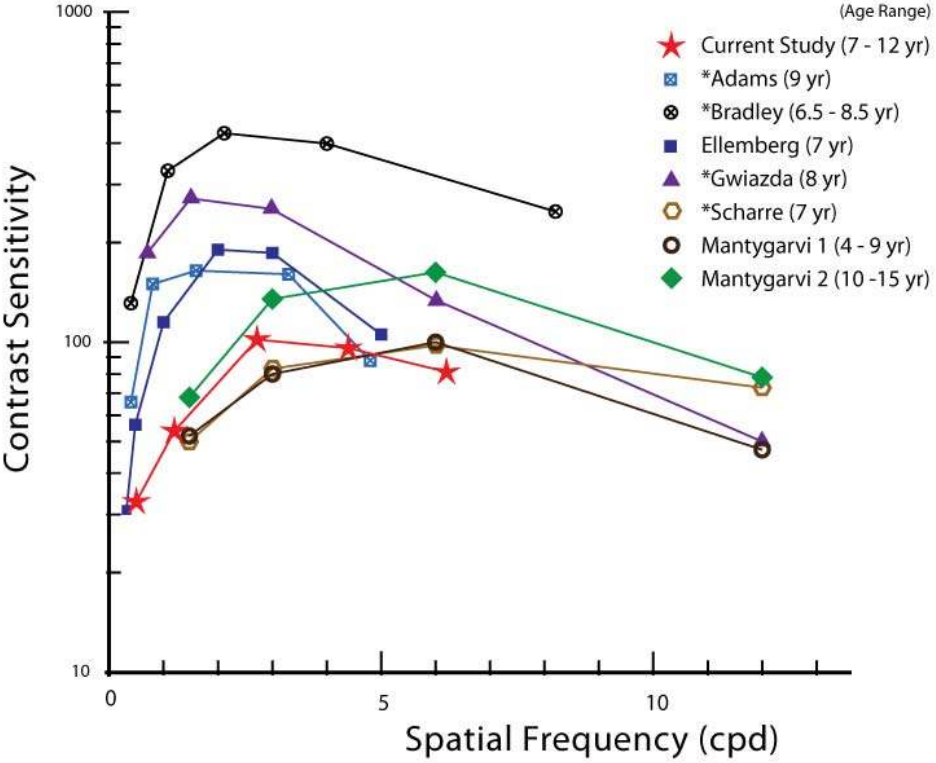


Figure 3.3 Contrast sensitivity of our children compared to that of other studies. The methods of measuring contrast sensitivity were also different across the studies. *Contrast thresholds were obtained binocularly.

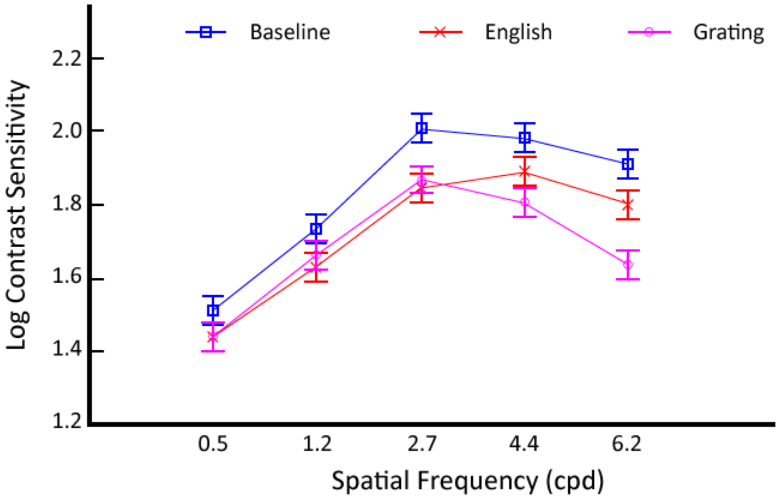
3.3.2 Post-adaptation Contrast Sensitivity

Figures 3.4 (a), (b) and (c) show the mean log contrast sensitivities at baseline and after adaptation for all subjects, emmetropic and myopic children respectively. All subjects showed reduced contrast sensitivity after near tasks (Figure 3.4 a), so nearly all adaptation effects were negative. There was a shift in the peak of contrast sensitivity after reading from 2.7 to 4.4 cpd for both emmetropic and myopic children (Figure 3.4 b and c).

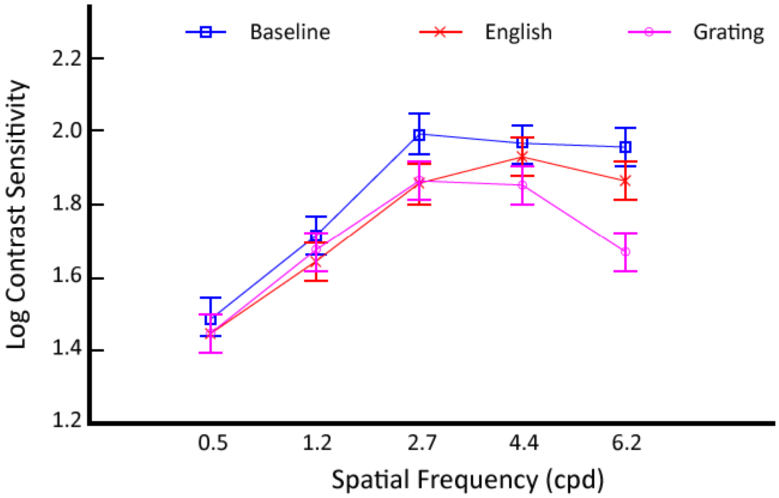
Table 3.2 shows the means and standard deviations of the contrast adaptation effect (log contrast sensitivity post-task – log contrast sensitivity pre-task) after reading and after viewing the horizontal gratings in myopic and emmetropic children. The post-adaptation log contrast sensitivity was significantly different from the baseline at all spatial frequencies except at 0.5 cpd in reading and at 0.5 and 1.2 cpd in the grating task (Table 3.2). Myopes showed significant difference between post-adaptation and baseline in reading at all spatial frequencies but for emmetropes the difference only occurred at 2.7 cpd. For the grating adaptation task, both myopes and emmetropes showed significant adaptation from baseline log contrast sensitivity at spatial frequencies from 2.7 to 6.2 cpd. These significance are indicated with * in Table 3.2.

In Table 3.2, the adaptation effect induced by reading English text and viewing of horizontal grating ranges from 0.077 to 0.161 and 0.070 to 0.273 log units respectively. For both adaptation tasks, the effect reduced continuously from 0.5 to 4.4 cpd, after which stronger adaptation effect was observed in the grating task when the test spatial frequency was at the adapting spatial frequency of 6.2 cpd (-0.273 ± 0.193 log units).

a. All Subjects



b. Emmetropes



c. Myopes

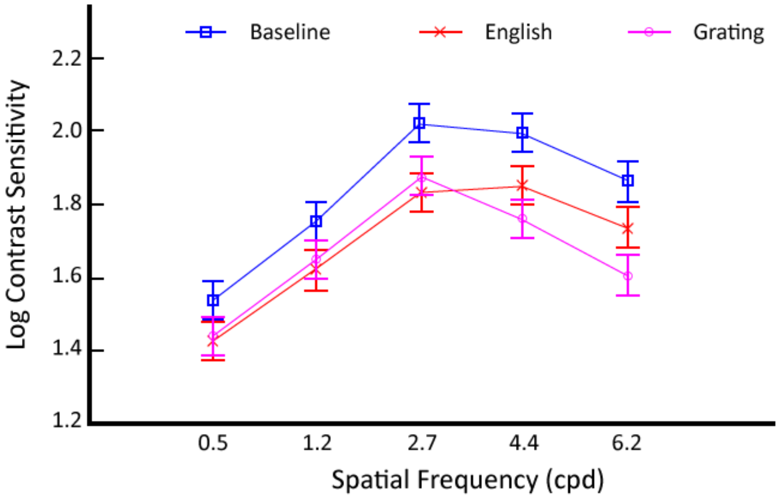


Figure 3.4 Mean log contrast sensitivities of (a) all, (b) emmetropic and (c) myopic children at baseline and after adaptation to English text and horizontal sine wave gratings. Error bars show the 95% confidence intervals.

Table 3.2 Mean and standard deviation of the contrast adaptation effect after reading and after viewing the horizontal gratings in myopic and emmetropic children.

AT		English					Gratings				
SF		0.5	1.2	2.7	4.4	6.2	0.5	1.2	2.7	4.4	6.2
Mean contrast (log unit) ± SD	All	-0.077 ± 0.146	*-0.102 ± 0.130	*-0.161 ± 0.169	*-0.092 ± 0.186	*-0.110 ± 0.178	-0.070 ± 0.147	-0.075 ± 0.157	*-0.135 ± 0.135	*-0.175 ± 0.197	*-0.273 ± 0.193
	E	-0.041 ± 0.146	-0.075 ± 0.137	*-0.138 ± 0.157	-0.039 ± 0.170	-0.093 ± 0.189	-0.041 ± 0.153	-0.045 ± 0.162	*-0.128 ± 0.141	*-0.115 ± 0.175	*-0.287 ± 0.185
	M	*-0.113 ± 0.139	*-0.130 ± 0.118	*-0.184 ± 0.179	*-0.145 ± 0.187	*-0.126 ± 0.168	-0.099 ± 0.138	-0.104 ± 0.148	*-0.142 ± 0.130	*-0.235 ± 0.202	*-0.259 ± 0.202
Mean difference between E and M (greater adaptation effect in M)		-0.072	-0.055	-0.046	-0.106	-0.033	-0.058	-0.059	-0.014	-0.120	+0.028

Minus signs indicate there is a reduction of contrast sensitivity after near tasks.

AT – Adaptation task	**SF – Spatial frequency**
E – Emmetropic children	**M – Myopic children**
SD – Standard deviation	

***Spatial frequency at which there is significant difference in log contrast sensitivity of post adaptation and baseline.**

3.3.3 Comparison of Adaptation Effects in Myopes and Emmetropes

When all the data were analysed between the two refractive groups, the myopic group of children showed significantly greater adaptation effects of -0.154 ± 0.161 log units (mean ± SD) across both tasks than the emmetropic group (-0.100 ± 0.162) of children ($F_{1,\ 66}$ = 7.30; p = 0.009). The finding supports our hypothesis that myopic children exhibit greater contrast adaptation effects than emmetropic children (Figure 3.5).

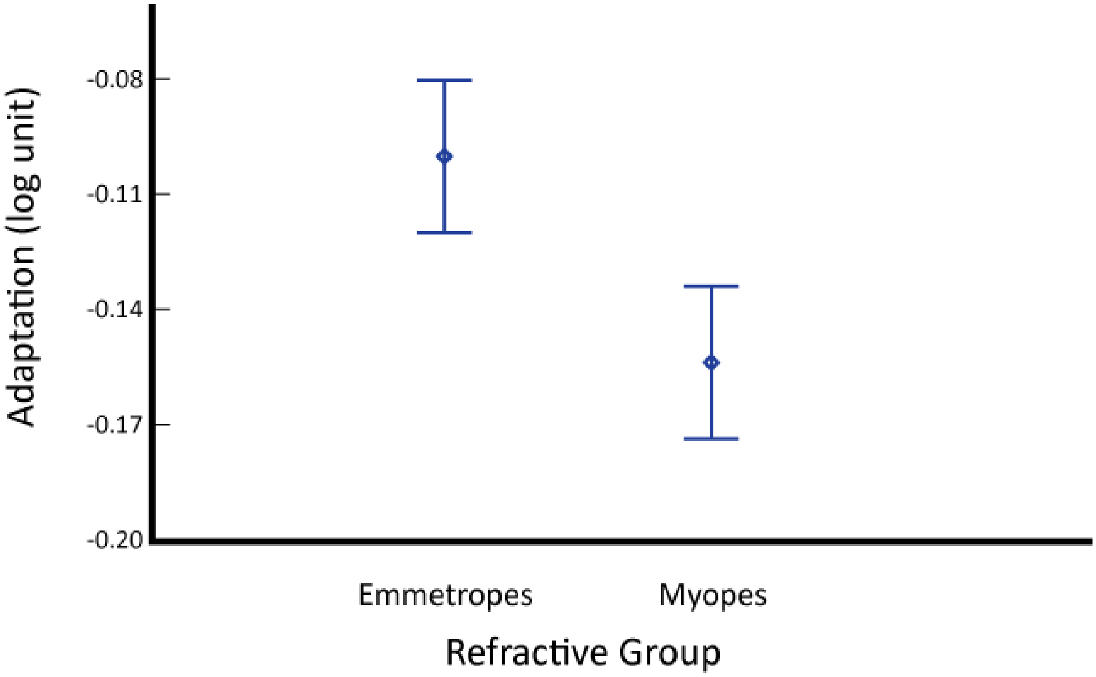


Figure 3.5 Myopic children showed greater contrast adaptation effect than emmetropic children. Error bars show LSD 95% confidence intervals.

There was no significant interaction between refractive error group and adaptation tasks ($F_{1, 594} = 0.21$; $p = 0.650$) nor between refractive error group and spatial frequency ($F_{4, 594} = 0.86$; $p = 0.495$). Myopic children showed greater adaptation effects for both English text (0.063 log units) and grating (0.045 log units) tasks across the tested spatial frequencies. The greatest difference in adaptation effect between myopic and emmetropic children occurs at 4.4 cpd with 0.106 log units in reading and 0.120 log units in the grating task (Table 3.2).

3.3.4 Adaptation Tasks and Spatial Frequencies

Adaptation to grating showed significantly greater adaptation effect (by an amount of 0.037 log units) than adaptation induced by reading English text ($F_{1, 594} = 10.69$; $p = 0.001$) (Figure 3.6).

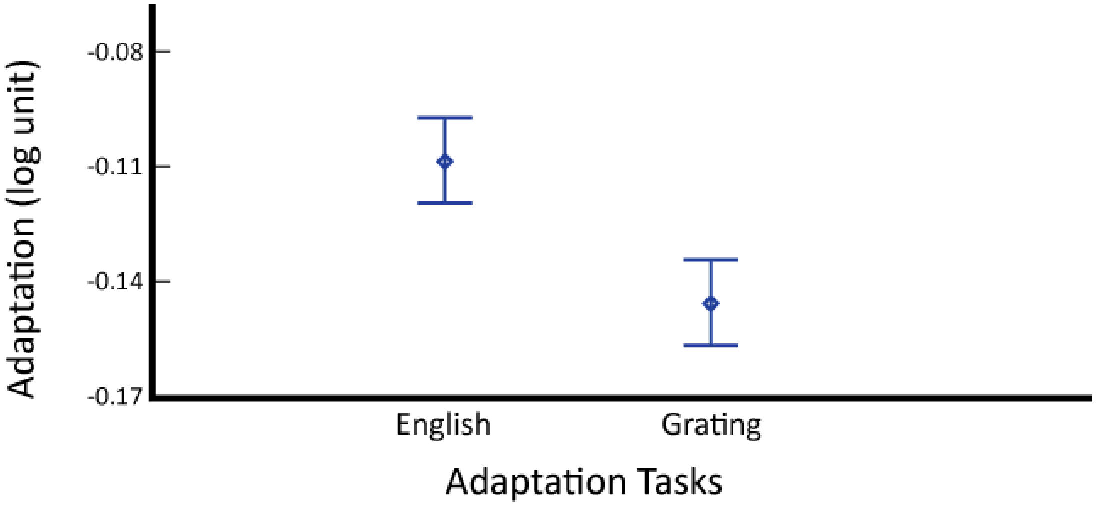


Figure 3.6 Adaptation effect was greater in grating than that induced by reading English text. Error bars show LSD 95% confidence intervals.

There was significant interaction between adaptation tasks and spatial frequencies ($F_{4, 594} = 10.86$; $p < 0.001$). Post-hoc analysis showed significant difference in adaptation effect between reading English and grating occur only at 4.4 (just significant) and 6.2 cpd (Figure 3.7).

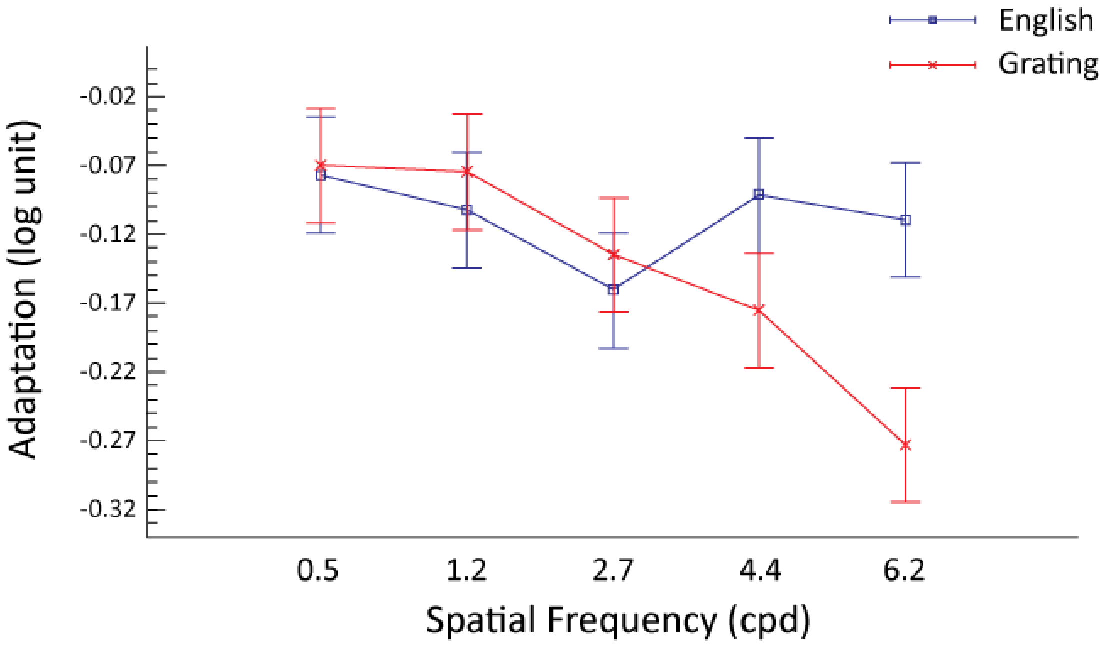


Figure 3.7 There was significant difference in adaptation effect between reading English and grating only at 4.4 (just significant) and 6.2 cpd. Error bars show the 95% confidence intervals.

3.3.5 Myopic Subgroup and Adaptation

When the progressing myopes were subdivided into faster (progression faster than 0.5 per year in any one of the 2 years) and slower progression groups, there was no significant difference in adaptation in these sub groups ($F_{1,32} = 0.44$, $p = 0.512$). There was also no significant relationship between the degree of myopia and the contrast adaptation or between the axial length and contrast adaptation (Table 3.3). In this table, a significance level of 0.01 was considered as statistically significant to reduce the chance of type 1 errors due to multiple comparisons. None of the P values displayed was significant and the relationship between contrast adaptation effects and axial length and contrast adaptation effects and degree of myopia are weak.

Table 3.3 Linear regression analysis between contrast adaptation and the degree of myopia (Rx) and axial length (AL)

	R^2 values and their respective P values at Tested Spatial Frequency (cpd)						
	Tasks		**0.5**	**1.2**	**2.7**	**4.4**	**6.2**
Rx	English	R^2	0.029	0.026	0.005	0.024	0.019
		P	0.162	0.189	0.561	0.204	0.265
	Grating	R^2	0.009	0.032	0.026	0.036	0.002
		P	0.446	0.143	0.192	0.120	0.751
AL	English	R^2	0.056	0.006	0.015	0.000	0.002
		P	0.052	0.535	0.314	0.974	0.698
	Grating	R^2	0.009	0.000	0.020	0.009	0.038
		P	0.447	0.974	0.249	0.434	0.111

3.4 Discussion

3.4.1 Magnitude and Spatial Frequency in Contrast Adaptation

Based on the spatial frequency content of the adapting targets and published literature (Blakemore and Campbell 1969; Schmid and Wildsoet 1997a; Diether, Gekeler and Schaeffel 2001; Majaj, Pelli, Kurshan et al. 2002), we expected to see contrast sensitivity reduction at and around 6 cpd for the sine wave grating and at or around either the row or stroke frequency of the text. Consistent with the past literature (Blakemore and Campbell 1969; Blakemore and Nachmias 1971; Georgeson and Harris 1984; Georgeson and Turner 1985; Ohlendorf and Schaeffel 2009), we observed contrast adaptations in response to the grating target and in addition we have shown here that hard-copy text display can produce a similar effect. Previous studies have shown that text displayed on VDU can induce contrast adaptation (Lunn and Banks 1986; Magnussen, Dyrnes, Greenlee et al. 1992), but as far as we know, this is the first study where a contrast adaptation experiment was performed on a large group of children. The findings of our study are in agreement with these studies (Lunn and Banks 1986;

Magnussen, Dyrnes, Greenlee et al. 1992) that contrast adaptation effect can be induced by reading the lines of text. Also, if contrast adaptation was involved in myopia development, the simple prediction was that myopic children would show greater adaptation effects than emmetropic children. Consistent with this, our data in general terms showed that myopic children were more susceptible to a loss of contrast sensitivity after reading. This data and the implications for myopia development involving near work are further discussed.

Contrast adaptation has been postulated as a potential error signal for emmetropization as the adaptation process alters the sensitivity of the visual system with defocused stimuli (Diether and Schaeffel 1997; Diether, Wallman and Schaeffel 1997; Diether and Schaeffel 1999). In this study, myopic children showed significantly reduced contrast sensitivity from baseline at tested spatial frequencies from 0.5 to 6.2 cpd, whereas the emmetropic children showed significantly reduced contrast sensitivity from baseline only at 2.7 cpd. Together with significantly greater reduction in contrast sensitivity function after reading in myopic children than emmetropic children, these observations lead to the suggestion that higher contrast adaptation induced by reading in myopic children alters the visual sensitivity of the eye and changes the ability of the eyes in detecting and resolving low to medium contrast images.

The corresponding decrease in firing of the cortical neurons which has been observed during contrast adaptation induced by gratings in animal studies (Movshon and Lennie 1979; Albrecht, Farrar and Hamilton 1984) may occur in the text induced contrast adaptation. The neural response gain would decrease and may have a similar extent as a degraded image caused by translucent diffusers in producing myopia in animal studies (Sivak, Barrie and Weerheim 1989; Bartmann and Schaeffel 1994). As a result, contrast adaptation could be perceived as “defocus” signals from the retina and potentially promote myopia development, in particular if contrast adaptation occurs at a young age of life. With children starting to read at a young age of 3 to 4 years of age, the dynamic neural plasticity of this age group results in the disruption of the emmetropization process due to external environmental changes in visual information with prolonged near work.

The magnitudes of contrast adaptation at 4.4 cpd observed were 0.039 log units in emmetropic children and 0.145 log units in myopic children in response to a period spent reading text. The difference in the two groups was 0.106 log units (28%). Although this different is small in magnitude, it is substantially larger than the within session variability of the measurement of average 13.23% (Table 2.2). Therefore, we believe this amount of contrast reduction is important as very minor changes in retinal image quality are reported to result in myopia (Robb 1977). In animal models, extremely minor deterioration of retinal image quality from translucent diffusers are more effective than opaque diffusers in producing high myopia (Sivak, Barrie and Weerheim 1989; Bartmann and Schaeffel 1994). Moreover, Mon-Williams, Tresilian and Strang et al (1998) reported that a change of contrast sensitivity of 0.1 log unit is a real difference since the contrast sensitivity function is normally stable. Therefore, although the magnitude of the difference may be considered relatively small (which is expected due to the short initial adaptation time of 5 min only), given the large impact of retinal image quality and the highly sensitive nature of the human visual system, it is a change likely to be more than sufficient to produce myopia. Furthermore, the magnitude of this difference is likely to be increased with longer reading duration and the myopigenic effect will be enhanced.

Of relevance to further understanding the impact of the degree of contrast adaptation on eye growth are data in the monkeys. The degree of image degradation required to trigger deprivation myopia in monkeys is relatively low (Smith and Hung 2000). Smith and Hung (2000) demonstrated that modest diffuser induced reductions in object contrast ranging from 0.1 log unit at 0.125 cpd to 0.75 log units at 8 cpd for a 95% contrast target were sufficient to cause deprivation myopia in two out of three monkeys (about 4 D). The 0.1 log unit reduction in image contrast that induces myopia in infant monkeys is similar in magnitude to the 0.106 log unit difference in the reduction in contrast sensitivity between the two groups of subjects in the current study. The amount of reduction occurred at 4.4 cpd and it was less than the overall reduction (0.154 log units) in the myopic children. This leads to a related question – if a reduction of 0.1 log unit is sufficient to cause myopia why didn't the emmetropic children who have an average of 0.100 log unit reduction also become myopic? The monkey study mentioned above showed high degrees of variability with some monkeys showing no myopia (Smith and Hung 2000). This may indicate that the threshold reduction in contrast required to cause myopia shows individual variability as well.

The magnitude of the measured reduction in the contrast threshold has been shown to be dependent on the contrast of the adapting task, with higher contrast stimuli resulting in greater threshold elevations (Blakemore and Campbell 1969; Blakemore, Nachmias and Sutton 1970; Blakemore, Muncey and Ridley 1973). This has important implications for reading, since books or any reading materials are usually of high contrast which may induce a high level of adaptation that would not dissipate quickly after a prolonged reading duration. Moreover, the occlusion of most distant objects by the page during the reading activity may exaggerate the effect of the contrast sensitivity loss since the eyes are locked in a near distance position at all times.

Myopes are reported to read blurred text better than emmetropes (Rosenfield and Abraham-Cohen 1999). Based on this, Wallman and Winawer have suggested that myopic eyes (not fully corrected) would see distant objects as blurred, thus attenuating high spatial frequencies. This, in turn, may result in boosting the amplification of these frequencies in their brain, thus leading to reduced accommodation during reading. By this rationale with contrast adaptation, the reduced visual sensitivity may results in reduced accommodation since the eye fails to sense the blurred text. This would result in hyperopic defocus which is myopigenic.

However, with the reports of increased accommodation response following blur adaptation (Vera-Diaz, Gwiazda, Thorn et al. 2004) and increased contrast threshold with VDU-induced transient myopia after a period of sustained near work (Jaschinski-Kruza 1984), there is a possibility that contrast adaptation induced in prolonged reading could reduce the perceived image quality of low contrast objects due to the reduced contrast sensitivity of the visual system. The perceived defocus image would act like a degraded image caused by translucent diffusers in producing myopia. Therefore, an alternative suggestion would be that the perceived defocus of the image results in a greater amount of accommodation and thus leads to a greater accommodative adaptation or NITM. Both accommodative accuracy and NITM were investigated in a separate experiment reported in Chapter 5 in this thesis.

It has been shown that the spatial frequency content of the visual environment is important in eye growth control (Schmid and Wildsoet 1997a; Smith and Hung 2000; Schmid, Brinkworth, Wallace et al. 2006). In the chick model, the exposure to mid spatial frequency targets of 0.86 cpd prevented more myopia than 0.086 cpd (low) and 4.3 cpd (high) spatial frequencies (or a combination of these) (Schmid and Wildsoet 1997a). In the chick, the peak of the contrast sensitivity function occurs at around 1 cpd (Schmid and Wildsoet 1998). Based on these data and that of the pigeon (Hodos 1993), it has been proposed that spatial frequencies around the peak of the contrast sensitivity function may be most critical for emmetropization (Schmid, Brinkworth, Wallace et al. 2006).

The peak of the contrast sensitivity function in children of 6 to 9 years of age is between 2 and 4 cpd (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997; Ellemberg, Lewis, Liu et al. 1999; Adams and Courage 2002) using different methods of measures. The spatial frequency of the text has a high spatial frequency content around this spatial frequency and thus it is around this spatial frequency that the adaptation effects we observed were greatest. This further supports the importance of the most affected spatial frequency of about 4.0 cpd (a mid-frequency for human subjects).

3.4.2 Duration of Contrast Adaptation

The time it takes for contrast sensitivity to return to normal, i.e. the contrast adaptation to dissipate, is also an important parameter in terms of the length of time that retinal activity might be reduced. Of course this would be in addition to the time spent performing the near task that caused the reduction. Recovery time has been shown to be dependent on adaptation time (Blakemore, Nachmias and Sutton 1970; Blakemore, Muncey and Ridley 1973); with some studies reporting a symmetric process that adaptation and recovery times are similar (Rose and Evans 1983; Magnussen and Greenlee 1985; Georgeson and Georgeson 1987) and others reporting that recovery takes much longer (Blakemore, Nachmias and Sutton 1970; Huggelund and Hohmann 1976; Mecacci and Spinelli 1976). Rose and Evans (1983) observe that it took 90 min for the adaptation effect to recover to baseline level after a 20 min adaptation period and Blakemore and co-workers report a dissipation time of several hours following 30 min adaptation (Blakemore, Nachmias and Sutton 1970). Furthermore, it is possible that contrast adaptation effect could be time-integrated and cumulative over the day and this could promote myopia in susceptible individuals performing considerable amount of near work.

The inability of the eye to discern a clear image after prolonged reading from the effects of contrast adaptation may induce a level of form deprivation that lingers over several hours. If 2-3 min exposure to defocus is sufficient to induce changes in eye growth (Zhu, Park, Winawer et al. 2005; Zhu and Wallman 2009), then reading of up to 1 hour (which is not uncommon) could be highly detrimental, particularly if the reading activity is not interspersed with a different activity. The decay function of contrast adaptation depends on the duration of adaptation: the longer the adaptation, the longer the recovery time. Therefore, if the cycle of near work is repeated constantly in a child without a complete dissipation of adaptation, the persistent degraded retinal image perceived may promote myopia development.

Having said that, the duration of contrast adaptation and the pattern of its decay were not investigated in this study. The dissipation time for reading induced contrast adaptation might be longer for myopes than emmetropes, like the longer dissipation time of accommodative adaptation in myopes (Ciuffreda and Wallis 1998; Wolffsohn, Gilmartin, Li et al. 2003). Hence, prolonged reading could result in a poor recovery of baseline contrast sensitivity which may be detrimental to young children who are still in the critical eye growth period. Both the time course of the development of contrast adaptation and the recovery from contrast adaptation induced by reading in children are important areas of future studies.

3.4.3 Grating versus Reading Task

The results obtained in this study agreed with the findings of previous studies that continuous viewing of a high contrast grating will decrease the visual system's sensitivity to the grating of the same orientation and spatial frequency (Blakemore and Campbell 1969; Georgeson and Harris 1984). In grating adaptation, greater loss of contrast sensitivity was observed as the test spatial frequency approached the 6.2 cpd of the adapting grating for both emmetropes and myopes.

Both myopes and emmetropes were affected by contrast adaptation induced by reading and viewing the gratings. The text letters form a broken uneven black row rather than the regular arrangement of the sine wave grating and thus may have less effective contrast at the row frequency which would generate a reduced adaptation response. Thus, although produced at the same contrast, the lower effective contrast of the text could have caused the lower adaptation effect of this stimulus.

There may be two different but related mechanisms of contrast adaptation displayed here. The grating adaptation involved continuous viewing of the grating without altering the gaze. For the reading induced contrast adaptation, the eye's gaze was moving constantly across the page while reading. Since M cells are important in motion and reading involves having the eye's focus moving across the page, reading induced contrast adaptation probably was mediated by M cells, whereas the grating adaptation was mediated by P cells and occurs at the cortical neurons since they are more spatial frequency and orientation specific. Moreover, Henrich and Bach (2002) found the 0.5 cpd channel was not adapted by 0.5 cpd spatial frequency using the pattern electroretinogram and the visual evoked potential. This finding supported an earlier experiment which showed that below 0.66 cpd, no after-effect could be obtained in a normal trichromat (Greenlee, Magnussen and Nordby 1988). But, in the current study, adaptation effect for 0.5 cpd was strong, especially in myopes after reading. The adaptation of contrast at low spatial frequencies may be an indication of mediation by M cells. Further studies investigating the origin of contrast adaptation induced by reading will be able to confirm this suggestion. As contrast adaptation induced by reading affected all tested frequencies from 0.5 to 6.2 cpd, it could be the low spatial frequencies (from 0.5 to 4.4 cpd) that are crucial for the normal emmetropization process to take place. Further studies can be performed by investigating contrast sensitivity after reading using an extended range of higher spatial frequencies such as 10, 20 and 30 cpd to confirm this observation.

3.4.4 Comparison with Other Studies on Contrast Adaptation

The current study is different from the studies on blur adaptation (Mon-Williams, Tresilian, Strang et al. 1998; Thorn, Cameron, Arnel et al. 1998; George and Rosenfield 2004; Rosenfield, Hong and George 2004; Ohlendorf and Schaeffel 2009) as the loss of contrast sensitivity was due to reading and also to viewing the grating with no other form of induced defocused by lenses or occluder involved. But, since myopes showed better visual acuity following blur adaptation (George and Rosenfield 2004; Rosenfield, Hong and George 2004), with the reduced contrast sensitivity at the range of spatial frequency (from 0.5 to 6.2 cpd), myopic subjects may not be aware of a reduction in vision in terms of contrast after prolonged reading, hence continue to involve themselves in reading activity.

