An investigation into reading ability using eye movement recordings in strabismic amblyopia

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by

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1. Introduction

1.1 Amblyopia

1.1.1 Definition

Amblyopia or 'lazy eye' has conventionally been defined as "a unilateral or bilateral decrease of visual acuity caused by deprivation of pattern vision or abnormal binocular interaction, for which no cause can be detected by physical examination of the eye and which in some cases can be reversed by therapeutic measures" (1).

Clinically, amblyopia is defined as a reduction in best-corrected visual acuity to less than 6/9 monocularly in Snellen optotype or as a two-line difference or more in best-corrected visual acuity between the eyes in LogMAR optotype. This compares with findings in normal subjects, in which the interocular difference in best-corrected visual acuity has been found to be less than two lines (0.2 LogMAR optotype) in both infants and adults (2). However, clinical definitions are debated with different studies using different inclusion criteria for the amblyopic subjects participated.

1.1.2 Prevalence

Amblyopia is a significant cause of unilateral visual deficit in childhood and is still considered as one of the most common causes of persistent unilateral visual impairment in adulthood, including populations in which advanced medical care is offered. The prevalence of amblyopia detected in children is estimated between 0.2-5.4% (3-30, 30-35) and in adults between 0.35-3.6% (36-41). It is also classified among the major causes of unilateral visual loss in visually impaired children (13, 42-47) and adults (48-60), in parallel with refractive error, retinal lesions, cataract, corneal opacities and age-related macular degeneration. However, prevalence estimates of amblyopia are affected by the criteria of visual loss used to define amblyopia, the socio-economic properties of the population, the efficacy of the applied screening programmes for amblyopia and amblyogenic risk factors and the effectiveness of the prescribed treatment regimens (1, 24, 61-72).

1.1.3 Aetiology

Amblyopia is a form of cerebral visual impairment, in the absence of an organic cause (73-76). It is considered to derive from the degradation of the retinal image associated with abnormal visual experience during the developmental period of the visual system in infancy and early childhood (73-76). Children with anisometropia, strabismus or any other condition causing a reduction in the clarity of the image in one or both eyes, thereby disrupting equal binocular vision, are at risk of developing amblyopia (74-76).

Amblyopia is therefore classified according to the type of pathology underlying the abnormal binocular interaction and/or form vision deprivation as (1, 77): (i) *Anisometropic*, in which a difference in the refractive error between the two eyes represents a risk for developing amblyopia due to creation of dissimilar images; (ii) *Strabismic*, in which the confusion and diplopia caused by the misalignment of the visual axes of the two eyes can lead to binocular rivalry and suppression of input from the deviating eye at the level of the visual cortex; (iii) *Mixed*, if anisometropic and strabismic amblyopia co-exist and, (iv) *Stimulus deprivation*, if there is some obstruction to vision during the sensitive period of visual development (opacities in the media e.g. cataract or severe