For grating adaptation, the current study agreed with the findings that an elevation in the contrast threshold following adaptation to a sine wave grating especially if the test and adaptation gratings are of the same frequency. However, in the present study, the increase in contrast threshold was about 0.3 log unit, rather than 1.5 log units in Blakemore and Campbell's study (Blakemore and Campbell 1969). The difference in magnitude could be due to three main reasons. Firstly, Blakemore and Campbell used the method of adjustment in which their subjects adjusted a potentiometer to set the contrast of the grating on the oscilloscope to threshold before and after adapting to a high contrast pattern. In the current study, contrast threshold was obtained by a 2 interval forced-choice method. The method of adjustment was found to have a greater variability compared to forced choice methods in contrast measurement (Higgins, Jaffe, Caruso et al. 1988). Secondly, the adapting and test gratings used were 12.5 cpd and 6.2 cpd in the previous and current study, respectively. Finally, Blakemore and Campbell used adults whereas the current study used young children as subjects.

3.4.5 Baseline Contrast Sensitivity

When the baseline contrast sensitivity of the children in this study is compared to values reported in other studies, the children in our study have slightly reduced contrast sensitivity of 0.3 to 0.5 log units at 1 to 5 cpd (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997; Ellemberg, Lewis, Liu et al. 1999; Adams and Courage 2002). The obvious reason was that these studies measured contrast thresholds binocularly (Bradley and Freeman 1982; Scharre, Cotter, Block et al. 1990; Gwiazda, Bauer, Thorn et al. 1997; Adams and Courage 2002; Adams, Dalton, Murphy et al. 2002) while the current study measured contrast threshold monocularly. Binocular viewing enhance the measurement of contrast sensitivity function (Ross, Clarke and Bron 1985). The ages of children varied between studies, and this could account for some of the differences in sensitivity given the age effect we observed in our data. The age of the subjects in the current study was younger compared to that of Mantyjarvi, Autere, Silvennoinen et al (1989).

The method of contrast sensitivity test used will also affect the threshold obtained. We used 2-interval forced choice (2-IFC) staircase procedure, the other studies used two-alternative forced-choice staircase procedure (i.e. the stimuli could appear on the left or the right) (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997). On using the 2-IFC, when the stimulus was presented on the first beep tone, due to the after image of the stimulus, it may create a phantom stimulus even though it was a blank screen in the second beep tone. That would affect the results and thus a lower contrast threshold may be registered. Ellemberg et al (1999) used the method of adjustment which is said to have a greater variability (Higgins, Jaffe, Caruso et al. 1988) than the forced-choice method. The results obtained using the Vistech contrast sensitivity test at 3 m (Mantyjarvi, Autere, Silvennoinen et al. 1989; Scharre, Cotter, Block et al. 1990; Adams and Courage 2002) are comparable to the thresholds obtained in the current study. Therefore, the difference in contrast thresholds obtained in different studies is affected by many factors.

The baseline contrast sensitivity (before reading) was not affected by the ethnic background of the children in our sample. A previous study found that Chinese adults performed poorer in contrast sensitivity testing compared to Malay and Indian adults for spatial frequencies 6.0 cpd and higher (Oen, Lim and Chung 1994). These differences in performance were independent of other confounding factors such as refractive error and age. The authors did not offer any explanation for this finding. They observed that among their subjects, aviators such as pilots and aircrews performed better than the non-aviators. They suggested that the stringent target acquisition training aviators went through may have helped to elevate their contrast sensitivity. There was no mention of the break down in terms of ethnicity among the aviators. The contrast sensitivity obtained in the previous study was higher than that of the current study and the difference could be due to the age of the subjects (age 17-51 yr in their study) and the range of spatial frequencies tested as the current study concentrate towards the lower spatial frequencies. Also, the method of testing and the testing environment were possible factors contributing to the difference between the current study and the study of Oen et al (1994).

The baseline contrast sensitivity test was not affected by refractive error group. This is in agreement with previous studies that myopia will not change the contrast sensitivity function if there is no retinal pathology present (Thorn, Corwin and Comerford 1986; Liou and Chiu 2001). Correcting lenses will reduce the apparent size of material and hence increase the effective spatial frequencies. Based on a vertex distance of 14 mm, or distance between the lens back entrance pupil of the eye of 17mm, the maximum change in effective spatial frequency for -6 D lens power will be 9%. As lenses were worn for all the experimental conditions for any subject, all conditions were affected the same for any subject. Furthermore, the subjects' refractive errors were less than -6 D and trial lenses were fitted closer to the eyes due to the 'Asian nose' feature, therefore the induced spectacle magnification was smaller than indicated.

Our results agree with some previous studies that there is no gender difference in contrast sensitivity (Owsley, Sekuler and Siemsen 1983; Solberg and Brown 2002). However, some studies found differences in contrast sensitivity between genders (Brabyn and McGuinness 1979; Oen, Lim and Chung 1994). Solberg and Brown attributed the contradictory findings to the mean luminance of the target used in different studies, which indicates the importance of experimental set up in contrast measurements.

3.4.6 Real World Implication

In the current study, the adaptation targets were English text of font size 12 points of Times New Roman. Unlike previous studies that often used the conventional adaptation target of sine wave gratings, the adaptation task in the current study used text targets of size that are often printed in most newspapers and books to simulate a situation that is as close to real life as possible. Neuronal response to naturalistic stimuli cannot be necessarily inferred from the response to conventional "laboratory" stimuli such as sine wave gratings. Therefore, we feel that we have used the correct target stimuli for adaptation.

Based on the findings of the study, children should be encouraged to take intermittent rests in between their reading activity to allow contrast adaptation effects to dissipate. The intermittent rests may involve outdoor activities which have been shown to protect against myopia (Rose, Morgan, Ip et al. 2008).

3.4.7 Limitation of the Study

One of the limitations of the study was that the amount of time spent in reading was only 5 min. In real life, children often read longer than 5 min without looking up at the distance to dissipate the adaptation effect. Mimicking the real life situation of prolonged reading was not practical. If the testing time is too long, the children would lose their attention and concentration when performing the contrast sensitivity test and the results of the contrast sensitivity will be adversely affected. The other limitation was the set up of the reading and testing tasks. When the subject swivels from the adaptation task to the test grating, there is an inevitable loss of adaptation effect. This could be overcome if the adapting task could be projected on the same computer as the test stimuli without disrupting the set up for the contrast sensitivity test.

3.4.8 Future Studies

Future studies could consider the effect of adaptation at peripheral retinal locations since studies have found form deprivation in the peripheral retina can influence the development of refractive error in primates (Smith, Kee, Ramamirtham et al. 2005). Homeostatic signals of the hyperopic periphery of a myopic eye may direct the eye to grow; the spatial summation signals from the much bigger area of peripheral than central retina would dominate the emmetropization process even though the density of the neurons is greater in the central retina (Wallman and Winawer 2004). As such, investigation of contrast adaptation at the retinal periphery may provide some vital information on its role on myopia development. In this case, lower spatial frequencies should be investigated as the peak of the contrast sensitivity function is displaced towards lower spatial frequencies as eccentricity is increased (Robson and Graham 1981).

Future studies could investigate the influence of the sign of defocus on contrast adaptation induced by reading with the aim of better understanding the role of contrast adaptation in myopia development. There is experimental evidence that the retina can distinguish the sign of imposed defocus since some retinal neurons display different patterns of gene and protein expression with defocus of the same amounts but of opposite sign (Bitzer and Schaeffel 2002). In a recent experiment, contrast sensitivity was lowered by wearing a positive lens only and thus contrast adaptation was induced by the defocus caused by a positive lens and not a negative lens (Ohlendorf and Schaeffel 2009). Once the sign of defocus is determined, the role of contrast adaptation induced by reading would be further established. Contrast adaptation studies may include middle to high spatial frequency as well because these frequencies are thought to provide clues to myopic defocus (Diether and Wildsoet 2005).

3.5 Conclusion

Both grating and reading tasks induced contrast adaptation in children, with myopes having significantly greater adaptation effects than emmetropes. Difference in adaptation effects between emmetropic and myopic children were found to be greatest at 4.4 cpd in both reading and viewing horizontal gratings. Viewing of horizontal gratings induced a greater adaptation effect than reading.

CHAPTER 4

EFFECT OF TEXT DESIGN ON NEAR WORK INDUCED CONTRAST ADAPTATION IN MYOPIC AND EMMETROPIC YOUNG ADULTS

Abstract

Purpose: To determine whether the magnitude of contrast adaptation varies with the type of text viewed in emmetropic and myopic young adults.

Methods: Contrast sensitivity was measured in emmetropic and myopic young adults under 3 adaptation conditions. Baseline contrast thresholds were determined using standard contrast sensitivity measurement for gratings of 0.5, 1.2, 2.7, 4.4 and 6.2 cpd. The effect of near tasks on contrast thresholds were determined by measuring contrast sensitivity testing following periods spent looking at (i) horizontal gratings, and following periods spent reading lines of (ii) English text and (iii) Chinese text. Contrast sensitivity measured after performing the near tasks was compared to the baseline measures and the difference was used as a measure of contrast adaptation.

Results: Almost all subjects showed reduced mean log contrast sensitivity after the near tasks. There was statistical significance in the contrast adaptation effect among 3 adaptation tasks ($F_{2, 672} = 43$, $P < 0.001$). There was no statistical significant difference in the adaptation effect between reading English and Chinese text across the spatial frequencies, but there was significant difference between reading induced adaptation (by either English or Chinese) and grating adaptation at 4.4 and 6.2 cpd. When adaptation data were analysed collectively, the myopic young adults (-0.09 ± 0.13) showed significantly greater adaptation effects than the emmetropic young adults (-0.05 ± 0.13) ($F_{1, 48} = 5$; $p = 0.03$) across the adaptation tasks.

Conclusion: Reading Chinese text induced similar amounts of contrast adaptation as reading English text. Myopic adults had greater contrast adaptation induced by reading material than did emmetropic adults.

4.1 Introduction

The prevalence of myopia is alarming in many developed East Asian countries including Hong Kong, Taiwan and Singapore (Edwards and Fan 1999; Tan, Saw, Lam et al. 2000; Lin, Shih, Hsiao et al. 2001; Wu, Seet, Yap et al. 2001; Edwards and Lam 2004; Lin, Shih, Hsiao et al. 2004; Saw, Tong, Chua et al. 2005). In the past, the primary cause of myopia was thought to involve genetics [reviewed in Feldkamper and Schaeffel (2003)] and there is a well known tendency for familial patterns of inheritance of myopia (Hammond, Snieder, Gilbert et al. 2001). However, the recent rapid increase in the prevalence of myopia in more developed countries with intensive and competitive education systems indicate that there is very strong environmental impact on common myopia development. Epidemiological correlation based studies suggest that lengthy periods spent performing near work (at close distances and young ages) are likely to be a contributory factor to the high myopia levels that are observed (Saw, Hong, Zhang et al. 2001; Saw, Wu, Seet et al. 2001).

In Singapore, the prevalence of myopia is higher among Chinese (82.2%) young adults than Malay (65%) and Indian (68.7%) young adults (aged 16 to 25 yr) (Wu, Seet, Yap et al. 2001). Here, the Malays, Indians and Chinese attend the same English based education system: learning English as their first language. However, each ethnic group also learns their relevant mother tongue as a second language in school - the Malays learn Malay, the Indians learn Tamil and the Chinese learn Chinese. As the prevalence rate of myopia is highest among the Chinese and Chinese language is taught at schools in countries such as Singapore, Taiwan and Hong Kong, there is a possibility that Chinese text may play a role in near work induced myopia development.

Written Chinese is considered to be a logographic system (Tan, Liu, Perfretti et al. 2001), in which the characters of the basic writing unit possess many strokes that are packed into a square shape. The strokes in Chinese words are also more closely packed than the strokes in English letters and words. This probably makes it harder to resolve Chinese words than English words. Examples of Chinese characters such as 读 and 船, which means 'read' and 'boat', respectively, consist of smaller strokes than the simple English counterparts.

Furthermore, in Chinese, each single character can be a whole word. The basic unit in each character in writing associates with a unit of meaning called a morpheme (Perfetti and Tan 1998). Unlike the use of phonemes in spoken English, Chinese character pronunciation is defined at the syllable level and must be learned through rote memory of the association of visual character form and sound, occasionally with the aid of sub-character units that are themselves real characters. These unique characteristics imply that the processing and neuro-cognitive mechanisms underlying Chinese logographic reading may differ from those underlying alphabetic word reading (Tan and Perfetti 1998).

In addition, Chinese reading differs from English reading in many dimensions (Li, Liu and Rayner 2011). There are more than 5000 Chinese characters (Hoosain 1991) in contrast to 26 letters in English, and the information density in Chinese character is much higher than in English letters. As each Chinese character is a logographic system, there are no spaces in Chinese text to separate the words. The text written in Chinese is formed by strings of equally spaced box-like characters. Chinese readers thus have to depend on lexical knowledge to segment characters into words (Li, Rayner and Cave 2009).

From Experiment 1, it was found that contrast sensitivity function was reduced in children after both viewing horizontal gratings and the reading of English text. The adaptation effect induced by reading was significantly higher by 0.106 log units at 4.4 cpd in myopic children than in emmetropic children. We proposed that the reduction in contrast sensitivity, as a result of the contrast adaptation, could result in perceived retinal image defocus, thus becoming a retinal error signal to drive axial elongation. The findings from Experiment 1 agree with the proposed theory that contrast adaptation, being a retinal mechanism that quantifies image focus with a long temporal integration acts as a retinal signal for enhanced eye growth (Diether, Gekeler and Schaeffel 2001; Ohlendorf and Schaeffel 2009).

Contrast adaptation is thought to be a process that can provide a measure of perceived image defocus (Heinrich and Bach 2002a). It is a mechanism that enhances or decreases contrast sensitivity depending on the input contrast from the visual scene (Ohlendorf and Schaeffel 2009). If the contrast is high, sensitivity is reduced and if it is low, sensitivity is enhanced. It has been shown in chicks that contrast sensitivity was enhanced after the removal of a diffuser or a defocusing lens that had been worn for 1.5 days (Diether, Gekeler and Schaeffel 2001). This experiment led to the belief that selective contrast adaptation to the altered contrast and spatial frequency spectrum of the environment could relate to a retinal error signal (Diether, Wallman and Schaeffel 1997). On the other hand, if contrast adaptation occuring during reading causes a restricting spatial frequency content and lowering of perceived image contrast, axial elongation could be induced. Moreover, contrast adaptation has been found to occur in the retina of salamander (Smirnakis, Berry, Warland et al. 1997; Kim and Rieke 2001), rabbit (Brown and Masland 2001; Baccus and Meister 2002), macaque (Chander and Chichilnisky 2001) and human (Heinrich and Bach 2002a). It would be a useful mechanism to guide emmetropization (Diether, Gekeler and Schaeffel 2001).

In neuro-physiological terms, contrast adaptation may result in either desensitized or neural fatigue of the visual system (Maffei, Fiorentini and Bisti 1973; Barlow, Macleod and Meeteren 1976; Georgeson and Harris 1984); Goldstein 2007). Following adaptation to a particular high contrast pattern, contrast sensitivity is reduced for stimuli similar to the adapter but is largely unaffected for other stimuli (Movshon and Lennie 1979), thus giving rise to the specificity of adaptation effects. The effect of neural adaptation could change the levels of neuro-transmitter agents that are involved in the axial growth of the eye.

Although we have shown (Experiment 1) that reading causes greater contrast adaptation in myopic children than emmetropic children, the effect of reading different types of text is not known. Furthermore, since the prevalence of myopia is highest amongst Chinese children and in countries where Chinese is taught in schools from a young age, we hypothesize that Chinese text will induce greater contrast adaptation effects than English text. To determine whether the magnitude of contrast adaptation varies with the type of text viewed, we measured contrast adaptation following periods of reading both English and Chinese texts, in emmetropic and myopic young adults.

4.2 Materials and Methods

This study used a similar methodology to that described in Experiment 1, with the addition of Chinese text as an adapting stimulus. Contrast sensitivity was measured in emmetropic and myopic young adults under 3 adaptation conditions. Baseline contrast thresholds were determined using standard contrast sensitivity measurement for gratings of 0.5, 1.2, 2.7, 4.4 and 6.2 cpd. The effect of near tasks on contrast thresholds was determined by measuring contrast sensitivity testing following periods spent looking at horizontal gratings, and following periods spent reading lines of English text and Chinese text. Contrast sensitivity measured after performing the near tasks was compared to the baseline measures and the difference was used as a measure of contrast adaptation.

Potential participants undertook a series of preliminary tests to ensure that they met the inclusion criteria. Subjective refraction was performed to measure refractive errors using the technique of maximum plus for best visual acuity (Elliott 2003). The subjects were screened for ocular disease using slit lamp biomicroscopy and direct ophthalmoscopy.

Contrast sensitivity was assessed using a Pelli-Robson chart and monocular visual acuity was measured using a Snellen projector chart.

This experiment was conducted with ethics approval in accordance with the "National Statement on Ethical Conduct in Human Research" published by the National Health and Medical Research Council of Australia. Approval was obtained from both Singapore Eye Research Institute Institutional Review Board and the Queensland University Technology (Ref 4251H), University Human Research Ethics committee. Written, informed consent was obtained from both the subject and a parent or guardian (if the subject was below 21 years old) prior to participation. The purpose of the study and details of the tests were explained to the subject and any questions answered. Testing was carried out at the Vision Science Centre at Singapore Polytechnic.

4.2.1 Subjects

Fifty young adults, comprising 25 emmetropes (mean SE ± SD: +0.11 ± 0.31 D) and 25 myopes (mean SE ± SD: -3.01 ± 1.30 D), aged 16 to 25 yr (mean: 18.4 ± 1.1 yr) were recruited. Emmetropia was defined as a mean best sphere refractive error between +0.75 to -0.25 D and myopia as equal or more than -0.50 D. The average axial lengths for the emmetropes and myopes were 23.38 ± 0.88 mm and 24.95 ± 0.86 mm, respectively.

Inclusion criteria were: at least 6/6 monocular VA and contrast sensitivity (Pelli-Robson CS) better than 1.65. The exclusion criteria included: cylinder > 1.00 DC, myopia > 6.00 D, hyperopia > 0.75 D and anisometropia > 1.00 DS, any ocular disease and strabismus. One extra criterion for participation in this experiment was that subjects had to be able to read both Chinese and English texts. Questions included past and present ocular history and details of ocular health. Since the majority of the subjects were optometry students or patients of the optometry centre, the rate of myopia progression was determined based on their optometric records, and if those were not available, an estimate was made by comparing the current spectacle prescription to the subjective refraction and reported age of spectacles. In this study, the myopes were all classed as stable myopes as none of them had myopia had progressed more than 0.25 D per year for the previous 2 years (McBrien and Adams 1997). All myopic subjects were full-time wearers of their prescription, including 3 myopes who were full time contact lens wearers. Contrast sensitivity testing was done on the right eye only. The left eye was used only if the right eye failed to meet the inclusion criteria. This occurred in 4 subjects where the right eye was excluded due to a higher astigmatism than -0.75 DC.

4.2.2 Study Protocol

Preliminary tests, apparatus used, contrast protocol, study protocol and contrast threshold measurements were as described in 2.2, 2.3 and 2.5. The sequence of presentation and testing of the 3 adaptation tasks was randomized across subjects. Contrast sensitivity was measured before and after task adaptation at 0.5, 1.2, 2.7, 4.4 and 6.2 cpd for myopic and emmetropic young adults. The flow chart in Figure 3.1 depicts the contrast adaptation experimental procedures.

4.2.3 Adaptation Tasks

Adaptation tasks investigated were reading English text and Chinese text and viewing the centre of the horizontal grating. The English text and the grating adaptation tasks used were as described in 3.2.4. For Chinese text, the simplified version of the Chinese characters was used as this version is used widely in Singapore and China. Both the English and Chinese text were presented with the same high contrast so that this parameter would not become a confounding factor to the results obtained.

The lines of text were assumed to form the black bars of the grating and the spaces in between formed the white bar of the grating. This forms the row frequency for both the English and Chinese text which was fixed at 1.2 cpd (Figure 4.1). The font size of the

Chinese text was set at SimSun 10.5 with a spacing of 17 points for the row frequency of 1.2 cpd.

Figure 4.1 Diagrammatic representation of row frequency.
The lines of letters correspond to the black bars and the spaces between the rows of text correspond to the white bars.

The stroke frequency was calculated using the method proposed by Majaj et al, (2002). It was found to be 6.21 strokes/degree. This was not very different from the English text (6.04 strokes/degree). The width was found to be bigger for each word (or letter in English text) even though the font size was smaller than the English text (SimSun 10.5 versus Times New Roman 12). The sizes of the texts were adopted based on the local newspaper prints on The Straits Times in English and My Paper in Chinese. Both the papers are widely read among the Singaporeans.

As the stroke frequencies of both the English and Chinese texts were calculated to be 6.04 and 6.21 respectively, the grating adaptation task of 6.2 cpd was created (Figure 4.2) and used in Experiments 1 (see 3.2.4) and 2.

A B C

Figure 4.2 Diagrammatic representation of stroke frequency
Adapting stimuli (A) Lines of Chinese text (B) Sine Wave Gratings at 6.2 cpd (C) Lines of English Text

4.2.4 Data Analysis

Contrast threshold measured in % before and after adaptation was converted to log contrast sensitivity for all measurements. Analysis of variance using the general linear models was used to analyze the data. Contrast adaptation effect, which was defined as the difference in log contrast sensitivity of adaptation task and the baseline, was the dependent variable. The independent variables were refractive error group nested in subjects, tested spatial frequencies and adaptation tasks. General linear models were analyzed at 5 spatial frequencies and 3 adaptation tasks (reading English text, reading Chinese text and viewing the horizontal gratings) in 2 refractive error groups with subject factor randomized, so that the goal of the study is to make a statement regarding the larger population. For two-level comparison, Fisher's Least Significant Difference (LSD) intervals were used for comparison of significant findings. For comparison of more than two-levels, Bonferroni corrected test was performed to reduce the type 1 error rate due to stepwise multiple comparison.

4.3 Results

4.3.1 Baseline Contrast Sensitivity

Contrast sensitivity was measured at 0.5, 1.2, 2.7, 4.4 and 6.2 cpd. The peak contrast sensitivity at baseline for all subjects was 2.156 ± 0.114 log units at spatial frequency 4.4 cpd, and the lowest contrast sensitivity was 1.661 ± 0.115 log units at 0.5 cpd. The baseline contrast sensitivity (before reading) of the young adults was not affected by gender ($F_{1,48} = 2.69$, $P = 0.107$), age ($F_{6,43} = 0.70$, $P = 0.649$) nor by refractive error group ($F_{1,48} = 1.98$, $P = 0.166$).

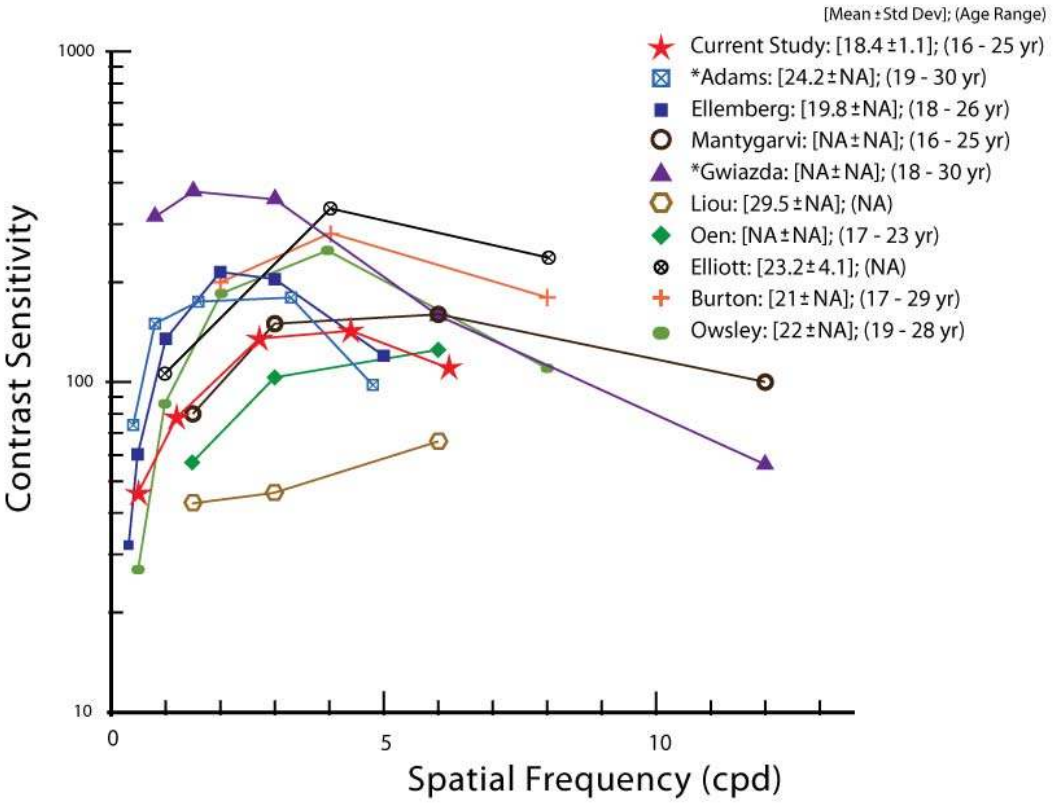


Figure 4.3 Contrast sensitivity functions of young adults in comparison to that obtained from other studies of similar age groups.
***Contrast thresholds were measured binocularly.**

Figure 4.3 shows the contrast sensitivity of the young adults obtained in the current study in comparison with other studies. Some of the studies (Gwiazda, Bauer, Thorn et al. 1997; Adams and Courage 2002) measured contrast sensitivity function binocularly and resulted in better sensitivity in their subjects. Some methodological differences across the studies are further discussed in 4.4.3.

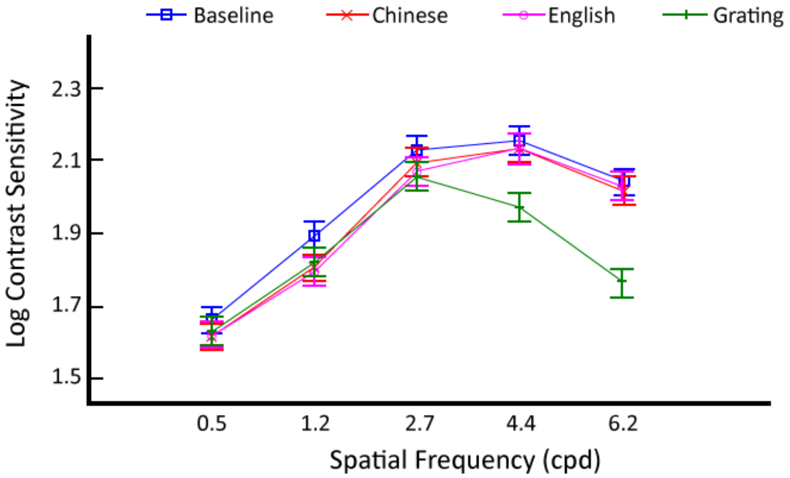
4.3.2 Post-adaptation Contrast Sensitivity

All subjects showed reduced mean log contrast sensitivity after the near tasks, be it reading English or Chinese text or viewing the horizontal sine wave grating (Figure 4.4 a). There was a shift in the peak of contrast sensitivity after reading (averaged log CS after adaptation to English and Chinese texts) from 2.7 (2.128 ± 0.144 log units) to 4.4

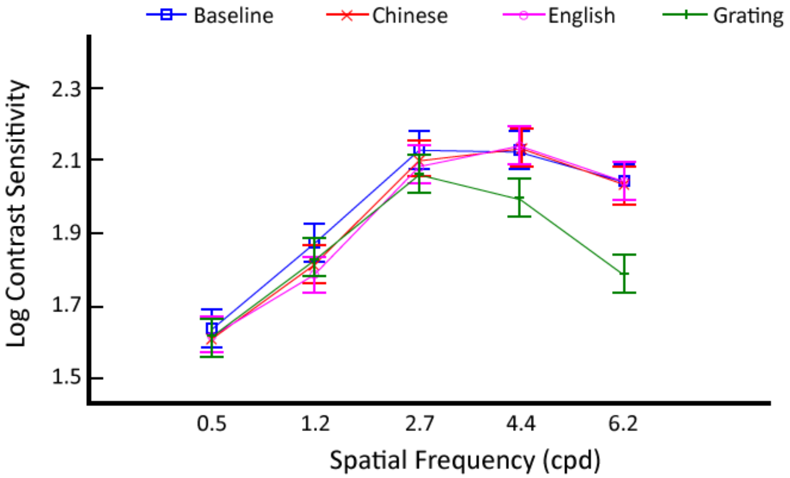
cpd (2.137 ± 0.131 log units) for emmetropes (Figure 4.4 b) but the peak of contrast sensitivity remained at 4.4 cpd (baseline peak 2.186 ± 0.136 log units; after adaptation peak: 2.132 ± 0.152 log units) for the myopes (Figure 4.4 c).

Table 4.1 shows the means and standard deviations of the contrast adaptation effect (log contrast sensitivity post-task – log contrast sensitivity pre-task) after reading and after viewing the horizontal gratings in myopic and emmetropic children. The post-adaptation log contrast sensitivity was significantly different from the baseline at spatial frequency 1.2 cpd for both English and Chinese adaptation tasks for myopes only. These significances are indicated as * in Table 4.1. The adaptation effects were 0.105 and 0.115 for English and Chinese respectively. In emmetropes, reading adaptation tasks did not show any significant different from the baseline at any tested spatial frequency. In terms of reading texts, the row frequency at 1.2 cpd showed a higher adaptation effect than the stroke frequency of the text at 6.2 cpd in the young adult population. This was not observed in Experiment 1.

a. All Subjects



b. Emmetropes



c. Myopes

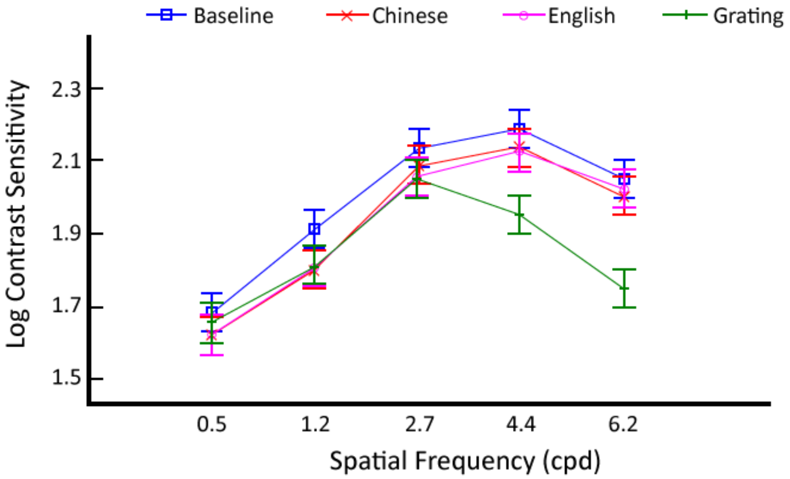


Figure 4.4 Mean log contrast sensitivities of (a) all, (b) emmetropic and (c) myopic young adults at baseline and after adaptation to English text, Chinese text and horizontal sine wave gratings. Error bars indicate the Bonferroni corrected 95% confidence intervals.

Table 4.1 Mean and standard deviation of contrast adaptation after reading and after viewing the horizontal gratings in myopic and emmetropic young adults

AT		E					M				
SF		0.5	1.2	2.7	4.4	6.2	0.5	1.2	2.7	4.4	6.2
English	Mean contrast (log unit) ± SD	-0.017 ± 0.116	-0.088 ± 0.136	-0.040 ± 0.115	+0.018 ± 0.116	+0.005 ± 0.158	-0.062 ± 0.119	*-0.105 ± 0.097	-0.079 ± 0.088	-0.062 ± 0.136	-0.025 ± 0.150
Chinese	Mean contrast (log unit) ± SD	-0.026 ± 0.075	-0.058 ± 0.123	-0.024 ± 0.158	+0.006 ± 0.098	-0.005 ± 0.166	-0.064 ± 0.127	*-0.115 ± 0.112	-0.049 ± 0.109	-0.046 ± 0.156	-0.043 ± 0.138
Grating	Mean contrast (log unit) ± SD	-0.024 ± 0.090	-0.042 ± 0.152	-0.065 ± 0.148	*-0.131 ± 0.110	*-0.253 ± 0.145	-0.028 ± 0.134	-0.105 ± 0.140	-0.084 ± 0.130	*-0.237 ± 0.154	*-0.301 ± 0.175

The minus sign of the contrast adaptation effect showed that contrast sensitivity reduced after adaptation except for emmetropic young adults reading at 4.4 cpd. There was limited adaptation effect among the emmetropes at 4.4 and 6.2 cpd after reading (contrast sensitivity was similar to before reading).
***Spatial frequency at which there is significant difference in log contrast sensitivity between post adaptation and baseline.**

AT – Adaptation task **SF – Spatial frequency**
E – Emmetropic young adults **M – Myopic young adults**
SD – Standard deviation

For the grating adaptation task, the log contrast sensitivity was significantly different from baseline at 4.4 and 6.2 cpd in both emmetropes and myopes. The strongest adaptation effect was observed in the grating task when the test spatial frequency was at 6.2 cpd, the adapting spatial frequency. The mean log contrast sensitivities for grating adaptation for emmetropes were -0.131 ± 0.110 log units and -0.253 ± 0.145 log units at 4.4 cpd and 6.2 cpd respectively, and for myopes were -0.237 ± 0.154 log units and -0.301 ± 0.175 log units at the same spatial frequencies (Table 4.1).

4.3.3 Comparison of Adaptation Effects Among Different Adaptation Tasks

Contrast adaptation effect was significantly different among the 3 adaptation tasks ($F_{2, 672} = 42.97$, $P < 0.001$). Adaptation effect was also significantly different across the spatial frequencies ($F_{4, 672} = 7.52$, $P < 0.001$). There was significant interaction between adaptation tasks and spatial frequencies ($F_{8, 672} = 19.28$, $P < 0.001$). Post-hoc Bonferroni test showed there was no statistical significant difference in the adaptation effect between reading English and Chinese text across the spatial frequencies (Figure 4.5), but there was significant different between reading induced adaptation (by either English or Chinese) and grating adaptation at 4.4 and 6.2 cpd only. The results did not support our hypothesis that reading Chinese text result in a higher adaptation effect than reading English text.

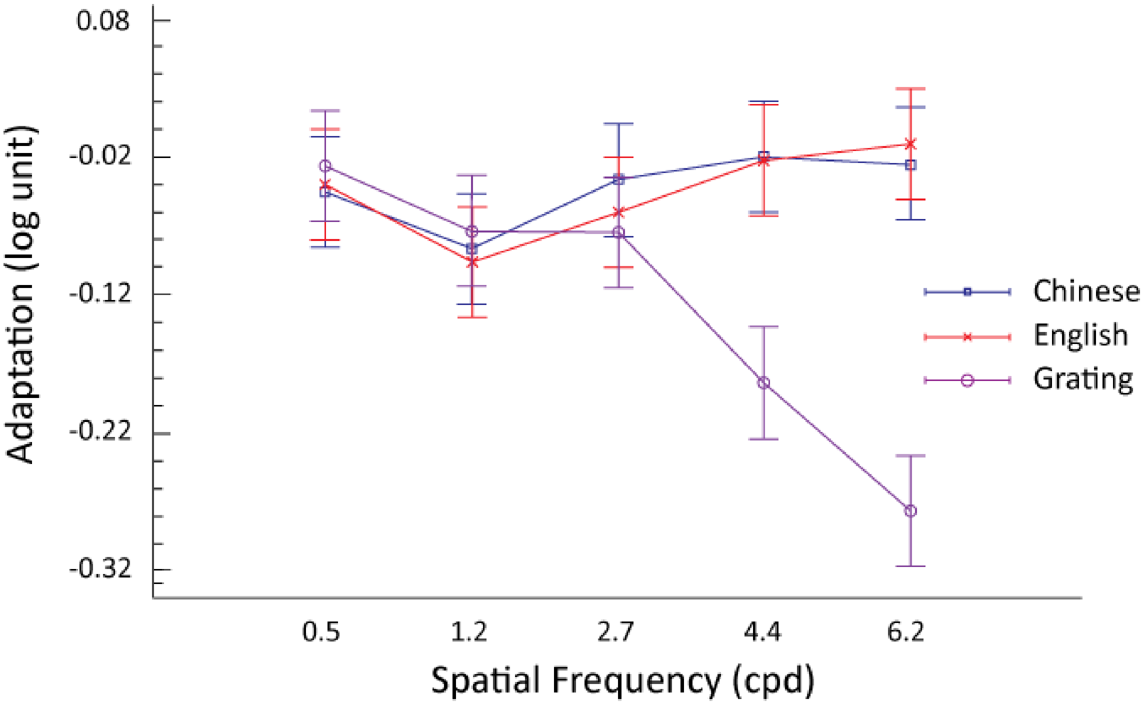


Figure 4.5 No significant effect was found between reading English and Chinese text at all the tested spatial frequencies. Significant contrast adaptation effect was found between reading and viewing of grating at spatial frequencies 4.4 and 6.2 cpd only. Error bars indicate the Bonferroni corrected 95% confidence intervals.

4.3.4 Comparison of Adaptation Effects in Myopes and Emmetropes

Figures 4.4 b and 4.4 c show the mean log contrast sensitivities at baseline and after adaptation for emmetropic and myopic subject groups respectively. When the data were pooled together across five spatial frequencies, the myopic (-0.094 ± 0.131 log units) young adults showed significantly greater adaptation than the emmetropic (-0.050 ± 0.127 log units) young adults ($F_{1, 48} = 5.01$; $p = 0.030$) (Figure 4.6). Interaction between refractive error group and adaptation task was not significant ($F_{2, 672} = 0.06$, $P = 0.946$), and neither was the interaction between refractive error group and spatial frequency significant ($F_{4, 672} = 0.23$, $P = 0.92$). English and Chinese tasks induced similar amounts of adaptation effect while the grating induced greater adaptation effect than reading texts in both myopic and emmetropic young adults (Figure 4.7).

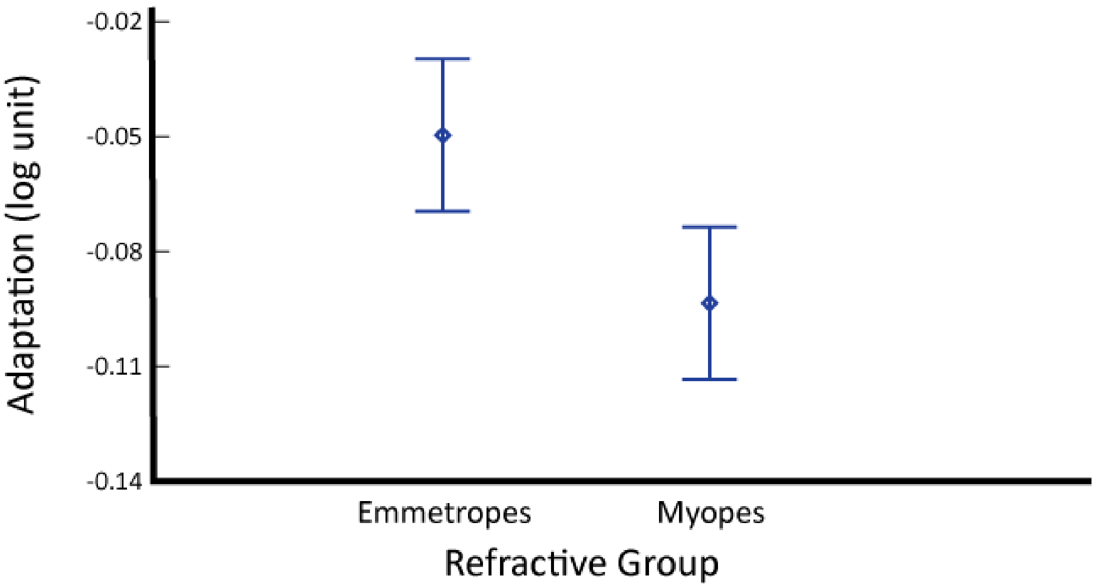


Figure 4.6 Myopic young adults showed greater adaptation effect than emmetropic young adults. Error bars show LSD 95% confidence intervals.

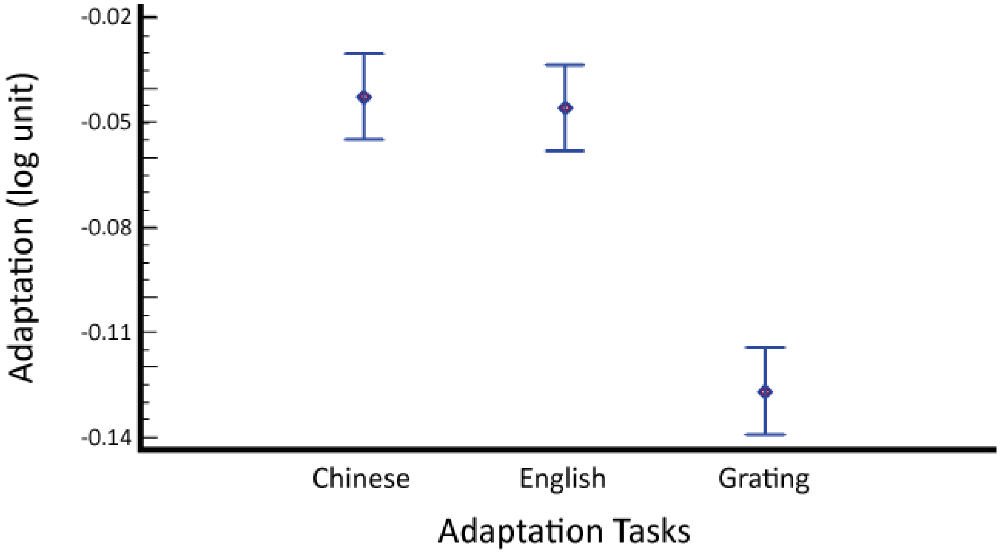


Figure 4.7 No significant difference in contrast adaptation effect induced by reading English and Chinese texts. However, viewing of grating induced a stronger adaptation effect than reading. Error bars indicate the Bonferroni 95% confidence interval.

When regression analysis was performed between the degree of myopia and the magnitude of contrast adaptation, there were no significant relationships found (Table 4.2). Here, a significance level of 0.01 was considered as statistically significant to reduce the chance of type 1 errors due to multiple comparisons. The only p value that was significant was the grating task at 4.4 cpd. However, the relationship between contrast adaptation effect and the degree of myopia is weak.

Table 4.2 Regression analysis between degree of myopia and contrast adaptation

Tasks	**R^2 and the Respective P values at Tested Spatial Frequency**					
		0.5	1.2	2.7	4.4	6.2
English	R^2	0.026	0.025	0.023	0.113	0.002
	P	0.259	0.272	0.289	0.017	0.740
Grating	R^2	0.003	0.109	0.007	0.162	0.024
	P	0.708	0.019	0.553	*0.004	0.286
Chinese	R^2	0.084	0.096	0.113	0.048	0.019
	P	0.041	0.028	0.463	0.126	0.335

*P value is significant (with significant level at 0.01).

4.4 Discussion

Reading Chinese text induced similar amounts of contrast adaptation to reading English text (and in both cases less than viewing a horizontal sine wave grating). Myopic young adults showed a significantly greater contrast adaptation effect than emmetropic young adults. The processing of different text types, the calculation of stroke frequencies of the texts and the effect of contrast adaptation and refractive errors are further discussed.

4.4.1 Chinese versus English Text

Both Chinese and English text caused a similar reduction in contrast sensitivity, and the reduction was similar in magnitude. This could be due to several reasons. Firstly, the characteristics of the text such as the stroke and row frequencies of both texts were similar. The stroke frequency and row frequency of the Chinese text were calculated to be the same as the English text based on the reading material used in the study. The stroke frequency is a function of the number of strokes crossing the horizontal midline and the size of the letter/character. The number of strokes of the words depended on the words chosen in the story and the size of the character/letter was based on newspaper fonts. The choice of Simplified Chinese characters had also led to a lower number of strokes obtained in each Chinese character. The Simplified Chinese was chosen because the text type is now most widely used in Singapore and China. Even though the font is smaller than English (10.5 SimSun versus 12 Times New Roman), the width of each character is bigger than each letter in English, thus lead to a smaller stroke frequency calculated since the stroke frequency is equal to the average number of strokes divided by the average width of each letter.

Secondly, contrast adaptation induced by reading did not relate to the stroke frequency (6.2 cpd) as much as to the row frequency (1.2 cpd) of the text. Contrast adaptation induced by reading was about 0.09 log unit at 1.2 cpd compared to 0.02 log unit at 6.2 cpd. This shows that the contrast adaptation occurred more at row than stroke frequencies, but the difference was not significant. This is consistent with the greater repetitiveness of the rows and relatively greater variability in the strokes and thus relative strength of the row and stroke stimuli (Patching and Jordan 2005). Patching and Jordan reported that a broad range of spatial frequencies are used to recognize words and different individuals may rely on different spatial frequencies in the word content they are sensitive to for words recognition. Furthermore, as discussed in more detail below, visual word processing involve both the encoding of spatial frequency of the words and individual letters of a given word (Allen, Wallance and Weber 1995). These spatial frequencies may vary based on the letters in the word. In a small paragraph for example, there will be different spatial frequencies for different letters and words. Hence, the contrast adaptation effect may not be dependent on the stroke frequency or the data may have resulted from an imperfect system being used to calculate the stroke frequency of the Chinese text. Given the data that adaptation is primarily related to the row frequency, we predict that the degree of adaptation would be similar for both the Simplified and the Traditional forms of Chinese text.

Thirdly, the processing of the reading task is complex. The information processes involved in reading consists of perceptual and comprehension aspects. Since the subjects' comprehension process during the experiment was difficult to ascertain, we will concentrate on the perceptual process of reading. Chinese characters' pronunciation must be learned through rote memory of the association of visual character form and sound with the aid of sub-character units (Tan, Liu, Perfretti et al. 2001). As the subjects in the experiment did not read out the text, pronunciation learned through rote memory was not necessary in processing the words. Moreover, whether the subjects were constantly involving the cognitive demand to follow the stories during the experiment and understand what they were reading could not be ascertained. Therefore, the neural cognitive mechanism may not be 100% applicable in this experiment. Furthermore, unlike accommodative adaptation, which requires innervation and feedback mechanism on stimuli, contrast adaptation is a measurement of ability to discern visual stimuli. Hence, perceptual processing of the words in contrast adaptation becomes exclusively important.

The stroke frequency was calculated from each and every letter. However, it is believed that reading involves a rapid word encoding system that entails a holistic, combination of both word-level code and letter-level code, rather than a system that process words by resolving the component letters that use the letter-level channel alone (Allen, Wallance and Weber 1995). The holistic system consists of a hybrid model (Figure 4.8) of visual word processing which assumes the existence of 2 main pathways: orthographic (addressed) and phonological (assembled). The orthographic pathway is further divided into word-level, syllable-level, and letter-level routes. The word-level, syllable-level and letter-level channels in the hybrid system are involved in a "horse race" to the central processor. The central processor selects the winner input code in an attempt to complete the task at hand (e.g. lexical decision, naming or letter identification). The word-level channel encodes the spatial frequency of entire words, the letter-level channels encode the spatial frequency pattern of individual letters of a given word (Allen, Wallance and Weber 1995). Since the holistic system of word processing combines two channels: one processing words as holistic, word-level codes and the other processing words as analyzed strings of letter-level codes, this system allows a more rapid processing than the single channel system using the letter-level channel or word-level channel, thus enable the reader to achieve faster word-encoding times and more easily meet the demand for rapid information inflow than the single channel system (Allen, Wallance and Weber 1995). Hence, the holistic system has replaced the previous belief that words are formed from component letters and reading is encoded purely by the analysis of each and every letter (McClelland 1976; Humphreys, Evett and Quinlan 1990).

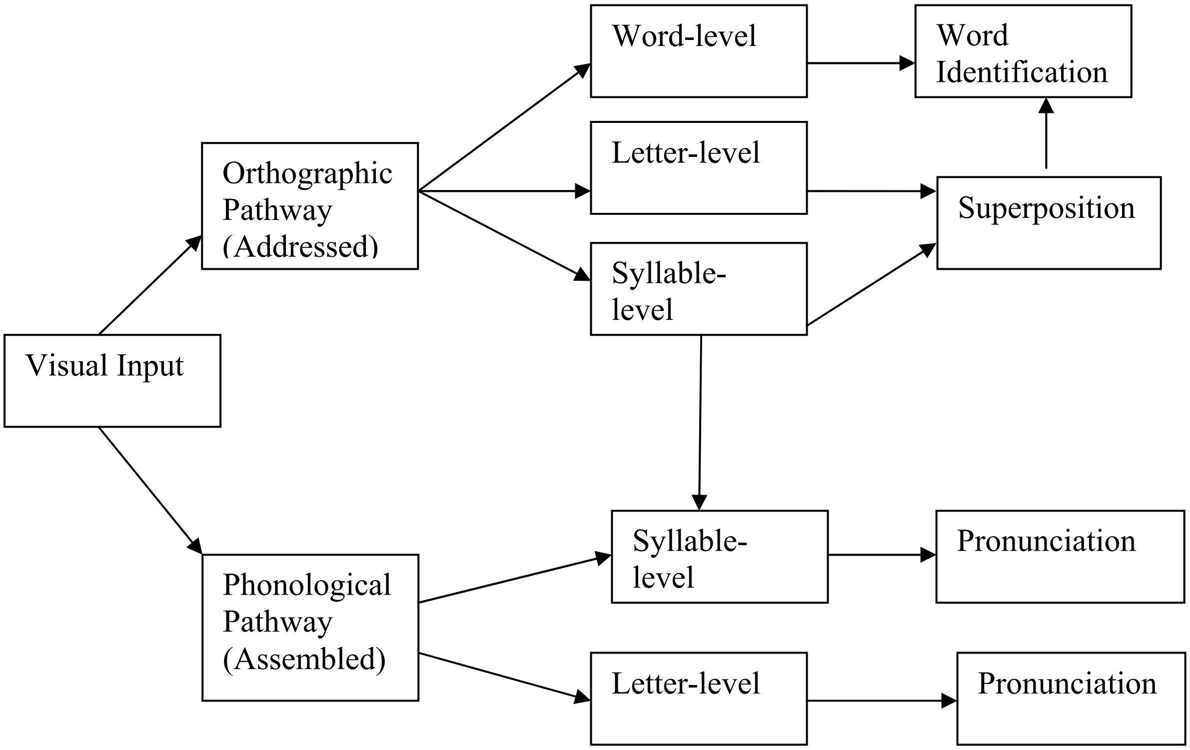


Figure 4.8 The holistic biased hybrid model of visual word processing. Adapted from Rayner and Pollastek, 1989

The holistic system holds true for the alphabetical system, such as in English text. It was also thought to hold true for logographic system, such as in Chinese text (Rayner and Pollatsek 1989). Evidence presented by Rayner and Pollastsek supports the fact that both routes are used even though the writing systems are very different in all languages. In addition, the spatial frequency of an individual letter which was thought to be important for letter identification may not play an important role in reading and comprehension. This could explain why the stroke frequency of the letters was not as important as row frequency in both the results obtained in this experiment and in the previous experiment on children.

Lastly, the way in which strokes were calculated for Chinese text may not be a good representation of the real number of strokes in the text. In terms of different types of characters between English and Chinese text, calculating the stroke frequency for the Chinese text may not produce the right centre frequency for each word. For example, the word “3” in Chinese is “三”. According to the stroke frequency, it is zero since none of the 3 strokes cross the horizontal midline. However, for a word like “川”, the stroke frequency is 3. Both words have 3 strokes but one with 0 cpd and the other word has 10 cpd (average strokes/average width of the letter). So the use of stroke frequency calculation may not work well in Chinese characters. The stroke frequency may accurately calculate the centre frequency of the English letters but it cannot be used to determine the centre frequency of the Chinese text.

A suggestion here is to include all the strokes in the calculation of Chinese characters, be it a horizontal stroke, a vertical stroke or an oblique stroke. For example, both “三” and “川” are calculated as 3 strokes. This method of calculation will ensure that each and every stroke in the Chinese character is counted and justified for the complexity of the character. If it is made up of a character of many strokes such as “鱼”, it should be calculated as having 8 strokes rather than 3 strokes that cross the horizontal midline. This method of calculation will ensure a better representation of the complexity of the character. Using the new method of calculation, the Chinese characters from the first row of the first page of the reading material was calculated to be 14 strokes/degree. Future studies could compare contrast adaptation effect induced by reading similar Chinese text using different methods to obtain the strokes to determine if adaptation effect increases with increasing strokes.

Therefore the way the stroke frequencies of the English and Chinese text were calculated might not be the best to represent the centre frequency of the letters or characters in this study. The final frequency for the whole page of text also depends on the correct mixture of words and the frequency of the words appearing in the passage. This is because not all the characters are complicated and the complicated characters appear less frequently than that of simpler characters. In the Chinese text, the more frequent words are those that join sentences, for example, 了, 不, 的. These words usually contain fewer strokes. In other words, the stroke frequency was not able to represent the Chinese text very well. Until there is a better way to quantify the strokes of the Chinese text in a fair manner when comparing with the English text, involvement of Chinese text in myopia development may be hard to establish.

4.4.2 Myopes versus Emmetropes

The total (3 levels of adaptation tasks and 5 levels of spatial frequencies) adaptation effects on myopes was significantly greater than that on the emmetropes. This confirmed our hypothesis (see Chapter 3) that myopes showed significantly greater adaptation than emmetropes. In contrast with the previous experiment, contrast adaptation was performed on a group of emmetropic and myopic young adults and the myopia in this group of subjects had mostly stabilized. The greatest difference in adaptation effect (0.066 log units more in myopes) between emmetropic and myopic young adults occurred at 4.4 cpd. This finding was similar but smaller than that obtained in Experiment 1. This suggests that there is difference in neural plasticity between the children and young adults group and spatial frequency of about 4.4 cpd may be involved in myopia progression.

The magnitude of contrast adaptation obtained in this study may seem small but as has been discussed in 3.4.1, it may still play a role in changing the perceived retinal image quality to result in myopia. This is because small amount of perceived retinal image defocus could result in myopia development in human as reported previously (Robb 1977). In animal studies, translucent diffusers that still allow light to the retina produce greater myopia than opaque diffusers which block all light (Sivak, Barrie and Weerheim 1989; Bartmann and Schaeffel 1994). Reduction of image contrast by as little as 0.1 log unit triggered deprivation myopia in monkeys (Smith and Hung 2000). Thus the magnitude of contrast adaptation need not be high to cause myopia. The degree to which contrast had to be degraded for myopia to occur varied for individual animals. Some animals developed myopia when the contrast was degraded to a lesser extent than those which remained isometropic (Schmid, Brinkworth, Wallace et al. 2006).

Another important factor is the rate of dissipation of the contrast adaptation as this will determine the duration of the reduced retinal activity. Prolonged reading from the effects of contrast adaptation may induce a reduction in the perceived retinal image quality that is similar to that of form deprivation that lingers over several hours. The reduced retinal activity due to the deprivation could become an error signal for eye growth. In chicks, 2-3 min exposure to defocus is sufficient to induce changes in eye growth (Zhu, Park, Winawer et al. 2005; Zhu and Wallman 2009), then reading of up to 1 hour (which is not uncommon especially when the young adults are preparing for their examinations) could be highly detrimental, particularly if the reading activity is not interspersed with other tasks. Therefore, if the recovery time for the contrast loss is long, persistent form deprivation may cause myopia progression. However, with young adults, the neural plasticity is not as high as in children and therefore the degree of detrimental effect is probably reduced as well. For example, axial elongation does not occur in an old eye where clear vision was affected by age-related cataract suggest the propensity of the changes in the image to produce axial elongation during the "critical period" of eye growth. From our results, both emmetropic and myopic children showed greater adaptation effects compared to emmetropic and myopic adults, respectively, thus suggesting that the age of exposure to contrast adaptation is important.

The exact mechanism by which contrast adaptation occurs is still unknown although both retinal (Smirnakis, Berry, Warland et al. 1997; Kim and Rieke 2001; Baccus and Meister 2004) and cortical (Blakemore and Campbell 1969; Ohzawa, Sclar and Freeman 1985; Sanchez-Vives, Nowak and McCormack 2000; Sanchez-Vives, Nowak and McCormick 2000) involvement is suggested. Since we have observed its occurrence in children whose myopia is progressing and young adults whose myopia is stabilized, the greater magnitude of contrast adaptation found in progressing myopes than stable myopes leads to our hypothesis that contrast adaptation is highly associated with myopia development (see 3.4.1).

4.4.3 Baseline Contrast Sensitivity of the Young Adults

The baseline contrast sensitivity of the young adults in this study was comparable to the values reported in other studies (Figure 4.3). Binocular contrast thresholds were better than monocular contrast thresholds (Gwiazda, Bauer, Thorn et al. 1997; Adams and Courage 2002). The difference could also be attributed to the differences in contrast stimuli used for testing, mean luminance and contrast sensitivity test methods. Two-interval forced choice staircase procedure was harder to perform than two-alternative forced-choice staircase procedure but with less variability than the method of adjustment as discussed in 3.4.5. Ellemberg et al (1999) used method of adjustment instead of forced-choice method to obtain contrast thresholds. Other studies used the Vistech contrast sensitivity test at 3 m (Mantyjarvi, Autere, Silvennoinen et al. 1989; Scharre, Cotter, Block et al. 1990; Oen, Lim and Chung 1994; Liou and Chiu 2001; Adams and Courage 2002) which is different from computer generated stimuli. The other aspects such as age of subjects, binocularity, luminance of target chart and method of testing probably also contributed to the differences in contrast thresholds obtained across different studies. However, an interesting observation from the comparison graphs is that Asian subjects (Oen, Lim and Chung 1994; Liou and Chiu 2001) showed lower contrast sensitivities than Caucasian subjects. This might be associated with the susceptibility of Asian eyes to changes in the perceived retinal images due to prolonged near work. However, further studies are required to confirm this suggestion.

The baseline contrast sensitivity test was not affected by refractive error groups and gender. As discussed in 3.4.5, if there is no retinal pathology detected (Thorn, Corwin and Comerford 1986; Liou and Chiu 2001), contrast sensitivity function of the myopes will not be affected. Moreover, the optical defocus induced by the distortion of high powered spectacle lenses (Liou and Chiu 2001) was not a big issue here because refractive error of our subjects were less than -6.00 D (see 3.4.5). There were contradictory findings in previous studies about gender differences in contrast sensitivity. The differences in findings could be due to the variability caused by different testing methods and environment.

4.5 Conclusion

Reading Chinese text induced the same amount of contrast adaptation effect as reading English text. Myopic adults had a greater contrast adaptation effect induced by reading than did emmetropic adults.

CHAPTER 5

CHINESE VERSUS ENGLISH TEXT ON ACCOMMODATIVE RESPONSES AND NEAR WORK-INDUCED TRANSIENT MYOPIA IN MYOPIC AND EMMETROPIC CHINESE CHILDREN

Abstract

Purpose: To measure the accuracy of accommodation responses during and NITM following reading of Chinese and English text, and based on this, determine if there are any differences that may be related to refractive error development in children.

Methods: Accuracy of accommodation during reading and NITM following the reading of Chinese and English text was measured with a free space autorefractor in myopic and emmetropic children. A total of four tasks were assessed – reading lines of English text (i) at 33 cm and (ii) at 25 cm; reading lines of Chinese text (iii) at 33 cm, and (iv) at 25 cm. Average near refraction measures were subtracted from the accommodation demands at 33 cm and 25 cm to obtain the accommodation accuracy. NITM was calculated by subtracting the pre-task closed-loop accommodation response value from the post-task value. Data for each subject were then divided into 6-s bin intervals, and magnitude of NITM was obtained at the first 6 s post task. Regression times were expressed in terms of the time taken for the post-task refraction to first reach the average pre-task refraction.

Results: There were significant effects of text type and reading distance on accommodation accuracy during reading but the magnitudes were small. Accommodation accuracy was similar for emmetropic and myopic children during the reading tasks ($F_{1,81} = 0.51$, $P = 0.475$). Neither text type nor distance had any significant effects on the magnitude of NITM (text: $F_{1,164} = 0.05$, $P = 0.82$; dist: $F_{1,164} = 0.00$, P =

0.99) nor its regression time (text: $F_{1,246} = 0.00$, P = 0.95; dist: $F_{1,246} = 2.1$, P = 0.15). However, refractive error group significantly affected both the magnitude of NITM ($F_{1,81} = 5.05$, P = 0.03) and regression time ($F_{1,81} = 31.1$, P < 0.001); myopes had greater NITM (by 0.07 D) and this took longer (by 50 s) to dissipate than for emmetropes.

Conclusion: Reading Chinese text resulted in a smaller accommodative lag than reading English text (accommodative lags of 0.97 D in Chinese vs. 1.00 D in English), but the effect was too small to be considered clinically important. Myopic children presented with significantly greater magnitude of NITM and longer regression time than emmetropic children for both types of texts.

5.1 Introduction

The current prevalence of myopia in some developed East Asian countries, such as Hong Kong, Taiwan and Singapore (Edwards and Fan 1999; Tan, Saw, Lam et al. 2000; Lin, Shih, Hsiao et al. 2001; Wu, Seet, Yap et al. 2001; Edwards and Lam 2004; Lin, Shih, Hsiao et al. 2004; Saw, Tong, Chua et al. 2005) is alarming. There is strong evidence that the rapid increase in the prevalence of myopia has been environmentally induced; high myopia prevalence in children being associated with increased education demands from schools and urbanization (Morgan and Rose 2005). In fact, many epidemiological studies report a correlation between high myopia prevalence and lengthy periods spent performing near work (Saw, Hong, Zhang et al. 2001; Saw, Wu, Seet et al. 2001) at close distances (Ip, Saw, Rose et al. 2008). Although current research (Rose, Morgan, Ip et al. 2008; Dirani, Tong, Gazzard et al. 2009) suggests that outdoor activity can ameliorate the myopia inducing effects of near work, it is clear from the high myopia prevalence that the level of outdoor activity in these East Asian countries is currently too low for this beneficial effect to be observed.

There are many possible mechanisms by which long periods spent reading (or performing near work) could result in myopia. One of the most researched aspects is the accommodation system; the accommodation response is activated during reading and therefore accommodation may play an important role in myopia development [see review by (Rosenfield and Gilmartin 1998)]. There are two main characteristics of accommodation that are considered to be important in myopia development. One is the accommodation error that occurs during reading (typically the response is less than the demand, i.e. a lag of accommodation is measured), and the second is the accommodation hysteresis that occurs following reading, i.e. accommodation takes time to relax for distance viewing after prolonged near tasks (Ebenholtz 1983; Ebenholtz and Zander 1987; Ehrlich 1987). The latter effect is termed accommodative adaptation or near work induced transient myopia (NITM). The lag of accommodation observed at near and the residual accommodation after near work induced hyperopic and myopic defocus, respectively, – the defocus is thought to play an important role in myopia development in those who perform prolonged near work.

Both myopic children and adults tend to have reduced accommodative responses, i.e. exhibit lags of accommodation at near (McBrien and Millodot 1986b; Gwiazda, Thorn, Bauer et al. 1993b; Abbott, Schmid and Strang 1998; Yeo, Kang and Tang 2006). A recent study reported that infants who showed the least robust emmetropization showed the poorest accommodative response and were exposed to the highest levels of hyperopic defocus (Mutti 2010). The resulting hyperopic retinal defocus may trigger the emmetropization process to produce compensatory myopia (Goss and Wickham 1995; Schmid and Wildsoet 1997b; Shaikh, Siegward and Norton 1999). It is usually accepted that lags in accommodation increase approximately linearly with the stimulus vergence (Charman 1999). Progressive addition spectacle lenses reduce myopia progression significantly compared to conventional single vision correction, in some studies (Leung and Brown 1999; Gwiazda, Hyman, Hussein et al. 2003; Yang, Lan, Ge et al. 2009; Cheng, Schmid, Woo et al. 2010). These works suggest that the increase in accuracy of the accommodative response imposed by a near addition during near work may help to slow the rate of myopia progression in juvenile onset myopia, presumably by reducing the blur signal resulting from accommodative lag at near.

Besides the accommodative lags, accommodative adaptation or NITM is suspected to play an important role in myopia development (Ciuffreda and Wallis 1998; Ciuffreda and Thunyalukul 1999; Wolffsohn, Gilmartin, Li et al. 2003; Ciuffreda and Vasudevan 2008). Near work induced transient myopia causes a myopic shift after a sustained period of near work measured under closed-loop condition (Ciuffreda and Wallis 1998; Ciuffreda and Thunyalukul 1999; Vera-Diaz, Strang and Winn 2002; Wolffsohn, Gilmartin, Li et al. 2003). Although the precise etiology of NITM remains unclear, the inability to relax accommodation rapidly and fully to the baseline far point is probably due to some neuro-pharmacological changes occurring to the innervation of the ciliary muscles [Lancaster and Williams (1914) cited by Ong and Ciuffreda (1995)]. Myopic young adults showed significantly greater post task myopic shift and prolonged NITM, which extended beyond the measured 120-s post task decay period, than emmetropes and hyperopes (Ciuffreda and Wallis 1998; Vera-Diaz, Strang and Winn 2002). Similar results were found in children where myopic children consistently presented with greater magnitude of NITM and longer decay rate than emmetropic children (Ciuffreda and Thunyalukul 1999; Wolffsohn, Gilmartin, Li et al. 2003).

A common prolonged near work activity for children is reading as they are often captivated by the stories in the books. Reading involves continuous eye movement following the words and constant cognitive demand. Besides reading stories in English, Singaporean children also read Chinese stories. Since there is higher myopia prevalence amongst Chinese children, we propose that the type of characters a child is exposed to at a young age, when learning to read, may play an important role in the development of myopia.

Written Chinese characters are made up of a number of strokes which are packed into a square shape. Depending on the complication of the word, the strokes in a Chinese word are usually more closely packed than the strokes in an English word. This probably makes it harder to resolve Chinese words than English words. Examples of Chinese characters such as 看 and 画, which means ‘see’ and ‘draw’ respectively consist of more strokes than their simple English counterparts. Furthermore, in a logography system (where a single character can be a whole word), the basic unit in writing is associated with a unit of meaning, a morpheme (Perfetti and Tan 1998). Therefore, Chinese characters map onto meaningful morphemes rather than phonemes (in English) in the spoken language. The Chinese characters' pronunciation is defined at the syllable level and must be learned through rote memory of the association of visual character form and sound, occasionally with the aid of sub-character units that are themselves real characters. There are more than 5000 Chinese characters (Hoosain 1991). Due to the box-like characters, Chinese text forms a "string" with no spaces to separate the words. Chinese readers have to depend on lexical knowledge to segment characters into words (Li, Rayner and Cave 2009). These unique characteristics imply that some of the neuro-cognitive mechanisms underlying Chinese logographic reading may differ from those underlying alphabetic word reading (Tan and Perfetti 1998). Although we have found no significant difference in contrast adaptation effect for Chinese and English text in Chapter 4, it remains a possibility that accommodation adaptations are different between the different texts.

The aim of this study was to measure the accuracy of accommodation responses and NITM during and following reading of Chinese and English text, and determine if there were any differences that may be related to refractive error. The effect of reading distance on NITM was also investigated. The hypothesis of this study was that NITM induced by reading Chinese text would be higher than that induced by reading English text. Since extra effort is required to resolve the words, this might improve accommodation accuracy during reading but further induce NITM. To our knowledge, no one has previously investigated the accommodative accuracy and NITM of children when reading Chinese text. This was also the first time where NITM were measured from a sample of Singaporean children.

5.2 Materials and Methods

Accuracy of accommodation and NITM during and following reading of Chinese and English text were measured with a free space autorefractor in myopic and emmetropic children. A total of four tasks were assessed – reading lines of English text (i) at 33 cm and (ii) at 25 cm; reading lines of Chinese text (iii) at 33 cm, and (iv) at 25 cm.

5.2.1 Subjects

Eighty-three children aged 7 to 12 yr (mean age: 10.1 ± 1.7 yr) were recruited - 40 were emmetropic (mean SE: +0.23 ± 0.25 D; mean age: 9.7 ± 1.9 yr) and 43 were myopic (mean SE: -2.87 ± 1.30 D; mean age: 10.3 ± 1.5 yr). The definition for emmetropia and myopia were ≤ +0.75 to -0.25 D and at least -0.50 D of myopia, respectively. The myopes in this study were progressing myopes, which were defined as having myopia increasing by at least 0.50 D per year for the previous 2 years (McBrien and Adams 1997). Subjects completed a questionnaire on their refractive error history and family ocular history. We made use of these data and past optometric records to classify myopes as progressing. All myopic subjects were full-time wearers of their prescription. Inclusion criteria comprised at least 6/6 monocular visual acuity, amplitude of accommodation of at least the minimum amplitude of the Duane-Hoffstetter's formula of (15.0 – 0.25 x age) and was measured with a RAF rule, cylinder ≤ 0.50 DC, myopia ≤ 6.00 D, hyperopia ≤ 0.75 D, anisometropia ≤ 1.00 DS and absence of any ocular disease including strabismus. All the children undertook screening tests to ensure that they met the inclusion criteria. The preliminary tests performed were subjective refractive error measurement, slit lamp biomicroscopy and direct ophthalmoscopy. Refractive power of the eye was measured subjectively using the maximum plus or best visual acuity methodology (Elliott 2003). All subjects were corrected with soft spherical contact lenses, including the emmetropes as described in 2.9.

The purpose of the study and details of the tests were explained to the children and their parents. Once all questions and queries had been addressed, the participant consent form was signed by each child and his/her guardian or parent. All experiments were conducted with ethics approval from the Singapore Eye Research Institute Institutional Review Board and in accordance with the "National Statement on Ethical Conduct in Human Research" published by the National Health and Medical Research Council of Australia.

5.2.2 Measures of Reading Distances

As there are no published data on reading distances adopted by children reading Chinese text, a study was conducted on 20 children (mean age: 10.2 ± 1.3 yr) to determine their typical reading distances for both English and Chinese books of appropriate age-based difficulty. The study was described in 2.12. The average reading distances for English and Chinese text were 34.4 ± 5.5 cm and 33.2 ± 5.7 cm, respectively, thus 33 cm was used as a reading distance. This shows, as has the other study (Rosenfield, Wong and Solan 2001), that the children adopt a habitual reading distance regardless of slight differences in the reading material. A reading distance of 25 cm was included for comparison purposes, as previous accommodation studies involving children have used this shorter reading distance (Gwiazda, Thorn, Bauer et al. 1993b; Vera-Diaz, Strang and Winn 2000; Vera-Diaz, Strang and Winn 2002).

5.2.3 Apparatus

A free-space auto refractor (WAM-5500, Grand Seiko Co. Ltd, Japan) was used in a static mode to measure the refractive state of the eye objectively. This device provides a relatively wide, open field-of-view of the test stimuli and surrounding environment. It was set at a resolution of 0.01 D. As the measurements are affected by eye movement, blinking, spherical aberrations, ophthalmic lens reflections and tear quality, this resolution setting has little effect on reliability and accuracy of the measurements (Chat and Edwards 2001). The vertex distance for the auto-refractor was set at zero as the refractive errors of the subjects were corrected using soft spherical contact lenses. The autorefractor was connected to a computer using a RS-232C cable, which allowed collection of high speed measurements. The data output was automatically converted to an Excel spreadsheet.

Reading materials were projected from a tablet PC, HP Pavilion TX 1000 with a screen luminance of 90 cd/m^2. The screen of the tablet PC was 26 cm by 16 cm, subtending 26° vertically by 38° horizontally at 33 cm and 33° vertically by 46° horizontally at 25 cm. The tablet PC was placed in front of the auto- refractor (see Figure 5.1). The use of a laptop computer with a turntable screen meant that the screen for display of the near task could be quickly positioned and removed and the required close working distance was achievable. When subjects were looking at the distance target, the screen was closed. When subjects performed the near reading task, the screen was quickly raised. After reading, the screen was immediately closed so that subjects could fixate the distance target after reading with little time delay (approximately 2 s).

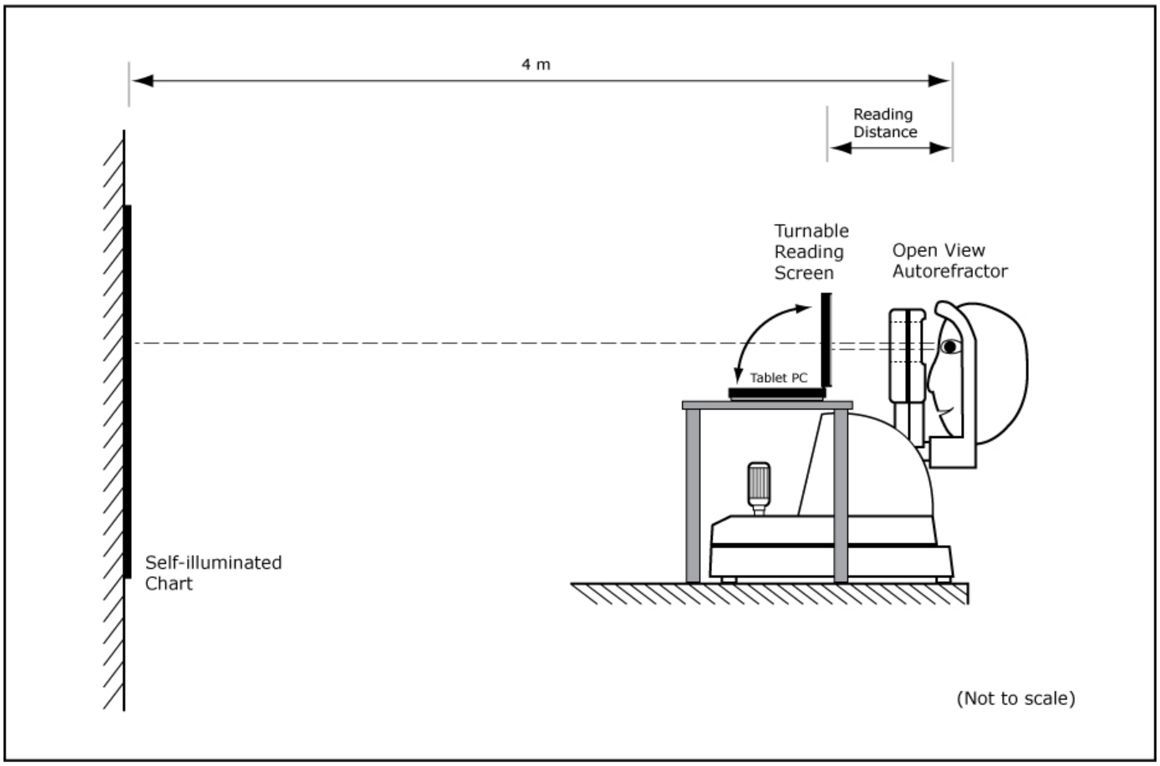


Figure 5.1 The experimental set up for refractive error measurement at distance and near to determine accommodation accuracy and NITM. Subjects viewed a self-illuminated chart at 4 m when the screen of the turntable tablet was closed. The screen was opened and displayed the required reading materials when subjects were engaged in the near reading task.

5.2.4 Reading and Distance Tasks

All subjects performed two different near tasks at two distances (33 and 25 cm), to give four reading tasks in total. The two near tasks were a) reading English texts of Times New Roman 12 point font and b) reading SimSun Chinese 10.5 point font. Both sets of print were of high contrast (maximum from the tablet screen). The luminances were measured using a Minolta Luminance Meter LS-100. The reading tasks were administered in a random order in terms of type of text but not in terms of distance. These materials subtended an angle equivalent to 0.7 log MAR at 33 cm and to 0.8 log MAR at 25 cm. Reading distance of 33 cm was always done first before the 25 cm. The reading distances of 33 cm and 25 cm were adjusted by moving the tablet PC away or towards the subjects (Figure 5.1). The reading and viewing tasks were performed binocularly with monocular measures taken using the auto-refractor. Refraction measures were taken before, during and after the reading period of 10 min. The 10 min reading time was chosen as 15 min was deemed too long for a repeat design experiment as it includes fatigue effects (Chen, Schmid and Brown 2005).

When the subjects were looking straight ahead at 4 m, an internally-illuminated distance visual acuity chart (LIGHTHOUSE modified ETDRS chart, Lighthouse International, USA) was used as the fixation target. Subjects were asked to fixate the middle letter of 0.2 logMAR (equivalent to Snellen 6/9). The mean luminance of the chart was approximately 110 cd/m^2 and measured by the Minolta Luminance Meter LS-100.

5.2.5 Measurement Protocol

The illuminance of the room was kept relatively low at 25 lux so that the ambient lighting would not interfere with the visibility of the near targets. The autorefractor performs monocular measurements; as in previous published work (Chen, Schmid and Brown 2005; Schmid, Hilmer, Lawrence et al. 2005), the right eye was chosen for measurement. If the right eye failed the criteria and the left eye met the criteria, the left eye was tested. This occurred in four subjects who had more than 0.75 D of astigmatism in the right eye.

Subjects initially spent 5 min in darkness to open the accommodation loop and dissipate the effects of any previous near activity (Ciuffreda and Wallis 1998; Chen, Schmid and Brown 2005; Schmid, Hilmer, Lawrence et al. 2005). Following this period, the lights were switched on and subjects viewed the distant chart at 4 m. Auto-refractor measurements commenced within three seconds and 30 measurements at two-second time intervals were made; the average of these gave the pre-task closed-loop accommodation value. The subjects then performed one of the near reading tasks. The computer screen was raised and the children were asked to read the text aloud. The screen of the tablet PC covered the entire view of the subject at the testing distance. Auto-refractor measures were taken at 2-min intervals; 10 measurements were made and averaged to give values at 2, 4, 6 and 8 min during the reading activity (a total of 40 measures were obtained). When measurements were taken, subjects were asked to briefly stop reading and view a highlighted word that aligned with the auto-refractor measurement system. The measurements taken were averaged at the reading time of 2, 4, 6 and 8 min and the grand total was averaged to give the overall estimate (over the 10 min reading) of the accommodation accuracy. Once the near task was completed, the computer screen was lowered and subjects were instructed to view the distance fixation target. Auto-refractor measurements were performed every 2 s over a 3-min period; the average of the first three measurements gave the post task 6 s NITM. The time taken for accommodation to return to pre-task levels was determined as the regression time. This completed one trial (about 20 min for each trial). In between trials, children took a break longer than 10 min. During this time they could go to the toilet, have a drink or snack and watch television at a distance of 4 m.

The accommodative adaptation or NITM in this experiment was measured in a closed-loop condition where the pre- and post-task measurements of accommodation were assessed while subjects viewed a distant letter chart. Thus normal blur-feedback mechanisms were allowed to operate (Rosenfield 1998). Under these conditions, a transient increase in the post-task response was observed immediately following completion of the near vision task. The post-task reading would be the combined response of the distance accommodation plus the output of the slow blur accommodative response, while the pre-task reading represents the distance accommodation exerted (Rosenfield 1998).

5.2.6 Data Analysis

Auto-refractor readings were converted to best sphere values by adding half the cylinder power to the spherical component. Invalid auto-refractor readings, which occurred as a result of blinking or momentary loss of fixation that gave outputs of large cylinder components of > -1.00 D were disregarded. To determine accommodation accuracy, the average of near refraction measures was subtracted from the accommodation demand at 33 cm and 25 cm accordingly. The accommodation accuracy during the 2nd, 4th, 6th and 8th minute of reading was also analyzed to determine whether accommodation accuracy changed over this time period.

Near work-induced transient myopia was calculated by subtracting the pre-task closed-loop accommodation response value from the post-task value with the myopic shift representing NITM expressed as a positive value (Chen, Schmid and Brown 2003). Individual post-task data (mean spherical equivalent) were normalized to each individual's pre-task closed-loop accommodation value. Data for each subject were divided into 6-s bin intervals, resulting in a total of 30 readings post-task. Previous studies compared the NITM values between myopes and emmetropes at the bin-interval of 10 and 30 s post task (Vera-Diaz, Strang and Winn 2002; Hazel, Strang and Vera-Diaz 2003). Since we used a 6 s bin interval, NITM between emmetropic and myopic children were compared at the first 6 s and 24 s post-task. As the accommodation responses post-task were measured at the interval of 2 s, NITM was obtained by the difference between the average of the first 3 distance refraction measures taken after reading (the first 6 s post-task) and the average pre-task refraction. Regression times were expressed in terms of the time taken (seconds) for the post-task refraction to first reach the average pre-task refraction (Schmid, Hilmer, Lawrence et al. 2005). Regression time was determined as the point where the plot of average refraction data from each refractive error group for each condition hit a horizontal line representing the pre-task refraction value against time. The NITM of some subjects in certain near tasks lingered beyond the 3 min post task period. The regression time for such cases was considered as the next 6-bin s, i.e. 186 s. The accommodative responses for the 2 refractive groups at initial post task time point at 6-s bin intervals were also analyzed.

Analysis of variance using the general linear model was performed to determine the significance of the results with refractive error group as the between-subject factor and type of text (English and Chinese) and reading distances as within-subject variables. The effect of type of text and reading distance on NITM magnitude and regression time and accommodation accuracy between the two refractive groups were analyzed. The effect of the 8 min reading duration on accommodation accuracy was also determined.

5.3 Results

There were significant effects of text type and reading distance on accommodation accuracy during reading but not on the degree or duration of NITM. Accommodation accuracy was similar for emmetropic and myopic children during the reading tasks, but both the magnitude and regression time of NITM were greater in myopes than emmetropes.

5.3.1 Accommodation Accuracy

The types of text read had a significant effect on accommodation accuracy when data from all subjects were pooled (irrespectively of their refractive error) over the entire 8 min of the near task ($F_{1,1230} = 7.24$, P = 0.007). Reading Chinese materials resulted in greater accommodation accuracy than reading English text (accommodative lags of -0.97 D vs. -1.00 D) (Table 5.1). Although the difference was statistically significant (Figure 5.2), the effect was too small to be clinically significant and therefore may not have any consequence in influencing the accommodation accuracy.

Table 5.1 Effect of text type and reading distance on accommodation responses averaged across all subjects (mean ± SD)

		33 cm		25 cm	
	Time into reading (min)	Chinese	English	Chinese	English
Accommodation Lags (D)	Average of entire 8 min	-1.00 ± 0.29	-1.01 ± 0.31	-0.94 ± 0.36	-1.00 ± 0.42
NITM (D)	First 6 s post-task	0.11 ± 0.21	0.11 ± 0.18	0.12 ± 0.23	0.11 ± 0.24
	First 24 s post-task	0.05 ± 0.20	0.02 ± 0.19	0.03 ± 0.20	0.02 ± 0.22
Regression Time (s)	When NITM returned to pre-task level	58.0 ± 60	67.2 ± 62	75.6 ± 68	67.1 ± 69

Accommodation lags reduced with reading Chinese text and at shorter reading distance of 25 cm than 33 cm. Type of text and reading distance, however, did not have any significant effect on the magnitude of NITM and its regression time.

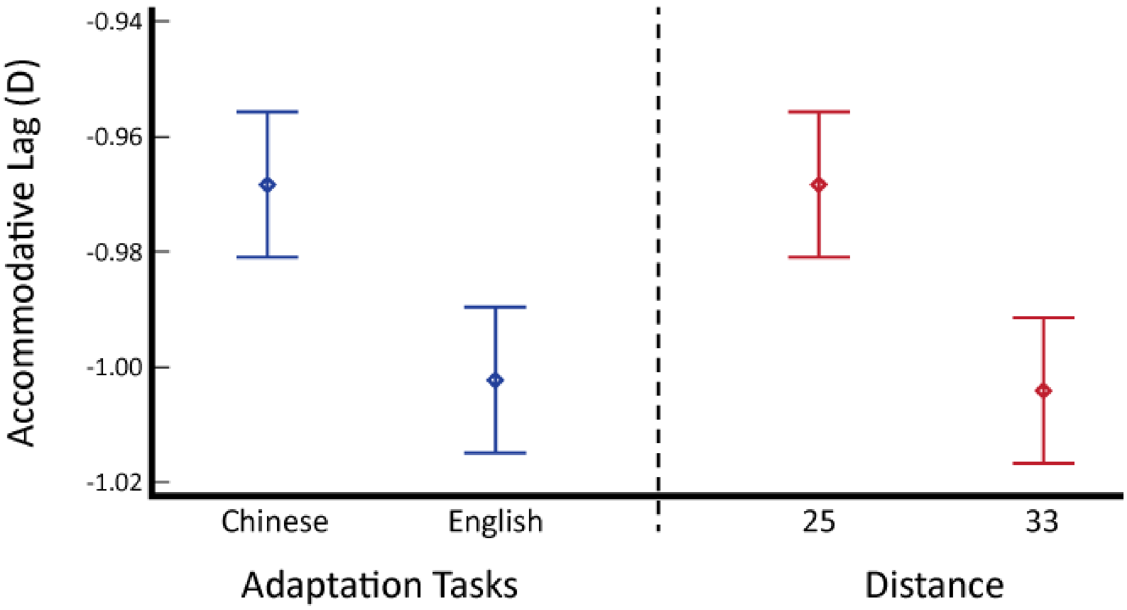


Figure 5.2 Text type and reading distance showed significant effect on accommodative lag. Reading English text showed significant increase in accommodative lag than reading Chinese text. Greater lag of accommodation was measured when reading at 33 cm than at 25 cm. Error bars show LSD 95% confidence intervals.

Reading distance also affected the accommodative lags significantly ($F_{1,1230} = 7.74$, $P = 0.005$) (Figure 5.2) accommodative lags were greater for the 33 cm distance (accommodative lag of 1.01 D at 33 cm versus 0.97 D at 25 cm). Again, the effect was deemed too small to be clinically significant and therefore may not have any consequence in influencing the accommodation accuracy.

As has been shown previously for children from other ethnic groups (Mutti, Mitchell, Hayes et al. 2006) and now here for Chinese children, the children under-accommodated at near i.e. had lags of accommodation. Lag of accommodation reduced as reading time increased ($F_{3,\ 1230} = 4.59$, $P = 0.003$) from 1.01 D at 2 min to 0.95 D at 8 min. The significant difference in accommodative lags occurred between the 2nd and 8th min reading time and 4th and 8th min reading time (Figure 5.3).

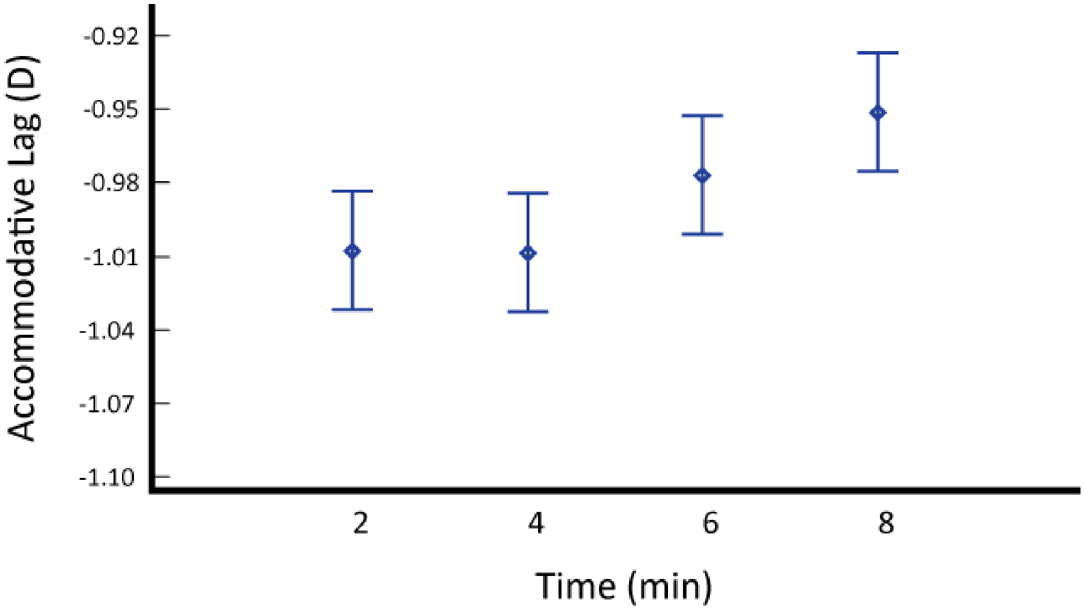


Figure 5.3 Significant differences in accommodative lag were observed between the 2nd and 8th reading times and between the 4th and 8th reading time. Error bars indicate the Bonferroni corrected 95% confidence intervals.

When data were analyzed with refractive error group included as the between subject factor in analysis of variance, the significant effect of text type and reading distance on accommodation accuracy were still observed (text: $F_{1,1216} = 7.02$, $P = 0.008$; dist: $F_{1,1216}$

= 7.09, P = 0.008). There was no significant difference in accommodation accuracy between emmetropic and progressing myopic children ($F_{1, 81} = 0.51$, P = 0.475) (Figure 5.4). The average accommodation lags across both text type and distances for emmetropes and progressing myopes were -0.96 ± 0.35 D and -1.01 ± 0.33 D, respectively, over the 8 min (Table 5.2). The interaction between refractive error group and reading distance was significant ($F_{1, 1216} = 12.69$, $P < 0.001$), and post-hoc analysis showed that reading distance had an effect on accommodative accuracy for the myopes only (Figure 5.5).

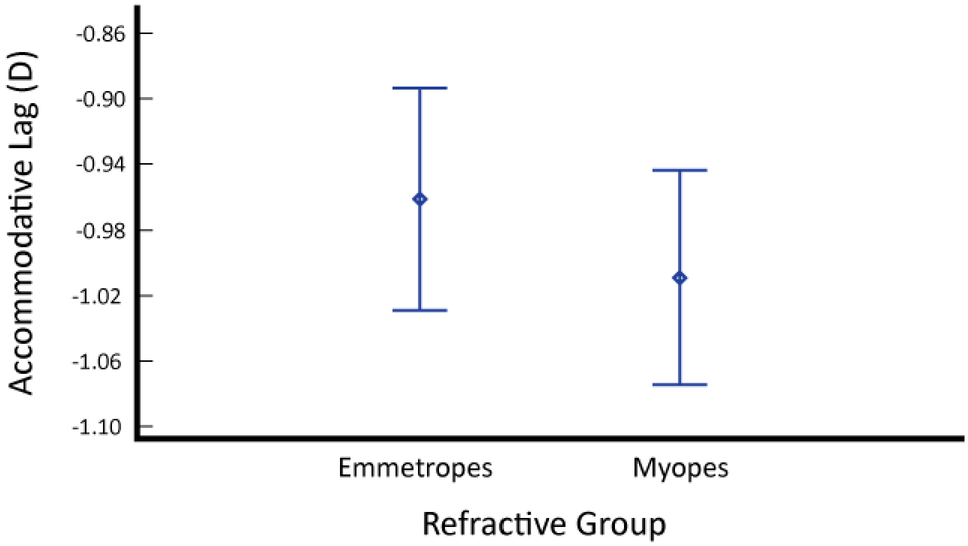


Figure 5.4 There was no statistical significant difference in accommodative lag in myopes and emmetropes. Error bars show LSD 95% confidence intervals.

Table 5.2 Effect of refractive error on accommodation responses (mean ± SD)

	33 cm		25 cm		Significance (P)
	Emmetropes	Myopes	Emmetropes	Myopes	
Accommodation Lags (D)	-0.96 ± 0.31	-1.05 ± 0.28	-0.97 ± 0.40	-0.97 ± 0.38	0.475
NITM (D) (6 s)	0.09 ± 0.22	0.14 ± 0.17	0.07 ± 0.21	0.16 ± 0.24	0.027
NITM (D) (24 s)	-0.01 ± 0.21	0.08 ± 0.17	0.00 ± 0.21	0.06 ± 0.21	0.006
Regression Time (s)	36.5 ± 47	87.0 ± 64	46.9 ± 60	94.1 ± 68	< 0.001

There were no significant difference in accommodation lags, but there were significant differences in magnitude and regression time in both emmetropic and myopic children.

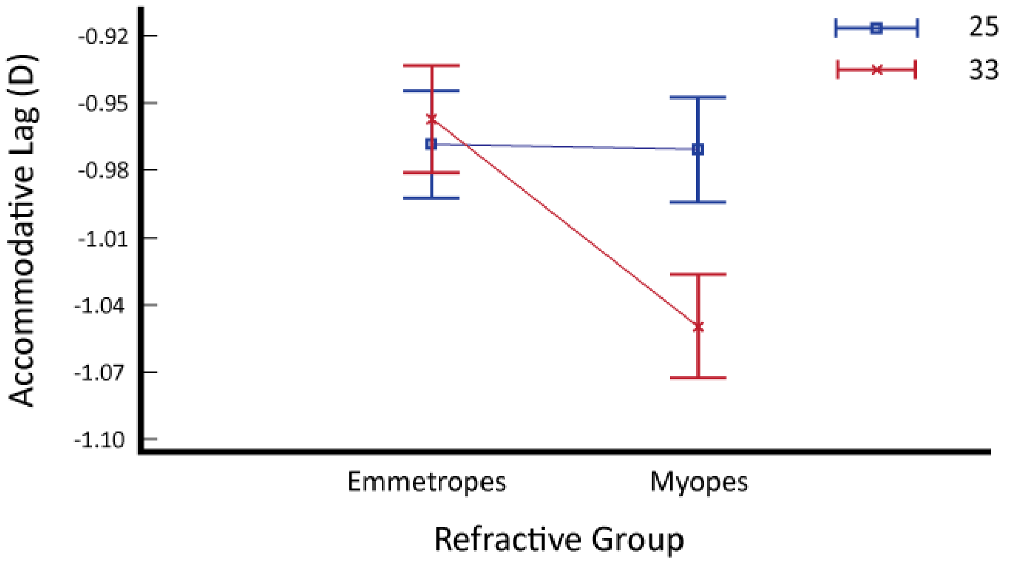


Figure 5.5 The interaction between refractive error group and distance was significant. Reading distance showed significant effect on accommodative accuracy in myopes only. Error bars indicate the 95% confidence intervals.

5.3.2 Near Work–Induced Transient Myopia and Its Regression Time

When data of all subjects were pooled, both text type and distance did not have significant effects on the magnitude of NITM (text: $F_{1,164} = 0.05$, $P = 0.824$; dist: $F_{1,164} = 0.00$, $P = 0.988$) (Figure 5.6) nor regression time (text: $F_{1,246} = 0.00$, $P = 0.954$; dist: $F_{1,246} = 2.06$, $P = 0.152$) (Figure 5.7).

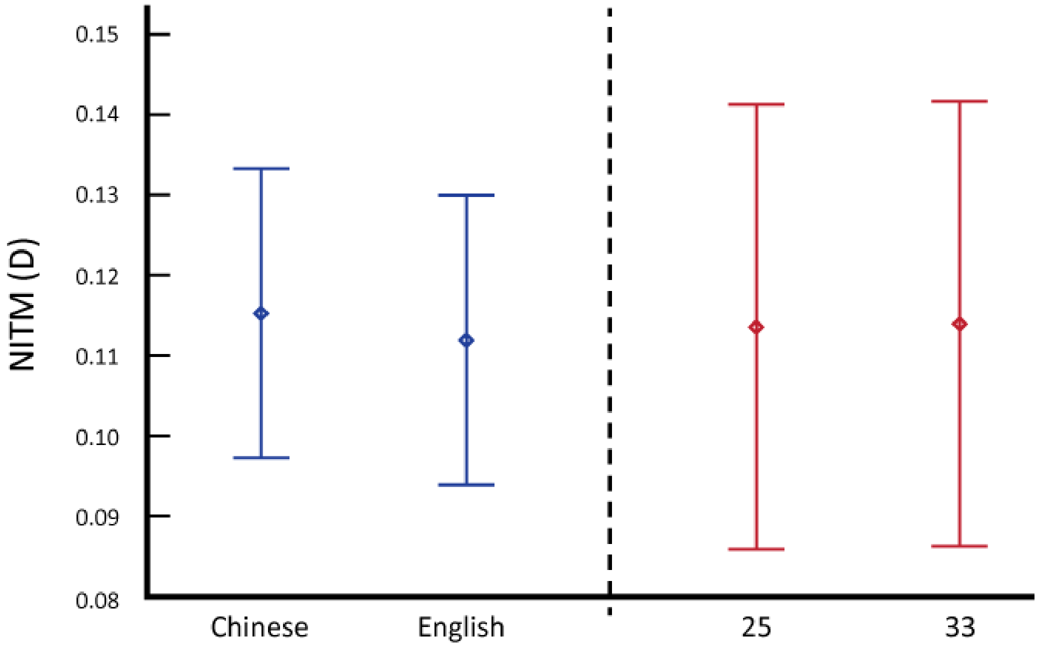


Figure 5.6 Text type and distance did not show any significant effect on the magnitude of NITM. Error bars show LSD 95% confidence intervals.

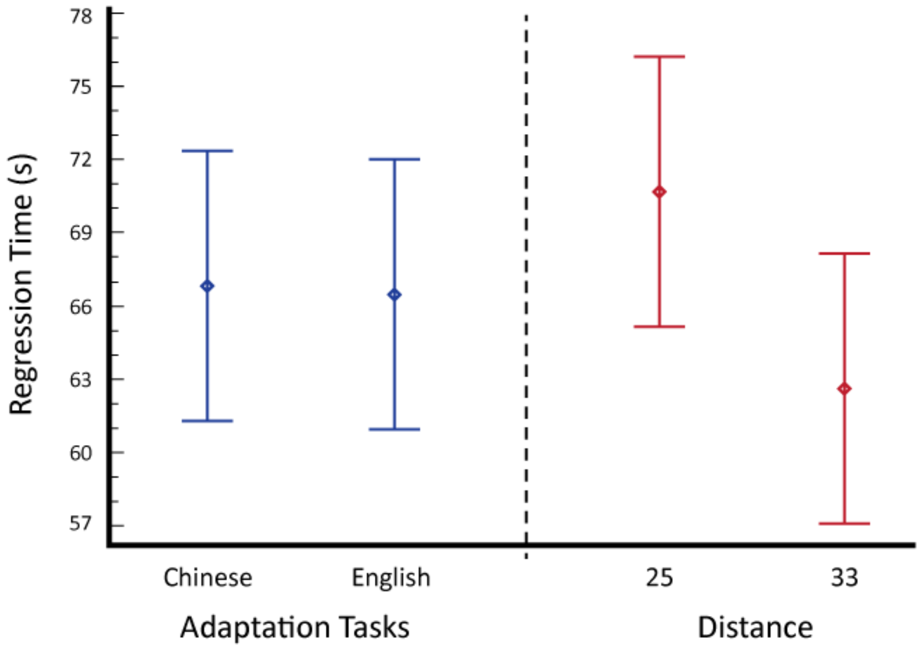


Figure 5.7 Both text type and distance did not show any significant effect on the regression time of NITM. Error bars show LSD 95% confidence intervals.

When data were analyzed with refractive error group included as the between subject factor, both text type and distance showed no significant effects on the magnitude of NITM (text: $F_{1,243} = 0.03$, $P = 0.874$; dist: $F_{1,243} = 0.00$, $P = 0.956$) nor regression time of NITM (text: $F_{1,243} = 0.00$, $P = 0.968$; dist: $F_{1,243} = 2.07$, $P = 0.151$). However, refractive error group affected significantly both the magnitude of NITM ($F_{1,81} = 5.05$, $P = 0.027$) and regression time ($F_{1,81} = 31.08$, $P < 0.001$); myopes had greater NITM (0.07 D) and this took longer (50 s) to dissipate (Figures 5.8 and 5.9).

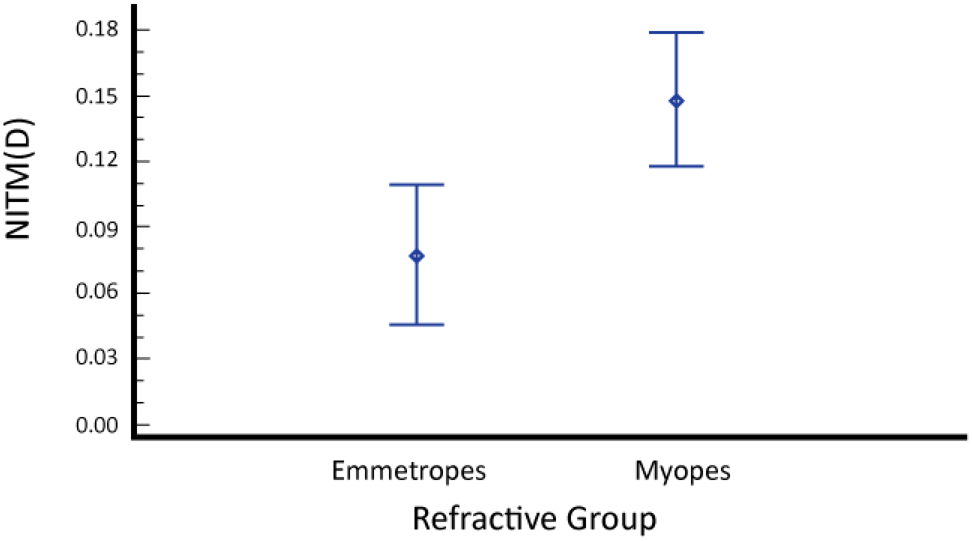


Figure 5.8 Myopic children showed significantly greater NITM magnitude than emmetropic children. Error bars show LSD 95% confidence intervals.

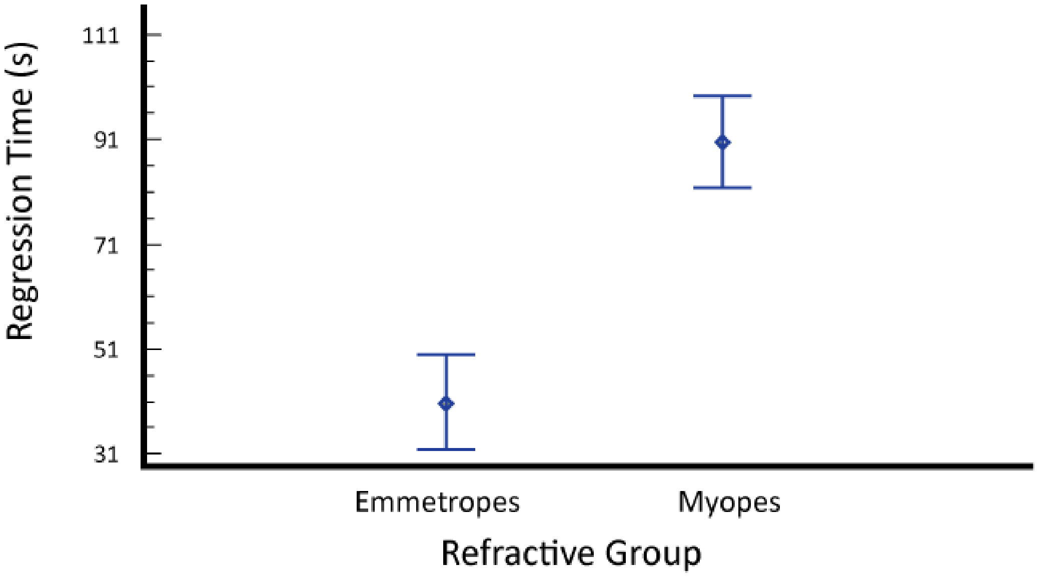


Figure 5.9 Myopic children showed significantly longer NITM regression time than emmetropic children. Error bars show LSD 95% confidence intervals.

Myopic children showed significantly larger NITM than emmetropic children at the first 6 s ($F_{1, 81}$ =5.05, P = 0.027) and 24 s ($F_{1, 81}$ = 7.92, P = 0.006) post task. At 24 s post task, the NITM induced by emmetropic children fell beyond the baseline of 0 D, but the NITM of myopic children stayed at a mean level of 0.07 D above their baseline 24 s after the near task (Table 5.2). About 20% of the myopic children had NITM regression times longer than the 3 min post task compared to only 8% of the emmetropic children. The NITM magnitude and regression times of the emmetropic and myopic children in four reading conditions are presented in Figures 5.10 and 5.11, respectively.

The mean accommodative responses during distance viewing before the task for emmetropic and myopic children were 0.19 D lag and 0.09 D lead, respectively. This shows that myopic children accommodated 0.28 D more at distance than the emmetropic children even before the near task.

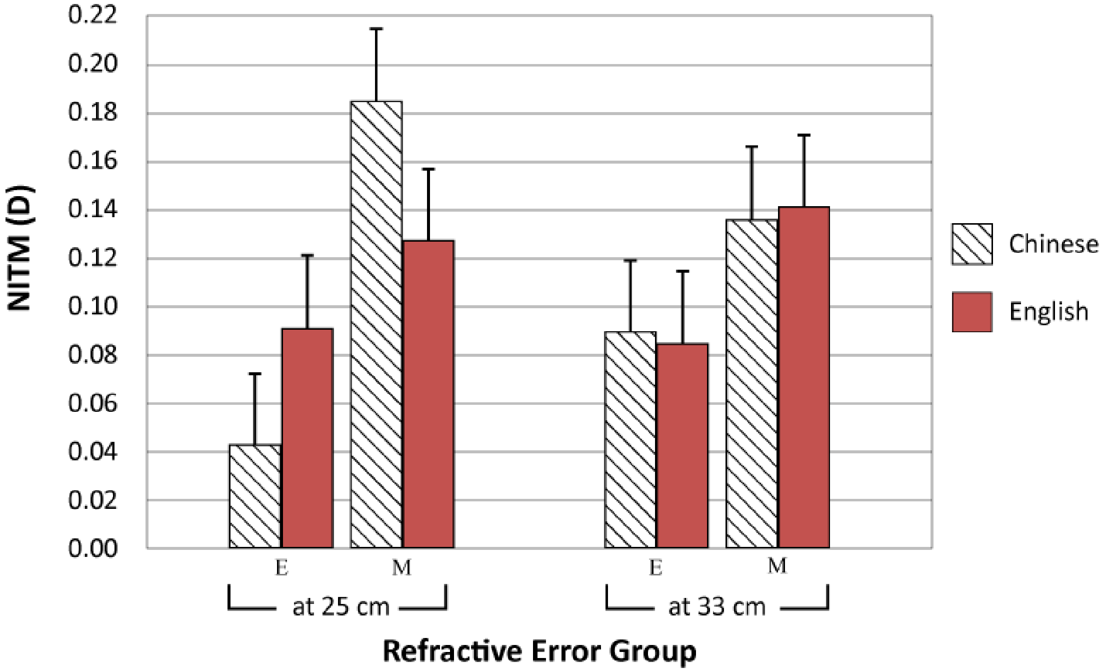


Figure 5.10 Effect of reading text on the magnitude of NITM at 25 and 33 cm reading distance. Error bars show LSD 95% confidence intervals.
E – Emmetropic children M – Myopic children

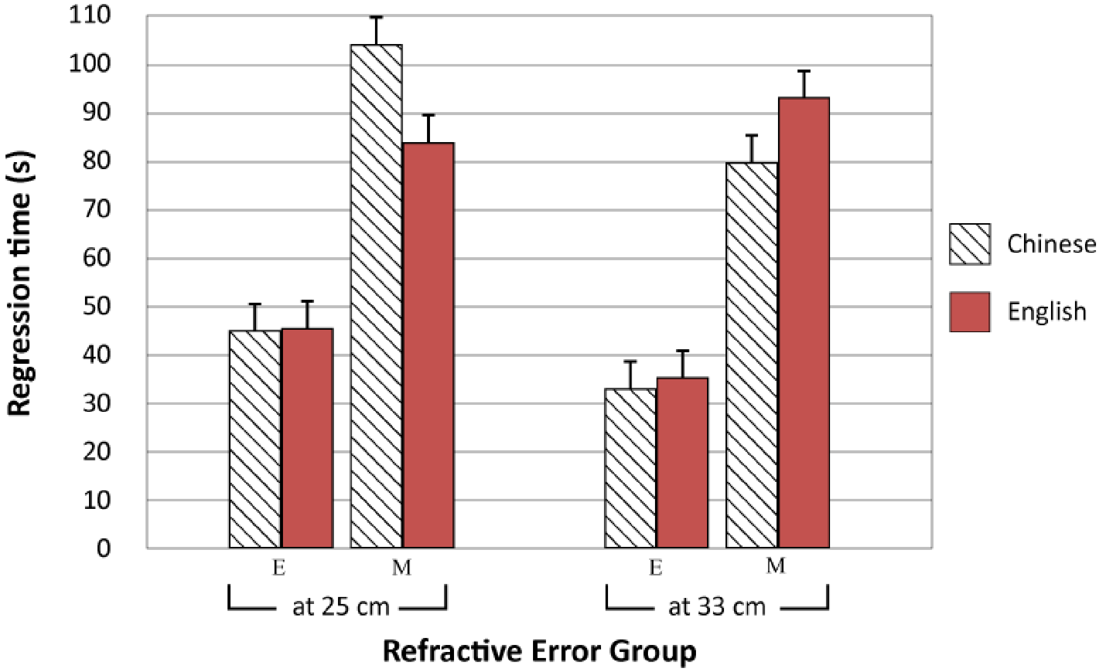


Figure 5.11 Effect of reading text on regression time at reading distance of 25 and 33 cm. Error bars show LSD 95% confidence intervals.
E – Emmetropic children M – Myopic children

5.4 Discussion

The accommodative accuracy and NITM magnitude and its duration were investigated and compared between reading Chinese and English texts in a group of Singaporean Chinese children. Reading Chinese text and changing reading distance significantly affected accommodation accuracy but not NITM magnitude or regression times. However, the effects of these significant findings were too small and may have no consequence to the accommodative accuracy.

Myopic children presented with greater magnitude of NITM and longer dissipation time than emmetropic children. as other studies have found (Ciuffreda and Thunyalukul 1999; Wolffsohn, Gilmartin, Li et al. 2003). This study has further confirmed findings from previous studies that myopes consistently show higher NITM and longer regression time than emmetropes (Ciuffreda and Wallis 1998; Vera-Diaz, Strang and Winn 2002; Schmid, Hilmer, Lawrence et al. 2005). However, unlike other studies (McBrien and Millodot 1986b; Gwiazda, Thorn, Bauer et al. 1993b), we found refractive error has minimal effect on accommodative accuracy. The effect of the data on accommodative accuracy and NITM is discussed separately below when considering their roles in myopia development.

5.4.1 Accommodative Accuracy

Reading Chinese text increased accommodation accuracy more than reading English text. This effect, however, was so small that it is not clinically significant. Table 1.3 shows the values of accommodative leads and lags in 3 studies. The value ranges from 0.1 D to 3.50 D across different studies. These values are affected by age and probably race of subjects, method of measures and the amount of accommodative stimulus. There are probably other factors which may affect the accommodation responses of a person at near, thus the accommodation accuracy. Gwiazda et al (1993b) described that the small but real difference of 0.40 accommodative lag in the myopic children may reflect the inability of myopic eyes to use blur cues for accommodation.

This slight difference could be due to the different input units (letters vs. characters) between English and Chinese, different mapping functions and different processing between letters and characters of both English and Chinese text (Prefetti, Liu and Tan 2002). The square shape of the logography in the Chinese text which requires an elaborated analysis of the spatial information and locations of the various strokes comprising the logographic character may involve a greater scrutiny of the characters which leads to a higher accommodation exerted.

Additional brain areas not often observed in processing English alphabets were observed in the processing of Chinese characters. For example, the left middle frontal gyrus is found activated in Chinese character reading, but rarely in alphabetic reading (Tan, Liu, Perfretti et al. 2001; Tan, Laird, Li et al. 2005). The additional activation of the brain areas found in these studies may result in an increase in neural transmission in processing Chinese characters, and thus lead to the differences in accommodation exerted between reading Chinese and English text.

Reading distance has an effect on accommodative accuracy, but again the effect was minimal. Reading distance of 33 cm induced higher accommodative lags than at 25 cm. This was unexpected as accommodative lags usually increased with accommodative demand. The increase in accommodative lag was also observed when duration of reading increased. This was consistent throughout the near task even though it became significantly different only at the 8th min into the reading task.

Previous studies have found some inconsistency between reading distance and significance of accommodative accuracy of different refractive error groups (Gwiazda, Thorn, Bauer et al. 1993b; Abbott, Schmid and Strang 1998; Yeo, Kang and Tang 2006). This could be due to considerable differences in methodology. The current study agreed with some of the previous findings that when accommodation was stimulated with changing target distance, the difference in accommodative lag between refractive groups was not significant (Abbott, Schmid and Strang 1998; Wolffsohn, Gilmartin, Li et al. 2003; Schmid, Hilmer, Lawrence et al. 2005; Yeo, Kang and Tang 2006). However, two of the above studies found reduced accommodation response in myopic subjects when accommodation was stimulated by minus lenses (Abbott, Schmid and Strang 1998; Yeo, Kang and Tang 2006). The reason could be that proximal cues in the changing target distance condition may have improved the accommodation responses of the myopes, reducing the difference in response between different refractive error groups (Chen, Schmid and Brown 2003).

Others found significantly different accommodative responses between myopes and emmetropes when accommodation was stimulated by changing reading distances from 25 to 20 cm (McBrien and Millodot 1986b) and from 33 to 25 cm (Gwiazda, Thorn, Bauer et al. 1993b). The differences between the McBrien and Millodot study and the current study are (i) the subjects in McBrien and Millodot study were young adults, (ii) they categorized myopia into EOM and LOM, and (iii) besides the two groups of myopic subjects, hyperopes and emmetropes were included in their study. What differentiates the current study from Gwiazda's study is that one eye was occluded in Gwiazda's subjects throughout the experiment. It has been found that the accommodative lag for each target was significantly smaller in myopes under binocular than in monocular viewing (Nakatsuka, Hasebe, Nonaka et al. 2003).

The reduced accommodation errors measured in binocular viewing condition was thought to be due to the constriction of the pupils which leads to reduced higher-order aberrations (Buehren and Collins 2006). The major contributor to higher-order aberrations is spherical aberration which shows the most systematic change with accommodation (Atchison, Collins, Wildsoet et al. 1995; Hazel, Cox and Strang 2003; Buehren and Collins 2006). With increasing accommodation levels, spherical aberration shifts from positive to negative, affecting the accommodation responses of different refractive error group measured by autorefractors.

However, the generally acceptable belief is that if the accommodative accuracy is not maintained during prolonged near work, the lag of accommodation may increase, and the resulting hyperopic retinal defocus may lead to myopia (Gwiazda, Thorn, Bauer et al. 1993b; Abbott, Schmid and Strang 1998). While some studies have observed a greater lag of accommodation in emmetropic children prior to them becoming myopic (Goss 1991; Portello, Rosenfield and O'Dwyer 1997), the others found lag of accommodation accompanies the development of myopia rather than precedes it (Mutti, Mitchell, Moeschberger et al. 2002b; Zadnik, Mitchell, Jones et al. 2004).

5.4.2 Near Work–Induced Transient Myopia

The magnitude and regression time of NITM were not affected by type of text and distance of near task. This could be due to both having similar text size. NITM was greater and decay longer for larger letters than smaller letters (Schmid, Hilmer, Lawrence et al. 2005). In the current study, both text types had letter size subtended at 1.0 cpd spatial frequency in row heights at 33 cm. Whether reading English or Chinese text, both are considered low cognitive demand tasks compared with doing arithmetic sums (Rosenfield and Ciuffreda 1994).

NITM magnitude and regression time were not affected by reading distances. This finding supports a previous study that found no significant reduction in NITM magnitude after doing near task at 20 cm and 40 cm (Wolffsohn, Gilmartin, Li et al. 2003). The influence of reading distance on NITM was relatively small because the primary determinant of NITM was blur-driven accommodation and that contribution from disparity and proximity were minimal under closed-loop viewing conditions (Ong, Ciuffreda and Rosenfield 1994).

Even though the magnitude of NITM measured in the current study was small, emmetropic subjects displayed about 0.07 D of NITM and myopes about 0.15 D, the results have not diminished the link between NITM and myopia development. NITM magnitude, measured in other studies, has ranged from 0.11 to 1.30 D and its duration from 30 s, for relatively short task durations, to as much as a few hours for longer near task durations (Ong and Ciuffreda 1995). The magnitudes measured in closed-loop conditions are usually small, so individual remain asymptomatic and blur-free. However, the magnitude of NITM was found to be additive over time (Vasudevan and Ciuffreda 2008) and therefore, a magnitude as small as 0.1 D after 10 min performing a near task could be suggestive of a greater degree of NITM after a longer near work period.

Ehrlich explained that the fatigue of accommodation system occurred after prolonged near work resulted in an increased innervation (due to increased accommodative convergence) which causes an increased pre-task accommodation, thus resulting in an increase in the near lags and distance leads among the myopes (Ehrlich 1987). Our results showed that NITM of myopic children was significantly higher than NITM of emmetropic children and the myopic children accommodated 0.28 D more than emmetropic children even at pre-task level. Thus NITM induces retinal image defocus, when cumulative over time, may play a role in myopia development.

The accommodation system receives dual innervation from the autonomic nervous system. It is thought that the sympathetic division, with its known slow or adaptive system in a time course of 10 to 40 s and its generally small magnitude with inhibitory (i.e. negative accommodation) in nature, may play an important role in accommodative adaptation and NITM (Gilmartin and Bullimore 1987; Gilmartin, Bullimore, Rosenfield et al. 1991). A deficit in sympathetic input leads to enhanced accommodative adaptation effects and a prolonged period of regression because of an un-antagonized parasympathetic tone [reviewed by Chen, Schmid and Brown (2003)]. Many studies hypothesized that a susceptibility to accommodative hysteresis leads to cumulative retinal defocus from enhanced transient pseudo-myopic changes in the distance refraction thus triggers an increase in axial length (Ehrlich 1987; Ciuffreda and Wallis 1998; Ciuffreda and Vasudevan 2008; Ciuffreda and Vasudevan 2010).

However, there are others who believe that myopes could exhibit an overall reduction of both sympathetic and parasympathetic innervation (Jiang 1995; Ong and Ciuffreda 1997; Woung, Lue and Shih 1998; Chen, Schmid and Brown 2003). This is because the level of sympathetic activation is positively correlated with the level of parasympathetic activity, with a decrease in the latter leading to decrease of the former (Ciuffreda and Vasudevan 2008). Unfortunately, some of these studies were not able to draw conclusive findings due to the complexity of the pharmacological events occurring at the autonomic neuro-effectors (Gilmartin and Winfield 1995; Chen, Schmid and Brown 2005). Moreover, the ß-adrenoceptor antagonism used in the studies may indeed have some differential effects with regard to the ciliary smooth muscle or other structures in the vicinity such as ciliary processes, choroidal and retinal vasculature and the central nervous system which may have indirect effect on accommodation response (Owens, Winn, Gilmartin et al. 1991). This makes the study of autonomic system on the control of accommodative adaptation difficult. Hence, the origin of NITM is still not known.

A recent study found axial length increases following prolonged near task of 30 min at 5 D accommodation in a group of young adults (Woodman, Read, Collins et al. 2010). This elongation persists for a short period of time after near work but returned to baseline level after 10 min. The authors suggest that larger amounts of near work, performed at closer distances might potentially be expected to lead to prolonged short-term eye length changes of greater magnitude that could potentially predispose a patient to greater amounts of eye elongation in the longer term (Woodman, Read, Collins et al. 2010).

5.4.3 The Rate of Regression

As mentioned, the NITM of some subjects in certain near tasks lingered on beyond the 3 min post task period. This was also observed in a previous study that involved children (Wolffsohn, Gilmartin, Li et al. 2003), where NITM was still evident 3 min after viewing a 5.0 D near task for 5 min (with reading duration shorter than the current study). Even a short reading time of 5 min could induce NITM that lasts beyond 3 min. If NITM is a function of task duration as believed (Ong and Ciuffreda 1995), then task duration and the time course of NITM decay support the notion that repeated occurrences of transient myopia lead to permanent myopia (Ong and Ciuffreda 1995).

In a recent study when NITM was measured after the 1st hr of reading and measured again after the 2nd hr of reading, it was found that progressing myopes showed an increase time constant for decay compared to stable myopes (Vasudevan and Ciuffreda 2008). Progressing myopes, but not stable myopes also exhibited additivity of NITM. The same study also found that EOM exhibited prolonged decay of NITM compared to the emmetropes and the LOM. About 60% of their myopic subjects did not experience decay to baseline over 120 s post task period. The finding of the current study is in agreement with the previous finding that myopic children showed significantly longer regression time (by 50 s) than emmetropic children. About 43% of the myopic children showed regression time ≥ 120 s post task compared to only 15% of the emmetropic children.

Therefore, myopes showed sustained NITM over a longer period post task than emmetropes. Furthermore, in a previous study, myopic shift (up to 1.50 D) can lead to prolonged decay and increased patient symptoms on a small group of symptomatic subjects (Ciuffreda and Ordonez 1995). This amount of myopic shift was not observed in the current study because there was no symptomatic subject in the current study. However, Individual susceptibility and genetic predisposition may play an important role in the adaptation effect of near work, hence the susceptibility of an individual in developing myopia.

The majority of the previous studies used near task distance of 20 cm with task durations lasting from 10 to 20 min. These produce small magnitudes of NITM that rapidly dissipate and are not significantly above baseline within the initial 30-50 s post-task interval (Rosenfield, Ciuffreda and Novogrodsky 1992). Therefore, the rate of regression obtained in the current study is similar to that in other studies.

5.4.4 Comparison Between Current and Other Similar Studies

The study shows that myopic children in Singapore have NITM which is greater than that of their emmetropic peers. The magnitude of NITM in this study was less than other reports (Ciuffreda and Wallis 1998; Vera-Diaz, Strang and Winn 2002; Wolffsohn, Gilmartin, Li et al. 2003). The difference in the results obtained could be due to differences in the nature and size of near tasks administered and the testing distance of NITM. In the previous studies, subjects were instructed to look at numbers and performed simple arithmetic operations with the numbers of size 0.00 log MAR (Wolffsohn, Gilmartin, Li et al. 2003) or 6/9 equivalent target (Vera-Diaz, Strang and Winn 2002; Ciuffreda and Vasudevan 2008) throughout the duration of the task. In the current study, the size of the targets were equivalent to N12 point, which is the print size commonly used in real life reading materials such as books and newspapers, which become 0.8 log MAR at 25 cm and 0.7 log MAR at 33 cm respectively.

The cognitive demand in performing arithmetic operations with numbers is probably stronger than reading text such as English and Chinese stories. Moreover, reading involves active eye movement from left to right and that might have caused some dissipation of accommodation induced during the active process. When the subjects fixated back to the word of interest for measurement, some of the NITM could have been lost. In previous studies, subjects fixated the numbers without active eye movement. Furthermore, in the study of Wolffsohn, the left eye was occluded during measurement. In the current experiment, all the measurements were taken when subjects were viewing the appropriate targets binocularly.

Since only spherical contact lenses were used to correct the refractive errors of both emmetropes and myopes, how individual children responded accommodatively to small uncorrected amounts of astigmatism might have impacted on the results. Astigmatic errors averaged 0.12 D in emmetropes and 0.26 D in myopes. The SER was the sphere plus half the cylinder, if subjects chose to accommodate to the central blur circle then there would be no effect on the data, if subjects chose to accommodate to the meridian with the most myopic power this might produce an extra lead of 0.14 D in myopes than in emmetropes. If subjects chose to accommodate to the meridian with the most hyperopic power this would produce an extra of 0.14 D lag in myopes than emmetropes. However most commonly uncorrected astigmatism produced fluctuations in accommodation between the two meridians and this would average to the best sphere reading over a number of measurements. We believe our testing conditions are close to the real, habitual environment in which the children are exposed to, where low astigmatic errors are not corrected.

5.4.5 Model of Adaptation

Increase in NITM, coupled with a higher accommodative lead at distance and slightly higher accommodative lag at near, were observed in the myopic children whose myopia was progressing. Although there was no significant difference in lag of accommodation at near task between emmetropic and myopic children in this study, we cannot rule out the possible role of accommodation accuracy in myopia progression. The accommodative lag was observed to decrease as reading time increased in the current study. It appears that if near focus is sustained over time, accommodative adaptation sets in to re-adjust the accommodation accuracy so as to reduce the residual accommodative error to a small extent over time (Ciuffreda and Wallis 1998) (this could be the reason why lags of accommodation reduced significantly as reading time increased and accommodative lags were no different between emmetropes and myopes). When subsequently focusing at far, there would also be a transiently increased accommodative error (NITM), especially in more susceptible people such as myopes that would act as another source of retinal defocus. This amount, even though small in magnitude, with accumulation over time could become significant in causing a higher accommodative lead when the eye is looking at distance objects. Hence, with the cumulative effect due to adaptation, that small magnitude will accumulate to create a larger lead of accommodation at distance, which over time may become a permanent fixture. Therefore, the transient increase in retinal defocus (with hyperopic defocus at near and myopic defocus at distance) as a result of accommodative adaptation - time-integrated and cumulative over months or even years in people performing considerable amounts of near work - could be myopigenic in nature.

An adaptation model of NITM was proposed to link NITM with myopia development (Hung and Ciuffreda 1999b). The model was based on animal studies that have found retinal image blur to be an important cue for regulating eye growth (Schaeffel, Troilo, Wallman et al. 1990). In the model, if the adaptation component is large, the time constant for the accommodative controller would be increased. This means the decay of NITM towards the pre-task baseline would be delayed. Over the long term, there are typically alternating periods of prolonged near work and brief distance viewing, which is representative of our everyday activities. Under this condition, both under-accommodation at near (lag of accommodation) and over-accommodation at far (lead of accommodation) typically occur (Ciuffreda and Wallis 1998). The accommodation lead or lags are the accommodative error, which becomes a useful measure of long-term effect of the resultant retinal defocus of an individual.

In addition, another hypothesis on the influence of the autonomic nervous system on myopia suggested that myopes have weak sympathetic or strong parasympathetic innervation, which would tend to reduce the attainable range of response in the sympathetic region of the response curve. This would adversely affect vision of more distant objects, rendering the subject relatively myopic (Charman 1982). By reviewing the studies on accommodation and drugs affecting the autonomic system, there is reasonable evidence that inhibition to sympathetic nervous system results in a greater magnitude and longer regression time in accommodative adaptation (Gilmartin, Bullimore, Rosenfield et al. 1992; Chen, Schmid and Brown 2003). However, significant inter-subject variations in response to the β-adrenergic antagonist timolol (Gilmartin, Mallen and Wolffsohn 2002) and inability to demonstrate any sympathetic inhibitory of accommodative control in closed-loop accommodation (Mallen, Gilmartin and Wolffsohn 2005) may hamper the progress of more research in this area.

5.5 Conclusion

Reading Chinese text resulted in a smaller accommodative lag than reading English text (difference of 0.03 D), but the effect was too small to be considered clinically important. Different text type also did not have any significant effect on the magnitude and regression time of NITM in different refractive groups. Therefore, reading Chinese text is unlikely to be the cause of greater accommodation inaccuracy and greater near work-induced adaptation that would exacerbate myopia development. Myopic children presented with significantly greater magnitude of NITM and longer regression time than emmetropic children.

CHAPTER 6

CONCLUSION AND SUMMARY

6.1 Summary of Major Findings

Given the reported association between near work and myopia (Rosenfield 1998), two near adaptations, contrast and accommodation were studied in emmetropic and myopic individuals in a country with high myopia prevalence (Singapore). The findings of the research are consistent with the fact that near work is associated with myopia development and these effects are likely to be induced regardless of the type of text read.

As has been observed previously for grating stimuli in adult observers (Blakemore and Campbell 1969; Blakemore, Nachmias and Sutton 1970; Blakemore, Muncey and Ridley 1973), we observed contrast adaptation in response to reading material in children – although of lesser magnitude than observed for grating stimuli in Experiment 1. In this experiment, the myopia of all the children was progressing and thus a sub-analysis based on whether the myopia was stable or not could not be made. Results of this experiment supported the hypothesis that myopic children show significantly greater contrast adaptation effects than emmetropic children. The degree of adaptation was greater in myopic versus emmetropic children at all tested spatial frequencies (0.5, 1.2, 2.7, 4.4 and 6.2 cpd); the difference between the refractive error groups was greatest at 4.4 cpd. The peak of the contrast sensitivity function in children of 6 to 9 years of age is between 2 to 4 cpd (Bradley and Freeman 1982; Gwiazda, Bauer, Thorn et al. 1997; Ellemberg, Lewis, Liu et al. 1999; Adams and Courage 2002). Since the greatest difference in contrast adaptation between emmetropic and myopic children was at 4.4 cpd, we suggest that spatial frequencies around this value are likely to be particularly important for the emmetropization system.

In Experiment 2, it was demonstrated in young adult subjects that the magnitude of contrast adaptation induced by Chinese text was similar to that induced by English text. This finding did not support the hypothesis that Chinese text induces greater contrast adaptation effects than English text. However, as in the first experiment on children, the myopic young adults showed greater reductions in contrast sensitivity after reading than emmetropic young adults, but of a smaller magnitude than that obtained in Experiment 1 for children. Here both the age of the participants and their myopia progression status differed. The reason for a greater adaptation effect in children could be that children have a stronger neural plasticity than young adults. The neural plasticity is discussed at 6.3.

Results of Experiment 3 showed that there were significant effects of text type and reading distance on accommodation accuracy during reading but the magnitude of the differences were too small to be of any clinical importance. Both text type and distance did not have any significant effects on the magnitude and regression time of NITM. The findings did not support the hypothesis that NITM induced by reading Chinese text is higher than that induced by reading English text. However, refractive error group affected both the magnitude and regression time of NITM significantly with myopic children having greater NITM by 0.07 D and longer regression by 50 s than emmetropic children.

6.2 Adaptation to Different Text Types

There was no significant difference in the effects of reading Chinese and English text in terms of contrast and accommodation adaptation (Figure 6.1). This suggests that the two visual tasks are similar. We have discussed in Chapters 4 and 5 that the visual word processing between the two text types is probably similar, although the written Chinese words are logographic. We have also discussed that stroke frequency may not represent the Chinese text well as sides strokes of the words are often ignored if they do not cross the horizontal midline. Moreover, different articles chosen for the near task may have different frequency of complicated characters, which would also affect the stroke frequency calculated on a page. In the contrast adaptation studies, subjects did not read the stories aloud. In the accommodation adaptation study, subjects were required to read the stories aloud and were told to skip the words that they did not know how to pronounce. In both cases, it was impossible to determine if the subjects understood what they read from the story. Investigations with fMRI (functional magnetic resonance imaging) suggest that, although brain activations during reading aloud of Chinese characters are bi-lateralized (Tan, Liu, Perfretti et al. 2001), silent reading of Chinese is dominated by the activity of the left hemisphere (Chee, Caplan, Soon et al. 1999). In conclusion, our research helps to establish that reading Chinese text will not lead to greater contrast and accommodation adaptation (Figure 6.1).

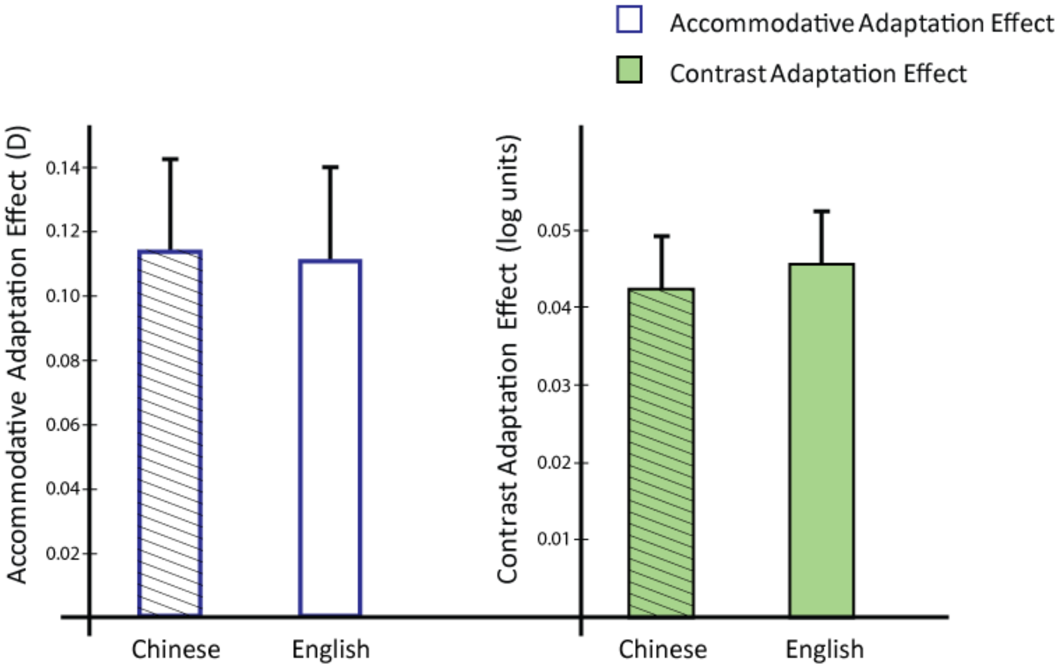


Figure 6.1 Adaptation Effects of Chinese and English are similar in both the accommodative and contrast adaptations. Error bars show LSD 95% confidence intervals.

6.3 Neural Plasticity

Combining the data from Experiments 1 and 2, the analysis of variance showed that progressing child myopes from Experiment 1 had significantly greater contrast adaptation than stable young adult myopes from Experiment 2 ($F_{1,57} = 4.47$, $p = 0.039$) (shown on the right of Figure 6.2). The significant difference in contrast adaptation effect was not observed in the emmetropic groups between children and young adults ($F_{1,57} = 2.93$, $p = 0.093$) (on the left of Figure 6.2). The two contrasting results in emmetropic and myopic subjects demonstrate that the increased in contrast adaptation in myopes is due to progression in refractive error and not an “age effect”.

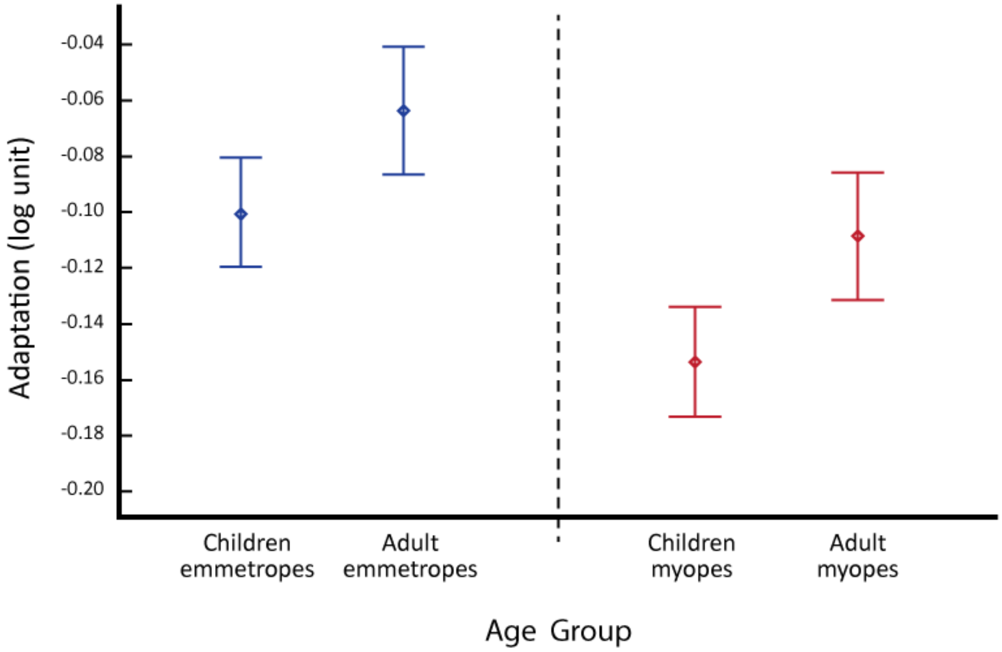


Figure 6.2 Contrast adaptations showed significant difference in progressing child myopes from Experiment 1 and stable young adult myopes from Experiment 2 (on the right), but not in emmetropic children and emmetropic young adults (on the left). Error bars show LSD 95% confidence intervals.

The adaptation effects observed in progressing (child) myopes is greater than stable (adult) myopes. This may reflect the underlying greater neural plasticity at younger versus older ages (Wiesel 1981). Neural plasticity refers to the response properties of neurons that can be shaped by an animal's or a person's perceptual experience (Goldstein 2007). This process is part of what makes humans so able to adapt to a broad range of circumstances, so that the physiology of the brain changes in response to a given set of conditions.

Furthermore, there is a critical period in terms of ocular and visual development between eye opening and puberty (Wiesel and Hubel 1963; Wiesel 1981) during which the visual system is susceptible to growth changes due to environmental impacts. For example, there is permanent vision loss if congenital cataracts are not removed till adulthood, but the loss is not evident if cataracts developing during adult life are not removed for many years. Thus, reading induced adaptations could lead to myopia when reading activity is started at a young age. In Singapore and other Asian countries, children start reading as young as 3 years of age. At young ages such as this emmetropization processes are strongest and thus the propensity for myopia development greatest.

Further evidence for age related differences in susceptibility to environmental impacts comes from animal studies (Sclar, Ohzawa and Freeman 1985). When contrast adaptation effects were assessed both qualitatively and quantitatively, the effects were greater for kittens than for adult cats, and greater for 4-week old kittens than for those aged 6 weeks. This suggests that susceptibility to adaptation varies as a function of age or the time course of this change may be similar to that of the 'critical period' for the effects of visual deprivation. The degree to which the cells in a kitten's visual cortex are susceptible to the effects of an adapting stimulus decreases during development (Sclar, Ohzawa and Freeman 1985). Based on the review of this type of data, Wallman and Winawer (2004) speculated that the age at which reading starts may be important in terms of its impact on refractive development.

One difficulty in comparing the contrast sensitivity of children and young adults is the known effect of age on contrast sensitivity performance and measurement (Mantyjarvi, Autere, Silvennoinen et al. 1989; Scharre, Cotter, Block et al. 1990; Gwiazda, Bauer, Thorn et al. 1997; Ellemberg, Lewis, Liu et al. 1999; Adams and Courage 2002). Consistent with past findings (Scharre, Cotter, Block et al. 1990; Ellemberg, Lewis, Liu et al. 1999), here the age of the children was found to affect contrast sensitivity; increasing age was associated with greater contrast sensitivity, i.e. better performance, for all spatial frequencies tested. The reduction of contrast sensitivity function in younger children could be due to less well-developed retinal and neural mechanisms (Scharre, Cotter, Block et al. 1990; Ellemberg, Lewis, Liu et al. 1999) or possibly an artifact of the measurements (Scharre, Cotter, Block et al. 1990).

Besides the visual factors, there are nonvisual factors such as the child's attention and understanding of the test may affect the measurement of contrast sensitivity in young children. Atkinson, French and Braddick (1981) observed in their experiment that for children (age 3-5 yr) to recognise their own state of sensory uncertainty and to make the best guess is too sophisticated for them. Children who perform confidently on easy discriminations often appear to abandon any attempt to make a visual discrimination when the task becomes difficult and instead adopt some 'strategy' or rule of behavior unrelated to the stimulus presented, such as always choosing the same side or regularly alternating between sides. Fortunately in the current study, all the children were 5 years of age or older and thus more able to make the required decisions. Furthermore, the coefficient of variation obtained in the study shown in Table 2.2 is consistent across the spatial frequencies for both children and young adults. Although comparison of data between children and adults may be affected by different maturity level, this does not impact on the contrast adapation effect since the measurements were obtained from the difference in contrast sensitivity before and after reading for each individual.

6.4 Contrast Adaptation Myopia Inducing Effects

The reduced contrast sensitivity that occurs after prolonged reading may give rise to a low level of form deprivation that lingers over several hours. Rose and Evans (1983) observed that it took 90 min for the adaptation effect to recover to baseline level after a

20 min adaptation period and Blakemore and co-workers report a dissipation time of several hours following 30 min adaptation (Blakemore, Nachmias and Sutton 1970). Therefore the contrast adaptation effect may persist in prolonged reading.

Since 2-3 min exposure to optical defocus is sufficient to induce changes in eye growth in animal studies (Zhu, Park, Winawer et al. 2005; Zhu and Wallman 2009), the contrast adaptation effect associated with reading of up to 1 hour (which is not uncommon) could be highly detrimental, particularly if the reading activity is not interspersed with a different activity. If a child's reading duration is longer than the period of distant viewing, there is probably no chance for the adaptation effect to dissipate completely. It is this lingering effect of adaptation which results in the perception of chronically degraded retinal image that may promote myopia development.

Relevant neurons have been observed to fire less during contrast adaptation (Maffei, Fiorentini and Bisti 1973; Albrecht, Farrar and Hamilton 1984; Ohzawa, Sclar and Freeman 1985; Abbonizio, Langley and Clifford 2002) and thus reading induced contrast adaptation is likely to give rise to reduced retinal activities. The reduced retinal activities may stimulate eye growth in a similar way that diffusers result in form deprivation myopia in animal models. We speculate that the reduced retinal activity alters the retinal signaling cascade initially at the level of the bipolar or amacrine cells [this is where the contrast adaptation originates from the retina (Baccus and Meister 2002)]. This then alters the release of neuro-transmitters or neuro-modulators that diffuse through the choroid to the sclera stimulating the growth of the eye.

Possible neurotransmitters or neuromodulators involved in the contrast adaptation effect are glutamate and dopamine. It has been reported that slow contrast adaptation results from reduced glutamate release from the presynaptic bipolar cells (Manookin and Demb 2006); glutamate is the neurotransmitter of the neurons of the vertical pathways through the retina (Massey 1990; Marc, Murry and Basinger 1995). Dopamine is a global modulator of retinal function and it is thought to be the key chemical messenger for retinal luminance adaptation (Witkovsky 2004). Currently, we are not able to find a direct link between light adaptation and contrast adaptation. However, it has been reported that dopamine interferes with the excitatory and inhibitory transmission at the postsynaptic site in striatal neurons (Mercuri, Bernardi, Calabresi et al. 1985) and that dopaminergic modulated ganglion cells to some extent could produce the network (inter-neurons and retinal ganglion cells) adaptation (Vaquero, Pignatelli, Partida et al. 2001). Reduced dopamine levels have been observed in form deprivation myopia (Stone, Lin, Laties et al. 1989; Megaw, Morgan and Boelen 1997).

We speculate that since the adaptation was not specific to row and stroke frequencies, it is probably broadly tuned and mediated by the magnocellular (M) pathway (Solomon, Peirce, Dhruv et al. 2004). M cells are on average 8 to 10 times more sensitive than parvocellular (P) cells to contrast (Kaplan and Shapley 1986). When contrast adaptation in M cells, P cells and in neurons that received input from S-cones in the lateral geniculate nucleus of the macaque were investigated, a reduction in contrast sensitivity after exposure to a moving grating with high contrast was found in M cells, but was absent in P cells (Solomon, Peirce, Dhruv et al. 2004). An earlier study observed that moving stimuli may stimulate the magnocellular pathway whereas a stationary grating stimulates the parvocellular pathway (Kaplan and Shapley 1982). Even though there were no moving stimuli in the current experiment, the eye's focus moved across the page when reading, thus creating an effect of moving stimuli in the subjects' field of view.

We have observed that increased contrast adaptation in myopes is due to progression in refractive error and is not an age effect (see 6.3). This suggests that contrast adaptation is associated with the cause rather than being a consequence of myopia. However, the determining factor for myopia development is still hinged on the genetic makeup and individual susceptibility to temporal integration of vision-dependent eye growth.

6.5 Accommodative Adaptation Myopia Inducing Effects

Our results showed that accommodative adaptation or NITM of myopic children was significantly higher in magnitude than NITM of emmetropic children at both 6 s and 24 s post-task. The regression time of NITM was also more prolonged in myopic children than emmetropic children. Both higher magnitude and longer regression time are thought to be associated with myopia development or progression [reviewed in (Ong and Ciuffreda 1995)]. In animal studies, however, myopic defocus produces a compensatory eye growth which results in hyperopia in chicks (Schaeffel, Glasser and Howland 1988; Irving, Sivak and Callender 1992), tree shrews (McBrien, Gentle and Cottriall 1999) and monkeys (Smith and Hung 1999). These studies predicted that myopic defocus would inhibit and not promote myopia development. However, two clinical trials in human myopes involving purposeful under-correction of 0.5 to 0.75 D which created increased myopic defocus at far found that under-correction resulted in increased myopic progression relative to full correction of myopia (Chung, Mohidin and O'Leary 2002; Alder and Millodot 2006). In these studies, the researchers question the validity of applying the results of animal studies to humans (Alder and Millodot 2006) and suggested that presence of blurred vision at any distance may stimulate the progression of myopia regardless of the sign of defocus in eyes which are susceptible (Chung, Mohidin and O'Leary 2002).

The prolonged effect of NITM has been observed in myopic children previously (Wolffsohn, Gilmartin, Li et al. 2003) and in the current study; NITM was still evident 3 min after viewing at 3 D and 4 D near task for 5 min. If NITM is a function of task duration as believed (Ong and Ciuffreda 1995), then task duration and the time course of NITM decay support the notion that repeated occurrences of transient myopia eventually lead to permanent myopia (Ong and Ciuffreda 1995).

The non-decay of NITM acts like an addition of a low-powered plus lens that creates myopic defocus, which reduce the image quality of distant objects. With repeated cycles of near-far-near work over an extended period (days or months), this residual NITM persisted after brief distance viewing. This persistent myopic shift could become more permanent if it is not dissipated away quickly when near work is continuously performed, thus may play a role in the aetiology of permanent myopia (Ong and Ciuffreda 1995; Ciuffreda and Vasudevan 2008). This is especially true for progressing myopes, who were found to exhibit additivity of NITM (Vasudevan and Ciuffreda 2008).

In their recent review, Ciuffreda and Vasudevan (2010) proposed that since the myopic eye has more peripheral hyperopic defocus than emmetropic eyes, the small myopic defocus (about 0.25 D) at the fovea interacts with the peripheral hyperopic defocus (about 0.75 D) to create retinal defocus which results in axial eye growth. Of course, more studies need to be conducted in order to ascertain the claim, but we believe that myopic defocus induced by NITM may play a role in myopia development.

6.6 Critical Nature of Temporal Integration

The time-integrated or temporal integration property of vision-dependent eye growth in animals is not linear (Kee, Hung, Qiao et al. 2007). The non-linear time integrated property has been demonstrated in animal studies. In form deprived chicks (Napper, Brennan, Barrington et al. 1995; Napper, Brennan, Barrington et al. 1997), monkeys (Smith, Hung, Kee et al. 2002) and negative lens-reared chicks (Schmid and Wildsoet 1996) and tree shrews (Shaikh, Siegward and Norton 1999), the degree of relative myopia decreases exponentially with increasing durations of the daily period of unrestricted vision. In all species, a daily 1-hour period of unrestricted vision reduces the amount of myopia by at least 50% compared with animals that experienced continuous form deprivation or hyperopic defocus. Here, we believe the reverse may be true so that intermittent blur and defocus induced by contrast and accommodative adaptation after prolonged near work (if not dissipated quick enough) may induce retinal image degradation and result in myopia development. In the animal studies, there is a high degree of variability which reflects individual differences in the integration properties of the emmetropization process or the sensitivity of the process to defocus, with some variability reflect individual differences in visual experience (Kee, Hung, Qiao et al. 2007). As such, an individual's sensitivity to the intermittent blur and defocus after reading and variability in the time integration emmetropization process may determine if he/she will develop myopia.

The non-linearity property in time integrated vision dependent eye growth would greatly constrain the effects of visual experience on the development of myopia. This may explain why it has been so difficult to establish a quantitative relationship between visual experience and the degree of myopia, at least on an individual basis (Kee, Hung, Qiao et al. 2007). For example, when quantifying near work, some studies used diopter hour and some used number of books read per week. Such measures do not take into consideration the manner in which different types of visual experience are integrated over time, which resulted in these studies finding no association between near work and myopia (Zadnik, Santariano, Mutti et al. 1994; Mutti, Mitchell, Moeschberger et al. 2002a; Saw, Zhang, Hong et al. 2002). These measures are commonly used to quantify near work but the element of time integration is missing. It is however, challenging to include the time integration factor because there are many variables to individual susceptibility in myopia development.

Wallman and Winawer (2004) have argued that the way in which one reads may be an important factor in determining whether near work promotes the development of myopia. We propose that the duration of reading without intermittent vision breaks on distant objects is probably an important factor because near adaptation during reading allows visual information to provide slow signals suited for control of eye growth to take place. This proposal agrees with the recent findings that outdoor activities seem to have a protective effect on myopia development (Rose, Morgan, Ip et al. 2008). The authors hypothesize that the increased light intensity of outdoor environment constrict the pupils and result in a greater depth of field and less image blur. Based on this hypothesis, we speculate that outdoors allows contrast of low spatial frequency objects to be detected much easier than indoors due to the higher light intensity, thus allowing a quicker return of the loss of contrast after prolonged reading. Although accommodative adaptation may not return quickly to normal, the clear image perceived is able to negate the retinal image degradation, thus preventing myopia from developing. A recent study has shown evidence that the cumulative effect of NITM can be prevented by short rest periods of 5 min in between near tasks (Arunthavaraja, Vasudevan and Ciuffreda 2010). An alternative hypothesis was put forward by Rose et al (2008) that release of dopamine from the retina is known to be stimulated by light, and dopamine can act as an inhibitor of eye growth (McCarthy, Megawa, Devadas et al. 2007).

6.7 Contrast and Accommodative Adaptation Ocular Mechanisms

Although both contrast and accommodative adaptations are near adaptation processes activated during near work, we are unsure whether they are two separate mechanisms or they are related and influence each other. Regression analysis was performed on the average values of accommodation and contrast adaptations at each spatial frequency for the data of 15 children who participated in both the contrast and accommodative adaptations experiments. There was no statistical significant relationship between contrast and accommodative adaptations (Table 6.1). This could be due to the small sample being analyzed in the study.

Table 6.1 Regression analysis between contrast and accommodation adaptations of 15 children

	Spatial frequency (cpd)				
	0.5	1.2	2.7	4.4	6.2
R^2	0.063	0.082	0.023	0.172	0.020
P values	0.366	0.301	0.586	0.124	0.612

Although contrast and accommodative adaptations did not show significant relationships, they could play important roles in myopia development. From Experiment 1, we found that text induced contrast adaptation reduces contrast perceived at low spatial frequencies up to about 6 cpd. The most prominent reduction in contrast sensitivity was found at 2.7 cpd for all children but the difference in contrast sensitivity between emmetropic and myopic children was highest at 4.4 cpd.

One of the possible outcomes could be that myopes with a greater contrast adaptation than emmetropes may be oblivious to the blur (due to loss of contrast sensitivity) because of the higher blur tolerance of myopes than emmetropes as has been found in previous studies (Rosenfield and Abraham-Cohen 1999; George and Rosenfield 2004). Therefore, myopes who do a lot of near work such as reading may not be aware that there is blur in the text during or intermittently throughout the near task. Wallman and Winawer (2004) speculated that blur adaptation may lead to a reduced need for accurate accommodation, with the greater hyperopic blur from the resultant large lag of accommodation. However, there was no significant difference in lag of accommodation between myopic and emmetropic children in our study.

Instead, our results showed greater magnitude and longer decay time of NITM in myopic than emmetropic children after reading. This leads us to believe that the blur experienced with the greater loss of contrast after reading in myopes has resulted in a greater innervation of accommodation, thus inducing a greater magnitude of NITM and prolonging the regression time in myopic compared to emmetropic children. This is in agreement with the findings that myopes showed a significant increase in the near accommodative response after 3 min of blur adaptation, while the accommodation to near target in emmetropes did not change (Vera-Diaz, Gwiazda, Thorn et al. 2004).

With the findings that prolonged reading leads to reduced contrast sensitivity at low to mid spatial frequencies, the other possible outcome is that contrast adaptation could lead to a greater accommodation adaptation at these frequencies. This is in agreement with the findings that steady-state accommodation is most responsive for intermediate spatial frequencies (3-5 cpd) of sinusoidal gratings (Owens 1980). However, Charman and Tucker (1977) found that accuracy of accommodation for sinusoidal gratings increases monotonically as a function of spatial frequency. The difference in the findings may be due to a significant difference in the instructions. In Charman and Tucker's study, observers were instructed to always try to obtain “best possible” focus, but in Owen’s study, observers were frequently reminded to view the gratings “naturally, without straining the eye”. Since contrast sensitivity affected most after reading occurred at around 3 – 5 cpd, it is possible that the contrast adaptations would further exacerbate accommodation adaptation, thus increase the NITM measured at near (Chapter 5), which have been implicated in myopia development.

On the other hand, one may argue that the measured reduction in contrast sensitivity could be explained by accommodative inaccuracy as the subject moved between the two different fixation distances of the adaptation stimuli and contrast sensitivity testing task. The adapting task was at the closer distance (2.5 D), and the test stimuli at the further distance (1 D); if the subjects stayed accommodated at near for a protracted time this would produce myopic defocus on the contrast sensitivity test pattern (at most 1.5 D if the subject did not relax focus at all). This degree of defocus (1.50 D myopic defocus) has been shown to reduce contrast sensitivity by more than 1 log unit (Woods, Strang and Atchison 2000). However, the accommodation response time required to change from 2.5 to 1 D is typically 0.25 to 0.30 s (Kasthurirangan, Vilupuru and Glasser 2003; Seidel, Gray and Heron 2003; Kasthurirangan and Glasser 2005) and no difference was observed between emmetropes and myopes (Schaeffel, Wilhelm and Zrenner 1993; Seidel, Gray and Heron 2005; Strang, Day, Gray et al. 2011). The relaxation time could be critical and this would be longer in the myopic children. The current investigations were not able to tell which mechanism alters first, whether it was contrast adaptation or accommodative inaccuracy. Therefore, both contrast and accommodation adaptations may augment or complement each other in the process of myopia development.

In summary, time-integrated retinal defocus could be augmented by both contrast and accommodative adaptations, which linger on in the visual system of susceptible individuals. It has been speculated that long-term, time-integrated increased retinal defocus of small amounts without regard to directional information would be sufficient to induce modest amounts of axial elongation, thereby resulting in low degrees of axial-based permanent myopia and/or in myopic progression (Ong and Ciuffreda 1995; Ong and Ciuffreda 1997; Chung, Mohidin and O'Leary 2002; Alder and Millodot 2006). In contrast adaptation, the perceived retinal image degradation induced is probably similar to that of an occluder in form deprivation, while in accommodative adaptation, it is like adding a low plus lens (myopic retinal defocus) which affects the image qualities. In both cases of adaptations, the magnitudes were small but if induced over a period of time through prolonged reading activity, may lead to myopia development.

A model combining accommodative and contrast adaptations in the inducing of myopia is proposed here (Figure 6.3). Reading induces contrast adaptation, which reduces the contrast sensitivity of the visual system and decreases retinal activity. This leads to decreased contrast at low to mid spatial frequencies from 0.5 to 6.2 cpd, in particular, the spatial frequency of 4.4 cpd. The reduction of perceived contrast of objects at these spatial frequencies result in reduced retinal activity, thus changing the retinal signal cascade and leading to decreased neurotransmitters or neuromodulators and axial elongation.

In addition the contrast adaptation induced decreased sensitivity to defocus will exacerbate the accommodation errors. This will lead to increased accommodative adaptation, hence increase defocus induced by NITM by increasing its magnitude and regression time. This increase will trigger another change in the retinal signal cascade and eventual axial elongation. Having said that, the determining factor for myopia development is still dependent on the genetic makeup and individual susceptibility to temporal integration of vision-dependent eye growth.

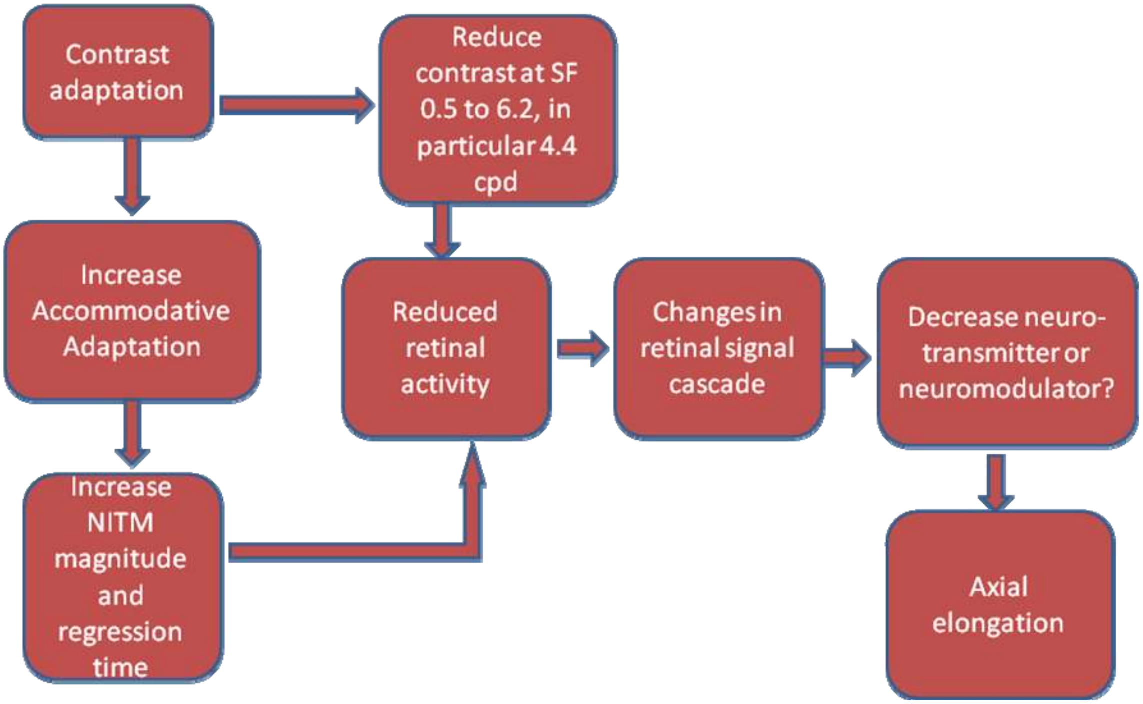


Figure 6.3 A model of contrast and accommodative adaptations inducing myopia.

Much has been discussed with regards to a combination of contrast adaptation, accommodative inaccuracy, and the duration of such effects likely in driving the process of myopia development. It would also be possible that these phenomena occur as a result of myopia development and progression. Due to the nature of the experimental design, we acknowledge that this thesis is not best placed to comment on cause and effect in the matter of myopia initiation. A protracted longitudinal study on very large groups of emmetropic children, some who go on to develop myopia and some who remain emmetropic, is the way to determine this.

6.8 Future Research

Future studies may consider investigating both contrast and accommodation adaptations together. The current experiment was limited by the display of the LCD monitor in displaying a wide range of contrasts compared to the CRT monitor. Therefore, contrast sensitivity function can only be measured using the bulky CRT monitor which is not portable and cannot be incorporated into a tablet form. With the advancement of LCD monitors in which a wider range of video bits can be displayed with better resolution, the contrast sensitivity test and the adapting tasks can be displayed on the same monitor of a tablet. The tablet can be placed in front of the open-field autorefractor, just like the apparatus set up in Experiment 3. Contrast adaptation can be measured with the adapt-test-readapt paradigm while NITM can be obtained at the end of the adaptation task. This experimental arrangement will also ensure that there is little loss of contrast adaptation as there is no need for subjects to swivel 90° between the adaptation task and contrast test.

The precise mechanisms by which retinal defocus lead to changes in the neuro-chemicals that are involved in eye growth are not known. It may involve cascades of neuro-chemical actions, or even parallel or local feedback processes (Hung, Fiedler and Ciuffreda 2010). Neuromodulators such as dopamine, serotonin and neuro-peptides act over long periods of time to modulate the cellular processes in the retina. Animal studies have demonstrated that changes in neuromodulator release cause predicted alterations in the structure of the sclera via modulation of proteoglycan synthesis (Troilo, Nickla, Mertz et al. 2006), thus causing a change in sclera growth rate. In contrast adaptation, we speculate that the perceived retinal defocus induced by reading could trigger a signaling cascade that begins in the bipolar or amacrine cells with the release of neuro-transmitters or neuro-modulators through the choroid to the sclera resulting in growth of axial length. In future, sophisticated equipment may be able to detect concentration of neurotransmitters or neuromodulators in a human being through brain signals or through skin contacts. With these non-invasive techniques, the concentration of neurotransmitter substances such as dopamine and glutamate can be determined during contrast adaptation.

An adaptive model of near work-induced transient myopia was proposed by Hung and Ciuffreda (1999a). The model includes both neuro-adaptive and biomechanical factors. For example, individuals may have a genetic predisposition to greater adaptive response during near viewing, resulting in transient over-accommodation at distance. This is seen as a slower accommodative decay of NITM that can eventually lead to an excess of cumulative, time-integrated retinal defocus (Hung and Ciuffreda 1999a). Future research could look into producing a similar model for contrast adaptation where it can be tested with simulation. This model should also take into account the theory proposed that eye growth is governed by the genetically programmed growth which provides information for directional modulation of growth rate and environmental programmed growth which is due to change in retinal defocus.

Other future studies have been discussed in Chapter 3 such as investigating contrast adaptation at the peripheral retinal locations and determine the signs of defocus of contrast adaptation. Other suggestions are to investigate the recovery time of contrast adaptation induced by reading in emmetropes and myopes, and to investigate the effect of contrast adaptation on higher spatial frequencies such as 10, 20 and 30 cpd.

6.9 Clinical Significance

Our research established that reading high contrast text can induce similar contrast adaptation effects as occurs for looking at high contrast gratings. Reading induced contrast adaptation effect is greater in myopes than emmetropes and thus could be associated with the development or progression of myopia. Accommodative adaptation was found to have a higher magnitude and longer regression time in myopic than emmetropic children. Our study also established that reading Chinese text will not lead to greater contrast and accommodative adaptations than reading English text. Reading Chinese text is likely no more myopigenic than reading English text and thus this does not account for the high myopia prevalence in countries where Chinese language is widely used.

In order to prevent strong contrast adaptation, the hard copy displays of text could be adjusted so that the blank space between character lines is larger than the size of the displayed characters. This approach could modify the duty cycle of the overall text display to reduce the spectral power of the fundamental of a single-spaced text display (Lunn and Banks 1986). Changing the duty cycle of a text display by varying the font characteristic might diminish the adaptation effects associated with periodic display patterns.

We propose that the duration of reading without intermittent vision breaks spent looking at distant objects is an important factor in myopia development because near adaptation during reading allows integration of retinal error signals on a slow time-scale to allow axial elongation to take place. Therefore, children should be encouraged to take intermittent vision breaks in between their reading activities to allow contrast and accommodation adaptation effects to dissipate. The vision breaks help to break the persistence in adaptation effects, thus reducing the retinal error signals and reducing myopia from developing.

References

Abbonizio, G., K. Langley and C. W. Clifford (2002). "Contrast adaptation may enhance contrast discrimination." *Spatial Vision* **16**: 45-58.

Abbott, M. L., K. L. Schmid and N. C. Strang (1998). "Differences in the accommodation stimulus response curves of adult myopes and emmetropes." *Ophthalmic and Physiological Optics* **18**(1): 13-20.

Abromov, I., L. Hainline, J. Turkel, et al. (1984). "Rocket-ship psychophysics: assessing visual functioning in young children." *Investigative Ophthalmology and Visual Science* **25**: 1307-1315.

Adams, A. J. and N. A. McBrien (1993). "A longitudinal study of the relationship between tonic accommodation (dark focus) and refractive error in adulthood." *Investigative Ophthalmology and Visual Science* **34 (ARVO Suppl)**: S1308.

Adams, R. J. and M. L. Courage (2002). "Using a single test to measure human contrast sensitivity from early childhood to maturity." *Vision Research* **42**: 1205-1210.

Adams, R. J., S. M. Dalton, A. M. Murphy, et al. (2002). "Testing young infants with the Welch Allyn Suresight non-cycloplegic autorefractor." *Ophthalmic and Physiological Optics* **22**(6): 546-551.

Albrecht, D. G., S. B. Farrar and D. B. Hamilton (1984). "Spatial contrast adaptation characteristics of neurones recorded in the cat's visual cortex." *Journal of Physiology* **347**: 713-739.

Alder, D. and M. Millodot (2006). "The possible effect of undercorrection on myopic progression in children." *Clinical and Experimental Optometry* **89**: 315-321.

Allen, P. A., B. Wallance and T. A. Weber (1995). "Influence of case type, word frequency, and exposure duration on visual word recognition." *Journal of Experimental Psychology: Human Perception and Performance* **21**(4): 914-934.

Arunthavaraja, M., B. Vasudevan and K. J. Ciuffreda (2010). "Nearwork-induced transient myopia (NITM) following marked and sustained, but interrupted, accommodation at near." *Ophthalmic and Physiological Optics* **30**: 766-775.

Atchison, D. A., M. J. Collins, C. F. Wildsoet, et al. (1995). "Measurement of monochromatic ocular aberrations of human eyes as a function of accommodation by the Howland Aberroscope Technique." *Vision Research* **35**(3): 313-323.

Atkinson, J., J. French and O. Braddick (1981). "Contrast sensitivity function of preschool children." *British Journal of Ophthalmology* **65**: 525-529.

Baccus, S. A. and M. Meister (2002). "Fast and slow contrast adaptation in retinal circuitry." *Neuron* **36**: 909-919.

Baccus, S. A. and M. Meister (2004). "Retina versus cortex: contrast adaptation in parallel visual pathways." *Neuron* **42**: 5-7.

Baker, R., B. Brown and L. Carney (1983). "Time course and variability of dark focus." *Investigative Ophthalmology and Visual Science* **24**: 1528-1531.

Bao, M., L. Yang, C. Rios, et al. (2010). "Perceptual learning increases the strength of the earliest signals in visual cortex." *The Journal of Neuroscience* **30**(45): 15080-15084.

Barlow, H. B., D. I. A. Macleod and A. V. Meeteren (1976). "Adaptation to gratings: no compensatory advantages found." *Vision Research* **16**: 1043-1045.

Bartmann, M. and F. Schaeffel (1994). "A simple mechanism for emmetropization without cues from accommodation or colour." *Vision Research* **34**(7): 873-876.

Bartmann, M., F. Schaeffel, G. Hagel, et al. (1994). "Constant light affects retinal dopamine levels and blocks deprivation myopia." *Visual Neuroscience* **11**: 199-208.

Beazley, L. D., D. J. Illingworth, A. Jahn, et al. (1980). "Contrast sensitivity in children and adults." *British Journal of Ophthalmology* **64**: 863-866.

Benardete, E. A., E. Kaplan and B. W. Knight (1992). "Contrast gain control in the primate retina: P cells are not X-like, some M cells are." *Visual Neuroscience* **8**: 483-486.

Bitzer, M. and F. Schaeffel (2002). "Defocus-induced changes in ZENK expression in the chicken retina." *Investigative Ophthalmology and Visual Science* **43**(1): 246-252.

Blakemore, C. and F. W. Campbell (1969). "On the existence of neurones in the human visual system selectively sensitive to the orientation and size of retinal images." *Journal of Physiology* **203**: 237-260.

Blakemore, C., J. P. J. Muncey and R. M. Ridley (1973). "Stimulus specificity in the human visual system." *Vision Research* **13**: 1915-1931.

Blakemore, C. and J. Nachmias (1971). "The orientation specificity of two visual aftereffects." *Journal of Physiology* **213**: 157-174.

Blakemore, C., J. Nachmias and P. Sutton (1970). "The perceived spatial frequency shift: Evidence for frequency-selective neurones in the human brain." *Journal of Physiology (London)* **210**: 727-750.

Brabyn, L. B. and D. McGuinness (1979). "Gender differences in response to spatial frequencies and stimulus orientation." *Perception and Psychophysics* **26**: 319-324.

Bradley, A. and R. D. Freeman (1982). "Contrast sensitivity in children." *Vision Research* **22**: 953-959.

Brainard, D. H., D. G. Pelli and T. Robson (2002). Display characterization. In: Encyclopedia of Imaging Science and Technology. J. P. Hornak (ed). Online http://onlinelibrary.wiley.com/book/10.1002/0471443395, Wiley**:** 172-188.

Brown, S. P. and R. H. Masland (2001). "Spatial scale and cellular substrate of contrast adaptation by retinal ganglion cells." *Nature Neuroscience* **4**(1): 44-51.

Buehren, T. F. and M. J. Collins (2006). "Accommodation stimulus-response function and retinal image quality." *Vision Research* **46**(10): 1633-1645.

Buehren, T. F., M. J. Collins and L. Carney (2005). "Near work induced wavefront aberrations in myopia." *Vision Research* **45**: 1297-1312.

Campbell, F. W., G. F. Cooper and C. Enroth-Cugell (1969). "The spatial selectivity of the visual cells of the cat." *Journal of Physiology* **203**: 223-235.

Campbell, F. W. and J. G. Robson (1968). "Application of Fourier Analysis to the visibility of gratings." *Journal of Physiology* **197**: 551-566.

Carandini, M. (2000). "Visual cortex: fatigue and adaptation." *Current Biology* **10**: R605-R607.

Carandini, M. and D. Ferster (1997). "A tonic hyperpolarization underlying contrast adaptation in cat visual cortex." *Science* **276**: 949-952.

Chakraborty, R., S. A. Read and M. J. Collins (2011). "Diurnal variations in axial length, choroidal thickness, intraocular pressure, and ocular biometrics." *Clinical and Epidemiologic Research* **52**(8): 5121–5129.

Chander, D. and E. J. Chichilnisky (2001). "Adaptation to temporal contrast in primate and salamander retina." *Journal of Neuroscience* **21**(24): 9904-9916.

Charman, W. N. (1982). "The accommodative resting point and refractive error." *The Ophthalmic Optician* **21**: 469-473.

Charman, W. N. (1999). "Near vision, lags of accommodation and myopia." *Ophthalmic and Physiological Optics* **19**(2): 126-133.

Charman, W. N. and J. Tucker (1977). "Dependence of accommodation response on the spatial frequency spectrum of the observed object." *Vision Research* **17**: 129-139.

Chat, S. W. S. and M. H. Edwards (2001). "Clinical evaluation of the Shin-Nippon SRW-5000 autorefractor in children." *Ophthalmic and Physiological Optics* **21**(2): 87-100.

Chee, M. W. L., D. Caplan, C. S. Soon, et al. (1999). "Processing of visually presented sentences in Mandarin and English studied with fMRI." *Neuron* **23**: 127-137.

Chen, J. C., B. Brown and K. L. Schmid (2006). "Changes in implicit time of the multifocal electroretinogram response following contrast adaptation." *Current Eye Research* **31**: 549-556.

Chen, J. C., K. L. Schmid and B. Brown (2003). "The autonomic control of accommodation and implications for human myopia development: a review." *Ophthalmic and Physiological Optics* **23**(5): 401-422.

Chen, J. C., K. L. Schmid and B. Brown (2005). "The effect of B-Adrenoceptor antagonist on accommodative adaptation in Hong Kong Chinese." *Current Eye Research* **30**: 179-188.

Cheng, D., K. L. Schmid, G. C. Woo, et al. (2010). "Randomized trial of effect of bifocal and prismatic bifocal spectacles on myopic progression." *Archives of Ophthalmology* **128**(1): 12-19.

Chew, S. J., S. C. Chia and L. K. H. Lee (1988). "The pattern of myopia in young Singaporean men." *Singapore Medical Journal* **29**: 201-211.

Chong, Y. S., Y. Liang, D. Tan, et al. (2005). "Association between breastfeeding and likelihood of myopia in children." *Journal of American Medical Association* **293**(24): 3001-3002.

Chow, Y. C., B. Dhillon, P. T. K. Chew, et al. (1990). "Refractive errors in Singapore medical students." *Singapore Medical Journal* **31**: 472-473.

Chung, K. M., N. Mohidin and D. J. O'Leary (2002). "Undercorrection of myopia enhances rather than inhibits myopia progression." *Vision Research* **42**: 2555-2559.

Ciuffreda, K. J., C. Colburn and D. Wallis (1996). "Effect of stimulus duration and dioptric demand on transient myopia." *Investigative Ophthalmology and Visual Science* **37** (**ARVO Suppl**): 164.

Ciuffreda, K. J. and M. Lee (2002). "Differential refractive susceptibility." *Ophthalmic and Physiological Optics* **22**(5): 372-379.

Ciuffreda, K. J. and X. Ordonez (1995). "Abnormal transient myopia in symptomatic individuals after sustained nearwork." *Optometry and Vision Science* **72**: 506-510.

Ciuffreda, K. J. and V. Thunyalukul (1999). "Myopic nearwork effects in children." *Investigative Ophthalmology and Visual Science* **40**: S448.

Ciuffreda, K. J. and B. Vasudevan (2008). "Near work-induced transient myopia (NITM) and permanent myopia - is there a link?" *Ophthalmic and Physiological Optics* **28**: 103-114.

Ciuffreda, K. J. and B. Vasudevan (2010). "Effect of nearwork-induced transient myopia on distance retinal defocus patterns." *Optometry* **81**: 153-156.

Ciuffreda, K. J. and D. M. Wallis (1998). "Myopes show increased susceptibility to nearwork aftereffects." *Investigative Ophthalmology and Visual Science* **39**(10): 1797-1803.

Collins, J. W. and L. G. Carney (1990). "Visual performance in high myopia." *Current Eye Research* **9**(3): 217-223.

Cordain, L., S. B. Eaton, J. Brand Miller, et al. (2002). "An evolutionary analysis of the aetiology and pathogenesis of juvenile-onset myopia." *Acta Ophthalmologica Scandinavica* **80**: 125-135.

Cufflin, M. P., C. A. Hazel and E. A. H. Mallen (2007). "Static accommodative responses following adaptation to differential levels of blur." *Ophthalmic and Physiological Optics* **27**: 353–360.

Cufflin, M. P., A. Mankowska and E. A. H. Mallen (2007). "Effect of blur adaptation on blur sensitivity and discrimination in emmetropes and myopes." *Investigative Ophthalmology & Visual Science* **48**(6): 2932-2939.

De Valois, K. K. (1977). "Spatial frequency adaptation can enhance contrast sensitivity." *Vision Research* **17**: 1057-1065.

Dealy, R. S. and D. J. Tolhurst (1974). "Is spatial adaptation an aftereffect of prolonged inhibition?" *Journal of Physiology* **241**: 261-270.

Diether, S., F. Gekeler and F. Schaeffel (2001). "Changes in contrast snsitivity induced by defocus and their possible relations to emmetropization in the chicken." *Investigative Ophthalmology and Visual Science* **42**(12): 3072-3079.

Diether, S. and F. Schaeffel (1997). "Local changes in eye growth induced by imposed local refractive error despite active accommodation." *Vision Research* **37**(6): 659-668.

Diether, S. and F. Schaeffel (1999). "Long-term changes in retinal contrast sensitivity in chicks from frosted occluders and drugs: relations to myopia?" *Vision Research* **39**: 2499-2510.

Diether, S., J. Wallman and F. Schaeffel (1997). "Form deprivation may change the contrast sensitivity function (CSF) of chicks." *Investigative Ophthalmology and Visual Science* **38**(S542).

Diether, S. and C. F. Wildsoet (2005). "Stimulus requirements for the decoding of myopic and hyperopic defocus under single and competing defocus conditions in the chicken." *Investigative Ophthalmology and Visual Science* **46**(7): 2242-2252.

Dirani, M., L. Tong, G. Gazzard, et al. (2009). "Outdoor activity and myopia in Singapore teenage children." *British Journal of Ophthalmology* **93(8 SUPPL)**: 997-1000.

Drexler, W., O. Findl, L. Schmetterer, et al. (1998). "Eye elongation during accommodation in humans: differences between emmetropes and myopes." *Investigative Ophthalmology and Visual Science* **39**(11): 2140-2147.

Ebenholtz, S. M. (1983). "Accommodative hysteresis: a precursor for induced myopia?" *Investigative Ophthalmology and Visual Science* **24**(4): 513-515.

Ebenholtz, S. M. and P. A. Zander (1987). "Accommodative hysteresis: influence on closed loop measures of far point and near point." *Investigative Ophthalmology and Visual Science* **28**(8): 1246-1249.

Edwards, M. H. and C. S. Fan (1999). "Is refraction in early infancy a predictor of myopia at the age of 7 to 8 years? The relationship between cycloplegic refraction at 11 weeks and the manifest refraction at age 7 to 8 years in Chinese children." *Optometry and Vision Science* **76**(5): 272-274.

Edwards, M. H. and C. S. Y. Lam (2004). "The epidemiology of myopia in Hong Kong." *Annals of the Academy of Medicine Singapore* **33**: 34-38.

Ehrlich, D. L. (1987). "Near vision stress: vergence adaptation and accommodative fatigue." *Ophthalmic and Physiological Optics* **7**(4): 353-357.

Ellemberg, D., T. L. Lewis, C. H. Liu, et al. (1999). "Development of spatial and temporal vision during childhood." *Vision Research* **39**: 2325-2333.

Elliott, D. (2003). Subjective Refraction. In: <u>Clinical Procedures in Primary Eye Care</u>. D. Elliott (ed), Butterworth-Heinemann**:** 172-188.

Elliott, D. B., K. Sanderson and A. Conkey (1990). "The reliability of the Pelli-Robson contrast sensitivity chart." *Ophthalmic and Physiological Optics* **10**(1): 21-24.

Fan, D. S. P., D. S. C. Lam, R. F. Lam, et al. (2004). "Prevalence, Incidence, and Progression of Myopia of School Children in Hong Kong." *Investigative Ophthalmology and Visual Science* **45**(4): 1071-1075.

Feldkaemper, M. P. and F. Schaeffel (2002). "Evidence for a potential role of glucagon during eye growth regulation in chicks." *Visual Neuroscience* **19**: 755-766.

Feldkamper, M. and F. Schaeffel (2003). "Interactions of genes and environment in myopia." *Developments in Ophthalmology* **37**: 34-49.

Fischer, A. J., I. B. Morgan and W. K. Stell (1999). "Colchicine causes excessive ocular growth and myopia in chicks." *Vision Research* **39**: 685-697.

Fisher, S. K., K. J. Ciuffreda and S. Levine (1987). "Tonic accommodation, accommodative hysteresis and refractive error." *American Journal of Optometry and Physiological Optics* **64**(11): 799-809.

Gardner, J. L., P. Sun, R. A. Waggoner, et al. (2005). "Contrast adaptation and representation in human early visual cortex." *Neuron* **47**: 607-620.

Gawron, V. J. (1981). "Differences among myopes, emmetropes, and hyperopes." *American Journal of Optometry and Physiological Optics* **58**: 753-760.

Gee, S. S. and K. F. Tabbara (1988). "Increase in ocular axial length in patients with corneal opacification." *Ophthalmology* **95**: 1276-1278.

George, S. and M. Rosenfield (2002). "Blur adaptation and the accommodative response." *Optometry and Vision Science* **79 (suppl)**: 25.

George, S. and M. Rosenfield (2004). "Blur adaptation and myopia." *Optometry and Vision Science* **81**(7): 543-547.

Georgeson, M. A. and J. M. Georgeson (1987). "Facilitation and masking of briefly presented gratings: time -course and contrast dependence." *Vision Research* **27**(3): 369-379.

Georgeson, M. A. and M. G. Harris (1984). "Spatial selectivity of contrast adaptation: models and data." *Vision Research* **24**(7): 729-741.

Georgeson, M. A. and R. S. E. Turner (1985). "Afterimages of sinusoidal, square-wave and compound gratings." *Vision Research* **25**(11): 1709-1720.

Gilinsky, A. S. (1968). "Orientation-specific effects of patterns of adapting light on visual acuity." *Journal of Optical Society of America* **58**: 13-18.

Gilmartin, B. and M. A. Bullimore (1987). "Sustained near-vision augments inhibitory sympathetic innervation of the ciliary muscle." *Clinical Vision Science* **68**: 22-26.

Gilmartin, B. and M. A. Bullimore (1991). "Adaptation of tonic accommodation to sustained visual tasks in emmetropia and late-onset myopia." *Optometry and Vision Science* **68**(1): 22-26.

Gilmartin, B., M. A. Bullimore, M. Rosenfield, et al. (1991). "Pharmacological effects on accommodative adaptation." *Optometry and Vision Science* **69**(4): 276-282.

Gilmartin, B., M. A. Bullimore, M. Rosenfield, et al. (1992). "Pharmacological effects on accommodative adaptation." *Optometry and Vision Science* **69**(4): 276-282.

Gilmartin, B., R. E. Hogan and S. M. Thompson (1984). "The effect of timolol maleate on tonic accommodation, tonic vergence and pupil diameter." *Investigative Ophthalmology and Visual Science* **25**: 763-770.

Gilmartin, B., E. A. H. Mallen and J. S. Wolffsohn (2002). "Sympathetic control of accommodation: evidence for inter-subject variation." *Ophthalmic and Physiological Optics* **22**(5): 366-371.

Gilmartin, B. and N. R. Winfield (1995). "The effect of topical B-adrenoceptor antagonists on accommodation in emmetropia and myopia." *Vision Research* **35**(9): 1305-1312.

Goh, P. P., Y. Abqariyah, G. P. Pokharel, et al. (2005). "Refractive error and visual impairment in school-age children in Gombak district, Malaysia." *Ophthalmology* **112**: 678-685.

Goldschmidt, E. (1968). "On the etiology of myopia." *Acta Ophthalmologica Scandinavica* **Suppl, 98**: 1-171.

Goldstein, E. (2007). Visual processing: the lateral geniculate nucleus and striate cortex. In: Sensation & Perception. E. Goldstein (ed). Pacific Grove, Brooks/Cole Publishing Company**:** 71-99.

Goss, D. A. (1991). "Clinical accommodation and heterophoria findings preceding juvenile onset of myopia." *Optometry and Vision Science* **68**(2): 110-115.

Goss, D. A. (2000). "Nearwork and myopia." *The Lancet* **356**: 1456-1457.

Goss, D. A. and J. B. Eskridge (1987). Myopia In: Diagnosis and Management in Vision Care J. F. Amos (ed). Boston, Butterworth-Heinemann USA**:** 121-148.

Goss, D. A. and T. W. Jackson (1996). "Clinical findings before the onset of myopia in youth: 2. Zone of clear single binocular vision." *Optometry and Vision Science* **73**: 263-268.

Goss, D. A. and M. G. Wickham (1995). "Retinal-image mediated ocular growth as a mecahnism for juvenile onset myopia and for emmetropization - a literature review." *Documenta Ophthalmologica* **90**: 341-375.

Greenlee, M. and S. Magnussen (1988). "Interactions among spatial frequency and orientation channels adapted concurrently." *Vision Research* **28**(12): 1303-1310.

Greenlee, M., S. Magnussen and K. Nordby (1988). "Spatial vision of the achromat: spatial frequency and orientation-specific adaptation." *Journal of Physiology* **395**: 661-678.

Greenlee, M. W., M. A. Georgeson, S. Magnussen, et al. (1991). "The time course of adaptation to spatial contrast." *Vision Research* **31**(2): 223-236.

Greenlee, M. W., M. A. Georgeson, S. Magnussen, et al. (1992). "The decay of adaptation to spatial contrast: a response to David Rose." *Vision Research* **32**(9): 1785-1788.

Greenlee, M. W. and F. Heitger (1988). "The functional role of contrast adaptation." *Vision Research* **28**(7): 791-797.

Grosvenor, T. and D. A. Goss (1999). Epidemiology of myopia. In: Clinical management of myopia. T. Grosvenor and D. A. Goss (ed). Woburn, USA, Butterworth Heinemann**:** 3-39.

Gwiazda, J., L. Hyman, M. Hussein, et al. (2003). "A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children." *Investigative Ophthalmology and Visual Science* **44**(4): 1492-1500.

Gwiazda, J. E., J. Bauer, F. Thorn, et al. (1995). "Shifts in tonic accommodation after near work are related to refractive errors in children." *Ophthalmic and Physiological Optics* **15**(2): 93-97.

Gwiazda, J. E., J. Bauer, F. Thorn, et al. (1997). "Development of spatial contrast sensitivity from infancy to adulthood: psychophysical data." *Optometry and Vision Science* **74**: 785-789.

Gwiazda, J. E., E. Ong, R. Held, et al. (2000). "Brief communication: Myopia and ambient lighting at night." *Nature* **404**: 144.

Gwiazda, J. E., F. Thorn, J. Bauer, et al. (1993a). "Emmetropization and the progression of manifest refraction in children followed from infancy to puberty." *Clinical Vision Science* **8**(4): 337-344.

Gwiazda, J. E., F. Thorn, J. Bauer, et al. (1993b). "Myopic children show insufficient accommodative response to blur." *Investigative Ophthalmology and Visual Science* **34**(3): 690-694.

Hammond, C. J., H. Snieder, C. E. Gilbert, et al. (2001). "Genes and environment in refractive error: The Twin Eye Study." *Investigative Ophthalmology and Visual Science* **42**(6): 1232-1236.

Han, W., M. K. H. Yap, J. Wang, et al. (2006). "Family-based association analysis of hepatocyte growth factor (HGF) gene polymorphisms in high myopia." *Investigative Ophthalmology and Visual Science* **47**(6): 2291-2299.

Hayes, B. P., F. W. Fitzke, W. Hodos, et al. (1986). "A morphology analysis of experimental myopia in young chickens." *Investigative Ophthalmology and Visual Science* **27**(6): 981-991.

Hazel, C. A., M. J. Cox and N. C. Strang (2003). "Wavefront aberration and its relationship to the accommodative stimulus-response function in myopic subjects." *Optometry and Vision Science* **80**(2): 151-158.

Hazel, C. A., N. C. Strang and F. A. Vera-Diaz (2003). "Open-and closed-loop regressions compared in myopic and emmetropic subjects." *Ophthalmic and Physiological Optics* **23**(3): 265-270.

Heggelund, P. and A. Hohmann (1976). "Long term retention of the "Gilinsky-effect"." *Vision Research* **16**: 1015-1017.

Heinrich, T. S. and M. Bach (2001). "Contrast adaptation in human retina and cortex." *Investigative Ophthalmology and Visual Science* **42**(11): 2721-2727.

Heinrich, T. S. and M. Bach (2002a). "Contrast adaptation in retinal and cortical evoked potentials: No adaptation to low spatial frequencies." *Visual Neuroscience* **19**: 645-650.

Heinrich, T. S. and M. Bach (2002b). "Contrast adaptation: paradoxical effects when the temporal frequencies of adaptation and test differ." *Visual Neuroscience* **19**: 421-426.

Higgins, K. E., J. M. Jaffe, R. C. Caruso, et al. (1988). "Spatial contrast sensitivity: effects of age, test-retest, and psychophysical method." *Journal of the Optical Society of America A* **5**(12): 2173-2180.

Hodos, W. (1993). The visual acapabilities of birds. In: Vision, Brain and Behavior in Birds. H. P. Zeigler and H. J. Bischof (ed). Cambridge, MIT Press**:** 63-76.

Hoosain, R. (1991). Psycholinguistic implications for linguistic relativity: A case study of Chinese. (ed). New Jersey, Lawrence Erlbaum Associates, Inc.

Hornbeak, D. M. and T. L. Young (2009). "Myopia genetics: a review of current research and emerging trends." *Current Opinion in Ophthalmology* **20**: 356-362.

Hoyt, C. S., R. D. Stone and C. Fromer (1981). "Monocular axial myopia associated with neonatal eyelid closure in human infants." *American Journal of Ophthalmology* **91**: 197-200.

Hubel, D. H. and T. N. Wiesel (1962). "Receptive fields, binocular interaction and functional architecture in the cat's visual cortex." *Journal of Physiology* **160**: 106-154.

Huggelund, P. and A. Hohmann (1976). "Long tern retention of the "Gilinsky-effect"." *Vision Research* **16**: 1015-1017.

Humphreys, G. W., L. J. Evett and P. T. Quinlan (1990). "Orthographic processing in visual word identification." *Cognitive Psychology* **22**: 517-560.

Hung, G. K. and K. J. Ciuffreda (1999a). "Adaptation model of nearwork-induced transient myopia." *Ophthalmic and Physiological Optics* **19**(2): 151-158.

Hung, G. K. and K. J. Ciuffreda (1999b). "Model of human refractive error development." *Current Eye Research* **19**(1): 41-52.

Hung, G. K. and K. J. Ciuffreda (2000). "Differential retinal-defocus magnitude during eye growth provides the appropriate direction signal." *Medical Science Monitor* **6**(4): 791-795.

Hung, G. K., A. J. Fiedler and K. J. Ciuffreda (2010). "Homeomorphic Matlab model of myopia development." *Journal of Computer Science and Systems Biology* **3**(2): 30-39.

Ip, J. M., S. M. Saw, K. A. Rose, et al. (2008). "Role of near work in myopia: findings in a sample of Australian school children." *Investigative Ophthalmology and Visual Science* **49**(7): 2903-2910.

Irving, E. L., J. G. Sivak and M. G. Callender (1992). "Refractive plasticity of the developing chick eye." *Ophthalmic and Physiological Optics* **12**: 448-456.

Jaschinski-Kruza, W. (1984). "Transient myopia after visual work." *Ergonomics* **27**(11): 1181-1189.

Javitt, J. C. and Y. P. Chiang (1994). "The socioeconimic aspects of laser refractive surgery." *Archives of Ophthalmology* **112**(12): 1526-1530.

Jiang, B. C. (1995). "Parameters of accommodative and vergence systems and the development of late-onset myopia." *Investigative Ophthalmology and Visual Science* **36**(8): 1737-1742.

Kaplan, E., K. Purpura and R. M. Shapley (1987). "Contrast affects the transmission of visual information through the mammalian lateral geniculate nucleus." *Journal of Physiology (London)* **330**: 25-143.

Kaplan, E. and R. M. Shapley (1982). "X and Y cells in the lateral geniculate nucleus of macaque monkeys." *Journal of Physiology (London)* **330**: 25-143.

Kaplan, E. and R. M. Shapley (1986). "The primate retina contains two types of ganglion cells, with high and low contrast sensitivity." *Proceedings of the Natural Academic of Science, USA* **83**: 2755-2757.

Kasthurirangan, S. and A. Glasser (2005). "Influence of amplitude and starting point on accommodative dynamics in humans." *Investigative Ophthalmology and Visual Science* **46**(9): 3463-3472.

Kasthurirangan, S. and A. Glasser (2006). "Age related changes in accommodative dynamics in humans." *Vision Research* **46** 1507–1519.

Kasthurirangan, S., A. S. Vilupuru and A. Glasser (2003). "Amplitude dependent accommodative dynamics in humans." *Vision Research* **43**: 2945–2956.

Katz, J., J. M. Tielsch and A. Sommer (1997). "Prevalence and risk factors for refractive errors in an adult inner city population." *Investigative Ophthalmology and Visual Science* **38**: 334-340.

Kee, C., L. F. Hung, Y. Qiao, et al. (2007). "Temporal constraints on experimental emmetropization in infant monkeys." *Investigative Ophthalmology and Visual Science* **48**(3): 957-962.

Kim, K. J. and F. Rieke (2001). "Temporal contrast adaptation in the input and output signals of salamander retinal ganagion cells." *Journal of Neuroscience* **21**(1): 287-299.

Kolb, H. (2003). "How the retina works." *American Scientist* **91**: 28-35.

Kroger, R. H. H., B. Hirt and H. J. Wagner (1999). "Effects of retinal dopamine depletion on the growth of the fish eye." *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology* **184**: 403-412.

Lam, C., W. Goh, Y. Tang, et al. (1994). "Changes in refractive trends and optical components of Hong Kong Chinese aged over 40 years." *Ophthalmic and Physiological Optics* **14**: 383-388.

Lam, C. S. Y., M. H. Edwards, M. Millodot, et al. (1999). "A 2-year longitudinal study of myopia progression and optical component changes among Hong Kong school children." *Optometry and Vision Science* **76**(6): 370-380.

Lam, C. S. Y. and W. S. H. Goh (1991). "The incidence of refractive errors among school children in Hong Kong and its relationship with the optical components." *Clinical and Experimental Optometry* **74**(3): 97-103.

Lancaster, W. B. and E. R. Williams (1914). "New light on the theory of accommodation, with practical applications." *Transactions of the American Academy of Ophthalmology and Otolaryngology* **19**: 170-195.

Leat, S. J., N. K. Yadav and E. L. Irving (2009). "Development of visual acuity and contrast sensitivity in children." *Journal of Optometry* **2**: 19-26.

Legge, G. E. (1981). "A power law for contrast discrimination." *Vision Research* **21**: 457-467.

Leung, J. T. M. and B. Brown (1999). "Progression of myopia in Hong Kong Chinese school children is slowed by wearing progressive lenses." *Optometry and Vision Science* **76**(6): 346-354.

Levine, M. W. and J. M. Shefner (1991). Spatial frequency representation. In: Sensation & Perception. M. Levine and J. Shefner (ed). Belmont, California, Brooks/Cole Publishing Company**:** 209-248.

Li, X. S., P. Liu and K. Rayner (2011). "Eye movement guidance in Chinese reading: is there a preferred viewing location?" *Vision Research* **51**(10): 1146-1156

Li, X. S., K. Rayner and K. R. Cave (2009). "On the segmentation of Chinese words during reading." *Cognitive Psychology* **58**: 525-552.

Lim, R., P. Mitchell and R. G. Gumming (1999). "Refractive associations with cataract: the Blue Mountains Eye Study." *Investigative Ophthalmology and Visual Science* **40**(12): 3021-3026.

Lin, L. L. K., Y. F. Shih, C. K. Hsiao, et al. (2004). "Prevalence of myopia in Taiwanese school children: 1983 to 2000." *Annals of the Academy of Medicine Singapore* **33**: 27-33.

Lin, L. L. K., Y. F. Shih, C. K. Hsiao, et al. (2001). "Epidemiologic study of the prevalence and severity of myopia among schoolchildren in Taiwan in 2000." *Journal of Formos Medical Association* **100**(10): 684-691.

Lin, L. L. K., Y. F. Shih, C. B. Tsai, et al. (1999). "Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1995." *Optometry and Vision Science* **76**(5): 275-281.

Liou, S. W. and C. J. Chiu (2001). "Myopia and contrast sensitivity function." *Current Eye Research* **22**(2): 81-84.

Lunn, R. and W. P. Banks (1986). "Visual fatigue and spatial frequency adaptation to video displays of text." *Human Factors* **28**(4): 457-464.

Luvone, P. M., M. Tigges, A. Fernandes, et al. (1989). "Dopamine synthesis and metabolism in rhesus monkey retina: development, aging and the effects of monocular visual deprivation." *Visual Neuroscience* **2**: 465-471.

Luvone, P. M., M. Tigges, R. A. Stone, et al. (1991). "Effects of apomorphine, a dopamine receptor agonist, on ocular refraction and axial elongation in a primate model of myopia." *Investigative Ophthalmology and Visual Science* **32**(1674-1677).

Määttänen, L. M. and J. J. Koenderink (1991). "Contrast adaptation and contrast gain control." *Experimental Brain Research* **87**: 205-212.

Maddock, R. J., M. Millodot, S. J. Leat, et al. (1981). "Accommodation responses and refractive error." *Investigative Ophthalmology and Visual Science* **20**(3): 387-391.

Maffei, L., A. Fiorentini and S. Bisti (1973). "Neural correlate of perceptual adaptation to gratings." *Science* **182**: 1036-1039.

Magnussen, S., S. Dyrnes, M. W. Greenlee, et al. (1992). "Time course of contrast adaptation to VDU-displayed text." *Behaviour and Information Technology* **11**(6): 334-337.

Magnussen, S. and M. W. Greenlee (1985). "Marathon adaptation to spatial contrast: saturation in sight." *Vision Research* **10**: 1409-1411.

Majaj, N. J., D. G. Pelli, P. Kurshan, et al. (2002). "The role of spatial frequency channels in letter identification." *Vision Research* **42**: 1165-1184.

Mallen, E. A. H., B. Gilmartin and J. S. Wolffsohn (2005). "Sympathetic innervation of ciliary muscle and oculomotor function in emmetropic and myopic young adults." *Vision Research* **45**: 1641-1651.

Mallen, E. A. H., P. Kashyap and K. M. Hampson (2006). "Transient axial length change during the accommodation responses in young adults." *Investigative Ophthalmology and Visual Science* **47**(3): 1251-1254.

Mallen, E. A. H., J. S. Wolffsohn, B. Gilmartin, et al. (2001). "Clinical evaluation of the Shin-Nippon SRW 5000 autorefractor in adults." *Ophthalmic and Physiological Optics* **21**(2): 101-107.

Manookin, M. B. and J. B. Demb (2006). "Presynaptic mechanism for slow contrast adaptation in mammalian retinal ganglion cells." *Neuron* **50**: 453-464.

Mantyjarvi, M. I. (1987). "Accommodation in hyperopic and myopic school children." *Journal of Pediatric Ophthalmology and Strabismus* **24**(1): 37–41.

Mantyjarvi, M. I., M. H. Autere, A. M. Silvennoinen, et al. (1989). "Observation on the use of three different contrast sensitivity tests in children and young adults." *Journal of Pediatric Ophthalmology and Strabismus* **26**(3): 113-119.

Marc, R. E., R. F. Murry and S. F. Basinger (1995). "Pattern recognition of amino acid signatures in retinal neurons." *Journal of Neuroscience* **15**: 5106–5129.

Marcelja, S. (1980). "Mathematical description of the responses of simple cortical cells." *Journal of Optical Society of America* **70**(11): 1297-1300.

Massey, S. C. (1990). "Cell types using glutamate as a neurotransmitter in the vertebrate retina." *Progress In Retinal Research* **9**: 399-425

Matsumura, H. and H. Hirai (1999). "Prevalence of myopia and refractive changes in students from 3 to 17 years of age." *Survey of Ophthalmology* **44**(Supp 1): S109-S115.

Mavracanas, T. A., A. Mandalos, D. Peios, et al. (2000). "Prevalence of myopia in a sample of Greek students." *Acta Ophthalmologica Scandinavica* **78**: 656-659.

McBrien, N. A. and D. W. Adams (1997). "A longitudinal investigation of adult-onset and adult-progression of myopia in an occupational group. Refractive and biometric findings." *Investigative Ophthalmology and Visual Science* **38**: 321-333.

McBrien, N. A., A. Gentle and C. Cottriall (1999). "Optical correction of induced axial myopia in the tree shrew: Implications for emmetropization." *Optometry and Vision Science* **76**(6): 419-427.

McBrien, N. A. and M. Millodot (1986a). "Amplitude of accommodation and refractive error." *Investigative Ophthalmology and Visual Science* **27**(7): 1187-1190.

McBrien, N. A. and M. Millodot (1986b). "The effect of refractive error on the accommodative response gradient." *Ophthalmic and Physiological Optics* **6**(2): 145-149.

McBrien, N. A. and M. Millodot (1987). "The relationship between tonic accommodation and refractive errors." *Investigative Ophthalmology and Visual Science* **28**(6): 997-1004.

McBrien, N. A. and M. Millodot (1988). "Differences in adaptation of tonic accommodation with refractive state." *Investigative Ophthalmology and Visual Science* **29**(3): 460-469.

McCarthy, C. S., P. Megawa, M. Devadas, et al. (2007). "Dopaminergic agents affect the ability of brief periods of normal vision to prevent form-deprivation myopia." *Experimental Eye Research* **84**(1): 100-107.

McClelland, J. L. (1976). "Preliminary letter identification in the perception of words and non-words." *Journal of Experimental Psychology: Human Perception and Performance* **2**: 80-91.

McFadden, S. A., M. H. C. Howlett and J. R. Mertz (2004). "Retinoic acid signals the direction of ocular elongation in the guinea pig eye." *Vision Research* **44**: 643–653.

McLean, J. and L. A. Palmer (1996). "Contrast adaptation and excitatory amino acid receptors in cat striate cortex." *Visual Neuroscience* **13**: 1069-1087.

Mecacci, L. and D. Spinelli (1976). "The effects of spatial frequency adaptation on human evoked potentials." *Vision Research* **16**: 477-479.

Megaw, P. L., I. G. Morgan and M. K. Boelen (1997). "Dopaminergic behavior in chicken retina and the effect of form deprivation." *Australian and New Zealand Journal of Ophthalmology* **25 Suppl**(1): S76-S78.

Mercuri, N., G. Bernardi, P. Calabresi, et al. (1985). "Dopamine decreases cell excitability in rat striatal neurons by pre- and postsynaptic mechanisms." *Brain Research* **358**: 110-121.

Metlapally, R., C. S. Ki, Y. J. Li, et al. (2010). "Genetic association of Insulin-like growth factor-1 polymorphisms with high-grade myopia in an international family cohort." *Investigative Ophthalmology and Visual Science* **51**(9): 4476-4479.

Mitchell, P., F. Hourihan, J. Sandbach, et al. (1999). "The relationship between glaucoma and myopia." *Ophthalmology* **106**: 2010-2015.

Mon-Williams, M., J. Tresilian, N. C. Strang, et al. (1998). "Improving vision: neural compensation for optical defocus." *Proceedings of the Royal Society London B* **265**: 71-77.

Morgan, I. G. and K. Rose (2005). "How genetic is school myopia?" *Retinal and eye research* **24**: 1-38.

Movshon, J. and P. Lennie (1979). "Pattern-selective adaptation in visual cortical neurones." *Nature* **278**: 850-852.

Mutti, D. O. (2010). "Hereditary and environmental contributions to emmetropization and myopia." *Optometry and Vision Science* **87** (4): 255–259.

Mutti, D. O., L. A. Jones, M. L. Moeschberger, et al. (2000). ""AC/A ratio, age, and refractive error in children"." *Investigative Ophthalmology and Visual Science* **41**(9): 2469-2478.

Mutti, D. O., G. L. Mitchell, J. R. Hayes, et al. (2006). "Accommodative lag before and after the onset of myopia." *Investigative Ophthalmology and Visual Science* **47**(3): 837-846.

Mutti, D. O., G. L. Mitchell, M. L. Moeschberger, et al. (2002a). "Parental myopia, near work, school achievement, and children's refractive error." *Investigative Ophthalmology and Visual Science* **43**(12): 3633-3640.

Mutti, D. O., G. L. Mitchell, M. L. Moeschberger, et al. (2002b). "Excess accommodative lag accompanies but does not precede the onset of myopia." *Investigative Ophthalmology and Visual Science* **43: E-Abstract** 1512.

Nakatsuka, C., S. Hasebe, F. Nonaka, et al. (2003). "Accommodative lag under habitual seeing conditions: comparison between adult myopes and emmetropes." *Japanese Journal of Ophthalmology* **47**: 291-298.

Napper, G. A., N. A. Brennan, M. Barrington, et al. (1995). "The duration of normal visual exposure necessary to prevent form deprivation myopia in chicks." *Vision Research* **35**(9): 1337-1344.

Napper, G. A., N. A. Brennan, M. Barrington, et al. (1997). "The effect of an interrupted daily period of normal visual stimulation on form deprivation myopia in chicks." *Vision Research* **37**(12): 1557-1564.

Nickla, D. L., C. F. Wildsoet and J. Wallman (1998). "Visual influences on diurnal rhythms in ocular length and choroidal thickness in chick eyes." *Experimental Eye Research* **66**: 163-181.

Norton, T. T. (1990). "Experimental myopia in tree shrews." *Ciba Foundation Symposium* **155**: 178-199.

Oen, F., T. H. Lim and M. Chung (1994). "Contrast sensitivity in a large adult population." *Annals of the Academy of Medicine Singapore* **23**(3): 322-326.

Ohlendorf, A. and F. Schaeffel (2009). "Contrast adaptation induced by defocus - A possible error signal for emmetropization?" *Vision Research* **49**: 249-256.

Ohngemach, S., G. Hagel and F. Schaeffel (1997). "Concentrations of bogenic amines in fundal layers in chickens with normal visual experience, deprivation and after reserpine application." *Visual Neuroscience* **14 (3 Suppl)**: 493-505.

Ohzawa, I., G. Sclar and R. D. Freeman (1982). "Contrast gain control in the visual cortex." *Nature* **298**: 266-268.

Ohzawa, I., G. Sclar and R. D. Freeman (1985). "Contrast gain control in the cat's visual system." *Journal of Neurophysiology* **54**(3): 651-667.

Onal, S., E. Toker, Z. Akingol, et al. (2007). "Refractive errors of medical students in Turkey: one year follow-up of refraction and biometry." *Optometry and Vision Science* **84**: 175-180.

Ong, E. and K. J. Ciuffreda (1995). "Nearwork induced transient myopia." *Documenta Ophthalmologica* **91**: 57-85.

Ong, E. and K. J. Ciuffreda (1997). Accommodation, nearwork and myopia. Santa Ana, CA, USA, Optometric Extension Program Foundation, Inc.

Ong, E., K. J. Ciuffreda and M. Rosenfield (1994). "Accommodation, vergence and nearwork-induced transient myopia (abstract)." *Optometry and Vision Science* **71**: 129.

Ong, E., K. J. Ciuffreda and M. Rosenfield (1995). "Effect of target proximity on transient myopia induced by equidioptric stimuli." *Optometry and Vision Science* **72**(7): 502-505.

Ong, E., K. J. Ciuffreda and M. Rosenfield (1996). "Accommodation, vergence and transient myopia." *Investigative Ophthalmology & Visual Science* **37 (ARVO Suppl)**: S164.

Owens, D. A. (1980). "A comparison of accommodative responsiveness and contrast sensitivity for sinusoidal gratings." *Vision Research* **20,**(2): 159-167.

Owens, H., B. Winn, B. Gilmartin, et al. (1991). "The effect of topical beta-adrenergic antagonists on the dynamics of steady-state accommodation." *Ophthalmic and Physiological Optics* **11**: 99-104.

Owsley, C., R. Sekuler and D. Siemsen (1983). "Contrast sensitivity throughout adulthood." *Vision Research* **23**(7): 689-699.

Pacella, R., J. McLellan, K. Grice, et al. (1999). "Role of genetic factors in the etiology of juvenile-onset myopia based on a longitudinal study of refractive error." *Optometry and Vision Science* **76**(6): 381-386.

Pantle, A. and R. Sekuler (1968). "Size-detecting mechanisms in human vision." *Science* **162**: 1146-1148.

Patching, G. R. and T. R. Jordan (2005). "Assessing the role of different spatial frequecies in word perception by good and poor readers." *Memory and Cognition* **33**(6): 961-971.

Pelli, E. (1990). "Contrast in complex images." *Journal of the Optical Society of America A* **7**(10): 2032-2040.

Pendrak, K., T. Nguyen, T. Lin, et al. (1997). "Retinal dopamine in the recovery from experimental myopia." *Current Eye Research* **16**: 152-157.

Perfetti, C. A. and L. H. Tan (1998). "The time course of graphic, phonological and semantic activation in Chinese character identification." *Journal of Experimental Psychology: Learning, Memory and Cognition* **24**(1): 101-118.

Pierro, L., F. I. Camesasca, M. Mischi, et al. (1992). "Peripheral retinal changes and axial myopia." *Retina* **12**: 12-17.

Portello, J. K., M. Rosenfield and M. O'Dwyer (1997). "Clinical characteristics of pre-myopic individuals." *Optometry and Vision Science* **74 (Suppl)**: 176.

Prefetti, C. A., Y. Liu and L. H. Tan (2002). How the mind meets the brain in reading: a comparative writing systems approach. In: Cognitive Neuroscience Studies of the Chinese Language. H. S. R. Kao, C. K. Leong and D. G. Gao (ed). Hong Kong, Hong Kong University Press**:** 35-70.

Quinn, G. E., C. H. Shin, M. G. Maguire, et al. (1999). "Myopia and ambient lighting at night." *Nature* **399**: 113-114.

Ramsdale, C. (1985). "The effect of ametropia on the accommodative response." *Acta Ophthalmologica Scandinavica* **63**: 167-174.

Raviola, E. and T. N. Wiesel (1985). "An animal model of myopia." *New England Journal of Medicine* **312**: 1609-1615.

Rayner, K. and A. Pollatsek (1989). Word perception. In: The Psychology of Reading. K. Rayner and A. Pollatsek (ed). Hillsdale, New Jersey, Lawrence Erlbaum Associates**:** 60-108.

Read, S. A., M. J. Collins, E. C. Woodman, et al. (2010). "Axial length changes during accommodation in myopes and emmetropes." *Optometry and Vision Science* **87**(9): 656-662.

Regan, D. (2000). How do we see objects? Conceptualizing the question and tackling it. In: Human Perception of Objects. D. Regan (ed). Sunderland, Massachusetts, Sinauer Associates, Inc.**:** 1-206.

Rieke, F. (2001). "Temporal contrast adaptation in salamander bipolar cells." *Journal of Neuroscience* **21**(23): 9445-9454.

Robb, R. M. (1977). "Refractive errors associated with hemangiomas of the eyelids and orbit in infancy." *American Journal of Ophthalmology* **83**(1): 52-58.

Robson, J. G. and N. Graham (1981). "Probability summation and regional variation in contrast sensitivity across the visual field." *Vision Research* **21**: 409-418.

Rose, D. and R. Evans (1983). "Evidence against saturation of contrast adaptation in the human visual system." *Perception and Psychophysics* **34**(2): 158-160.

Rose, K., I. G. Morgan, J. Ip, et al. (2008). "Outdoor activities reduces the prevalence of myopia in children." *Ophthalmology* **115**: 1279-1285.

Rosenfield, M. (1998). Accommodation and myopia In: Myopia and Nearwork. M. Rosenfield and B. Gilmartin (ed). Oxford, Butterworth-Heinemann**:** pp 91-116.

Rosenfield, M. and J. A. Abraham-Cohen (1999). "Blur sensitivity in myopes." *Optometry and Vision Science* **76**(5): 303-307.

Rosenfield, M. and K. J. Ciuffreda (1994). "Cognitive demand and transient nearwork-induced myopia." *Optometry and Vision Science* **71**(6): 381-385.

Rosenfield, M., K. J. Ciuffreda, G. K. Hung, et al. (1993). "Tonic accommodation: a review I. Basic aspects." *Ophthalmic and Physiological Optics* **13**(7): 266-284.

Rosenfield, M., K. J. Ciuffreda, G. K. Hung, et al. (1994). "Tonic accommodation: a review II. Accommodative adaptation and clinical aspect." *Ophthalmic and Physiological Optics* **14**(7): 265-277.

Rosenfield, M., K. J. Ciuffreda and L. Novogrodsky (1992). "Contribution of accommodation and disparity-vergence to transient nearwork-induced myopic shifts." *Ophthalmic and Physiological Optics* **12**: 433-436.

Rosenfield, M. and B. Gilmartin (1988). "Accommodative adaptation induced by sustained disparity-vergence." *American Journal of Optometry and Physiological Optics* **65**(2): 118-126.

Rosenfield, M. and B. Gilmartin (1989). "Temporal aspects of accommodative adaptation." *Optometry and Vision Science* **66**(4): 229-234.

Rosenfield, M. and B. Gilmartin (1998). Myopia and nearwork: causation or merely association? In: Myopia and Nearwork. M. Rosenfield and B. Gilmartin (ed). Oxford, Butterworth Heinemann**:** 193-206.

Rosenfield, M., S. E. Hong and S. George (2004). "Blur adaptation in myopes." *Optometry and Vision Science* **81**(9): 657-662.

Rosenfield, M., N. N. Wong and H. A. Solan (2001). "Nearwork distance in children." *Ophthalmic and Physiological Optics* **21**(1): 75-76.

Ross, J. E., D. D. Clarke and A. J. Bron (1985). "Effect of age on contrast senstivity function: uniocular and binocular findings." *British Journal of Ophthalmology* **69**: 51-56.

Rushton, W. A. H. (1965). "Visual adaptation (the Ferrier lecture, 1962)." *Proceedings of the Royal Society London B* **162**: 20-46.

Sanchez-Vives, M. V., L. G. Nowak and D. A. McCormack (2000). "Cellular mechanisms of long-lasting adaptation in visual cortical neurons in vitro." *Journal of Neuroscience* **20**(11): 4286-4299.

Sanchez-Vives, M. V., L. G. Nowak and D. A. McCormick (2000). "Membrane mechanisms underlying contrast adaptation in cat area 17 in vivo." *Journal of Neuroscience* **20**(11): 4267-4285.

Saw, S. M., W. H. Chua, C. Y. Hong, et al. (2002a). "Nearwork in early-onset myopia." *Investigative Ophthalmology and Visual Science* **43**(2): 332-339.

Saw, S. M., W. H. Chua, C. Y. Hong, et al. (2002b). "Height and its relationship to refraction and biometry parameters in Singapore Chinese children." *Investigative Ophthalmology and Visual Science* **43**(5): 1408-1413.

Saw, S. M., R. Z. Hong, M. Z. Zhang, et al. (2001). "Near-work activity and myopia in rural and urban schoolchildren in China." *Journal of Pediatric Ophthalmology and Strabismus* **38**: 149-155.

Saw, S. M., A. Shankar, S. B. Tan, et al. (2006). "A cohort study of incident myopia in Singaporean children." *Investigative Ophthalmology and Visual Science* **47**(5): 1839-1844.

Saw, S. M., S. B. Tan, D. Fung, et al. (2004). "IQ and the association with myopia in children." *Investigative Ophthalmology and Visual Science* **45**(9): 2943-2948.

Saw, S. M., L. Tong, W. H. Chua, et al. (2005). "Incidence and progression of myopia in Singaporean school children." *Investigative Ophthalmology and Visual Science* **46**(1): 51-57.

Saw, S. M., H. M. Wu, C. Y. Hong, et al. (2001). "Myopia and night lighting in children in Singapore." *British Journal of Ophthalmology* **85**: 527-528.

Saw, S. M., H. M. Wu, B. Seet, et al. (2001). "Academic achievement, close up work parameters, and myopia in Singapore military conscripts." *British Journal of Ophthalmology* **85**: 855-860.

Saw, S. M., M. Z. Zhang, R. Z. Hong, et al. (2002). "Near work activity, night-lights, and myopia in the Singapore-China Study." *Arch Ophthalmologica* **120**: 620-627.

Schaeffel, F., M. Bartmann, G. Hagel, et al. (1995). "Studies on the role of the retinal dopamine/ melatonin system in experimental refractive errors in chickens." *Vision Research* **35**: 1247-1264.

Schaeffel, F. and S. Diether (1999). "The growing eye: an autofocus system that works on very poor images." *Vision Research* **39**: 1585-1589.

Schaeffel, F., A. Glasser and H. C. Howland (1988). "Accommodation, refractive error and eye growth in chickens." *Vision Research* **28**: 639-657.

Schaeffel, F., D. Troilo, J. Wallman, et al. (1990). "Developing eyes that lack accommodation grow to compensate for defocus." *Visual Neuroscience* **4**: 177-183.

Schaeffel, F., S. Weiss and J. Seidel (1999). "How good is the match between the plane of the text and the plane of focus during reading?" *Ophthalmic and Physiological Optics* **19**(2): 180-192.

Schaeffel, F., H. Wilhelm and E. Zrenner (1993). "Inter-individual variability in the dynamics of natural accommodation in humans: relation to age and refractive errors." *Journal of Physiology* **461**: 301-320.

Scharre, J. E., S. A. Cotter, S. S. Block, et al. (1990). "Normative contrast sensitivity data for young children." *Optometry and Vision Science* **67**: 826-832.

Schmid, K. L., D. R. Brinkworth, K. M. Wallace, et al. (2006). "The effect of manipulations to target contrast on emmetropization in chick." *Vision Research* **46**: 1099-1107.

Schmid, K. L., K. S. Hilmer, R. A. Lawrence, et al. (2005). "The effect of common reductions in letter size and contrast on accommodation responses in young adult myopes and emmetropes." *Optometry and Vision Science* **82**(7).

Schmid, K. L. and C. F. Wildsoet (1996). "Effects on the compensatory responses to positive and negative lenses of intermittent lens wear and ciliary nerve section in chicks." *Vision Research* **36**(7): 1023-1036.

Schmid, K. L. and C. F. Wildsoet (1997a). "Contrast and spatial-frequency requirements for emmetropization in chicks." *Vision Research* **37**(15): 2011-2021.

Schmid, K. L. and C. F. Wildsoet (1997b). "The sensitivity of the chick eye to refractive defocus." *Ophthalmic and Physiological Optics* **17**(1): 61-67.

Schmid, K. L. and C. F. Wildsoet (1998). "Assessment of visual acuity and contrast sensitivity in the chick using an optokinetic nystagmus paradigm." *Vision Research* **38**: 2629–2634.

Schmid, K. L. and C. F. Wildsoet (2004). "Inhibitory effects of apomorphine and atropine and their combination on myopia in chicks." *Optometry and Vision Science* **81**(2): 137-147.

Schor, C. M., J. C. Kotulak and T. Tsuetaki (1986). "Adaptation of tonic accommodation reduces accommodative lag and is masked in darkness." *Investigative Ophthalmology and Visual Science* **27**: 820-827.

Schwartz, S. H. (1999). Spatial vision. In: Visual Perception - A Clinical Orientation. S. H. Schwartz (ed). New York, McGraw-Hill**:** 175-217.

Sclar, G., P. Lennie and D. DePriest (1989). "Contrast adaptation in striate cortex of macaque." *Vision Research* **29**(7): 747-755.

Sclar, G., I. Ohzawa and R. D. Freeman (1985). "Contrast gain control in the kitten's visual system." *Journal of Neurophysiology* **54**(3): 668-675.

Seet, B., T. Y. Wong, D. T. H. Tan, et al. (2001). "Myopia in Singapore: taking a public health approach." *British Journal of Ophthalmology* **85**: 521-526.

Seidel, D., L. S. Gray and G. Heron (2003). "Retinotopic accommodation responses in myopia." *Investigative Ophthalmology and Visual Science* **44**(3): 1035-1041.

Seidel, D., L. S. Gray and G. Heron (2005). "The effect of monocular and binocular viewing on the accommodation response to real targets in emmetropia and myopia." *Optometry and Vision Science* **82**(4): 279-285.

Seko, Y., M. Shimizu and T. Tokoro (1998). "Retinoic acid increases in the retina of the chick with form deprivation myopia." *Ophthalmic Research* **30**: 361-367.

Shaikh, A. W., J. T. Siegward and T. T. Norton (1999). "Effect of interrupted lens wear on compensation for a minus lens in tree shrews." *Optometry and Vision Science* **76**(5): 308-803.

Shapley, R. M. (1997). "Retinal physiology: Adapting to the changing scene." *Current Biology* **7**(7): R421-R423.

Shapley, R. M. and J. D. Victor (1978). "The effect of contrast on the transfer properties of cat retinal gangion cells." *Journal of Physiology* **285**: 275-298.

Shapley, R. M. and J. D. Victor (1981). "How the contrast gain control modifies the frequency responses of cat retinal ganglion cells." *Journal of Physiology* **318**: 161-179.

Sheppard, A. L. and L. N. Davies (2010). "Clinical evaluation of the Grand Seiko AutoRefractor/Keratormeter WAM-5500." *Ophthalmic and Physiological Optics* **30**: 143-151.

Siegward, J. T. and T. T. Norton (1999). "Regulation of the mechanical properties of tree shrew sclera by the visual environment." *Vision Research* **39**: 387-407.

Siegwart, J. T. and T. T. Norton (1999). "Regulation of the mechanical properties of tree shrew sclera by the visual environment." *Vision Research* **39**: 387-407.

Simonelli, N. M. (1983). "The dark focus of the human eye and its relationship to age and visual effect." *Human Factors* **25**: 85-92.

Sivak, J. G., D. L. Barrie and J. A. Weerheim (1989). "Bilateral experimental myopia in chicks." *Optometry and Vision Science* **66**: 854-858.

Smirnakis, S. M., M. J. Berry, D. K. Warland, et al. (1997). "Adaptation of retinal processing to image contrast and spatial scale." *Nature* **386**: 69-73.

Smith, E. L. and L. F. Hung (1999). "The role of optical defocus in regulating refractive development in infant monkeys." *Vision Research* **39**: 1415-1435.

Smith, E. L. and L. F. Hung (2000). "Form-deprivation myopia in monkeys is a graded phenomenon." *Vision Research* **40**: 371-381.

Smith, E. L., L. F. Hung, C. S. Kee, et al. (2002). "Effect of brief periods of unrestricted vision on the development of form-deprivation myopia in monkeys." *Investigative Ophthalmology and Visual Science* **19**: 135-150.

Smith, E. L., C. S. Kee, R. Ramamirtham, et al. (2005). "Peripheral vision can influence eye growth and refractive development in infant monkeys." *Investigative Ophthalmology and Visual Science* **46**: 3965-3972.

Smyth, D., B. Willmore, G. E. Baker, et al. (2003). "The receptive-field organization of simple cells in primary visual cortex of ferrets under natural scene stimulation." *The Journal of Neuroscience* **23**(11): 4746–4759.

Solberg, J. L. and J. M. Brown (2002). "No sex differences in contrast sensitivity and reaction time to spatial frequency." *Perceptual and Motor Skills* **94**: 1053-1055.

Soloman, S. G., J. W. Peirce, N. T. Dhruv, et al. (2004). "Profound contrast adaptation early in the visual pathway." *Neuron* **42**: 155-162.

Solomon, S. G., J. W. Peirce, N. T. Dhruv, et al. (2004). "Profound contrast adaptation early in the visual pathway." *Neuron* **42**: 155-162.

Stone, R. A., T. Lin, A. M. Laties, et al. (1989). "Retinal dopamine and form-deprivation myopia." *Proceedings of the Natural Academic of Science, USA* **86**: 704-706.

Strang, N. C., M. Day, L. S. Gray, et al. (2011). "Accommodation steps, target spatial frequency and refractive error." *Ophthalmic & Physiological Optics* **31**: 444-455.

Strang, N. C., B. Winn and B. Gilmartin (1994). "Repeatability of post-task regression accommodation in emmetropia and late-onset myopia." *Ophthalmic and Physiological Optics* **14**(1): 88-91.

Suzumura, A. (1979). "Accommodation in myopia." *Journal of Aichi Medical University Association* **7**: 6-15.

Tan, L. H., A. R. Laird, K. Li, et al. (2005). "Neuroanatomical correlates of phonological processing of Chinese characters and alphabetic words: A meta-analysis." *Human Brain Mapping* **25**: 83-91.

Tan, L. H., H. L. Liu, C. A. Perfretti, et al. (2001). "The neural system underlying Chinese logograph reading." *NeuroImage* **13**: 836-846.

Tan, L. H. and C. A. Perfetti (1998). "Phonological codes as early sources of constraint in Chinese word identification: A review of current discoveries and theoretical accounts." *Reading and Writing* **10**: 165-200.

Tan, N. W. H., S. M. Saw, D. S. C. Lam, et al. (2000). "Temporal variations in myopia progression in Singaporean children within an academic year." *Optometry and Vision Science* **77**(9): 465-472.

Tay, M. T. H., K. G. Au Eong, C. Y. Ng, et al. (1992). "Myopia and educational attainment in 421,116 young Singaporean males." *Annals of the Academy of Medicine Singapore* **21**(6): 785-791.

Thorn, F., L. Cameron, J. Arnel, et al. (1998). Myopia adults see through defocus better than emmetropes. In: Proceedings of the 6th International Myopia Conference. T. Tokoro (ed). Tokyo, Springer-Verlag**:** 368-374.

Thorn, F., T. R. Corwin and J. P. Comerford (1986). "High myopia does not affect contrast sensitivity." *Current Eye Research* **5**(9): 635-640.

Troilo, D., M. D. Gottlieb and J. Wallman (1987). "Visual deprivation causes myopia in chicks with optic nerve section." *Current Eye Research* **6**: 993-999.

Troilo, D. and S. T. Judge (1993). "Ocular development and visual deprivation myopia in the common marmoset (Callithrix jacchus)." *Vision Research* **33**(10): 1311-1324.

Troilo, D., D. Nickla and C. F. Wildsoet (2000). "Form deprivation myopia in mature common marmosets (Callithrix jacchus)." *Investigative Ophthalmology and Visual Science* **41**: 2043-2049.

Troilo, D., D. L. Nickla, J. R. Mertz, et al. (2006). "Changes in the synthesis rates of ocular retinoic acid and scleral glycosaminoglycan during experimentally altered eye growht in Marmoset." *Investigative Ophthalmology and Visual Science* **47**(5): 1768-1777.

Vannas, A. E., G. S. Ying, R. A. Stone, et al. (2003). "Myopia and natural lighting extremes: risk factors in Finnish army conscripts." *Acta Ophthalmologica Scandinavica* **81**: 588-595.

Vaquero, C. F., A. Pignatelli, G. J. Partida, et al. (2001). "A dopamine- and protein kinase A-dependent mechanism for network adaptation in retinal ganglion cells." *The Journal of Neuroscience* **21**(21): 8624–8635.

Vasudevan, B. and K. J. Ciuffreda (2008). "Additivity of near work-induced transient myopia and its decay characteristics in different refractive groups." *Investigative Ophthalmology and Visual Science* **49**(2): 836-841.

Vasudevan, B., K. J. Ciuffreda and B. Gilmartin (2009). "Sympathetic inhibition of accommodation after sustained nearwork in subjects with myopia and emmetropia." *Investigative Ophthalmology and Visual Science* **50**(1): 114-120.

Vasudevan, B., K. J. Ciuffreda and B. Wang (2007). "Nearwork-induced changes in topography, aberrations and thickness of the human cornea after interrupted reading." *Cornea* **26**(8): 917-923.

Vera-Diaz, F. A., J. Gwiazda, F. Thorn, et al. (2004). "Increased accommodation following adaptation to image blur in myopes." *Journal of Vision* **4**: 1111-1119.

Vera-Diaz, F. A., N. C. Strang and B. Winn (2000). "Accommodation in progressing myopia, stable myopia and emmetropia." *Investigative Ophthalmology and Visual Science* **41**(4): S815.

Vera-Diaz, F. A., N. C. Strang and B. Winn (2002). "Nearwork induced transient myopia during myopia progression." *Current Eye Research* **24**(4): 289-295.

Victor, J. D. (1987). "The dynamics of the cat retinal x cell centre." *Journal of Physiology* **386**: 219-246.

Vidyasagar, T. R. (1990). "Pattern adaptation in cat visual cortex is a co-operative phenomenon." *Neuroscience* **36**.

Villarreal, G. M., J. Ohlsson, H. Cavazos, et al. (2003). "Prevalence of Myopia among 12- to 13-Year-Old Schoolchildren in Northern Mexico." *Optometry and Vision Science* **80**(5): 369-373.

Vitale, S., L. Ellwein, M. F. Cotch, et al. (2008). "Prevalence of refractive error in the United States, 1999-2004." *Archives of Ophthalmology* **126**(8).

Wallman, J. and J. I. Adams (1987). "Developmental aspects of experimental myopia in chicks: susceptibility, recovery and relation to emmetropization." *Vision Research* **27**(7): 1139-1163.

Wallman, J., M. D. Gottlieb, V. Rajaram, et al. (1987). "Local retinal regions control local eye growth and myopia." *Science* **237**: 73-77.

Wallman, J. and J. Turkel (1978). "Extreme myopia produced by modest change in early visual experience." *Science* **201**: 1249-1251.

Wallman, J. and J. Winawer (2004). "Homeostasis of eye growth and the question of myopia." *Neuron* **43**: 447-468.

Wang, Q., B. E. Klein, R. Klein, et al. (1994). "Refractive status in the Beaver Dam Eye Study." *Investigative Ophthalmology and Visual Science* **35**: 4344-4347.

Whitefoot, H. and W. N. Charman (1992). "Dynamic retinoscopy and accommodation." *Ophthalmic and Physiological Optics* **12**: 8-17.

Wiesel, T. N. (1981). "The postnatal development of the visual cortex and the influence of environment." *Physiology of Medicine* **Nobel lecture** 61-83.

Wiesel, T. N. and D. H. Hubel (1963). "Single cell responses in striate cortex of kittens deprived of vision in one eye." *Journal of Neurophysiology* **26**: 1003-1017.

Wiesel, T. N. and E. Raviola (1977). "Myopia and eye enlargement after neonatal lid fusion in monkeys." *Nature* **266**: 66-68.

Wildsoet, C. F. (1997). "Active emmetropization - evidence for its existence and ramifications for clinical practice." *Ophthalmic and Physiological Optics* **17**(4): 279-290.

Wildsoet, C. F. and J. D. Pettigrew (1988). "Experimental myopia and anomalous eye growth patterns unaffected by optic nerve section in chickens: evidence for local control of eye growth." *Clinical Vision Science* **3**: 99-107.

Wildsoet, C. F. and K. L. Schmid (2000). "Optical correction of form deprivation myopia inhibits refractive recovery in chick eyes with intact or sectioned optic nerves." *Vision Research* **40**: 3273-3282.

Wildsoet, C. F. and J. Wallman (1995). "Choroidal and scleral mechanisms of compensation for spectacle lenses in chicks." *Vision Research* **35**(9): 1175-1194.

Wilson, H. R. and R. Humanski (1993). "Spatial frequency adaptation and contrast gain control." *Vision Research* **33**(8): 1133-1149.

Win-Hall, D. M., L. A. Ostrin, S. Kasthurirangan, et al. (2007). "Objective accommodation measurement with the Grand Seiko and Hartinger coincidence refractometer." *Optometry and Vision Science* **84**(9): 879-887.

Winawer, J. and J. Wallman (2002). "Temporal constraints on lens compensation in chicks." *Vision Research* **42**: 2651-2668.

Witkovsky, P. (2004). "Dopamine and retinal function." *Documenta Ophthalmologica* **108**: 17-40.

Wolffsohn, J. S., B. Gilmartin, R. W. H. Li, et al. (2003). "Nearwork-induced transient myopia in preadolescent Hong Kong Chinese." *Investigative Ophthalmology and Visual Science* **44**(5): 2284-2289.

Wolffsohn, J. S., C. O'Donnell, W. N. Charman, et al. (2004). "Simultaneous contiuous recording of accommodation and pupil size using the modified Shin-Nippon SRW-5000 autorefractor." *Ophthalmic and Physiological Optics* **24**(2): 142-147.

Wong, T. Y., P. J. Foster, J. Hee, et al. (2000). "Prevalence and risk factors for refractive errors in adult Chinese in Singapore." *Investigative Ophthalmology and Visual Science* **41**(9): 2486-2494.

Woodman, E. C., S. A. Read, M. J. Collins, et al. (2010). "Axial elongation following prolonged near work in myopes and emmetropes." *British Journal of Ophthalmology* **10.1136/bjo.2010.180323**.

Woods, R. L., N. C. Strang and D. A. Atchison (2000). "Measuring contrast sensitivity with inappropriate optical correction." *Ophthalmic and Physiological Optics* **20**(6): 442-451.

Woung, L. C., Y. F. Lue and Y. F. Shih (1998). "Accommodation and pupillary response in early-onset myopia among schoolchildren." *Optometry and Vision Science* **75**(8): 611-616.

Wu, H. M., B. Seet, E. P. H. Yap, et al. (2001). "Does education explain ethnic differences in myopia prevalence? A population-based study of young adult males in Singapore." *Optometry and Vision Science* **78**(4): 234-239.

Yang, Z., W. Lan, J. Ge, et al. (2009). "The effectiveness of progressive addition lenses on the progression of myopia in Chinese children." *Ophthalmic and Physiological Optics* **29**: 41-48.

Yap, M. K. H., L. F. Garner, R. F. Kinnear, et al. (1999). Tonic accommodation and refractive change in children. In: Proceedings of the 7th International Myopia Conference L. L. K. Lin, Y. F. Shih and P. T. Hung (ed). Taipei, Taiwan, New York: Springer-Verlag**:** 59-60.

Yap, M. K. H., M. Wu, Z. M. Liu, et al. (1993). "Role of hereditary in the genesis of myopia." *Ophthalmic and Physiological Optics* **13**: 316-319.

Yeo, A. C. H., K. K. Kang and W. Tang (2006). "Accommodative stimulus response curve of emmetropes and myopes." *Annals of the Academy of Medicine Singapore* **35**: 868-874.

Young, T. L., S. M. Ronan, A. B. Alvear, et al. (1998). "A second locus for familial high myopia maps to chromosome 12q." *The American Journal of Human Genetics* **63**: 1419-1424.

Young, T. L., S. M. Ronan, L. A. Drahozal, et al. (1998). "Evidence that a locus for familial high myopia maps to chromosome 18p." *The American Journal of Human Genetics* **63**: 109-119.

Zadnik, K. (1995). "Myopia development in childhood." *Optometry and Vision Science* **74**(8): 603-608.

Zadnik, K., L. A. Jones, B. C. Irvin, et al. (2000). "Brief communications: Myopia and ambient lighting at night." *Nature* **404**(143).

Zadnik, K., G. L. Mitchell, L. A. Jones, et al. (2004). Accommodative lag at the onset of myopia in children. In: Proceedings of the Tenth International Myopia Conference. D. J. O'Leary, H. Rakhakrishnan and S. Pardhan (ed). Cambridge, UK**:** 10.

Zadnik, K., D. O. Mutti, H. S. Kim, et al. (1999). "Tonic accommodation, age, and refractive error in children." *Investigative Ophthalmology and Visual Science* **40**(6): 1050-1060.

Zadnik, K., W. A. Santariano, D. O. Mutti, et al. (1994). "The effect of parental history of myopia on children's eye size." *Journal of the American Medical Association* **271**(17): 1323-1327.

Zhang, M. Z., S. M. Saw, R. Z. Hong, et al. (2000). "Refractive errors in Singapore and Xiamen, China- a comparative study in school children aged 6 to 7 years." *Optometry and Vision Science* **77**(6): 302-308.

Zhu, X., T. W. Park, J. Winawer, et al. (2005). "In a matter of minutes, the eye can know which way to grow." *Investigative Ophthalmology and Visual Science* **46**(7): 2238-2241.

Zhu, X. and J. Wallman (2009). "Temporal properties of compensation for positive and negative spectacle lenses in chicks." *Investigative Ophthalmology and Visual Science* **50**(1): 37-46.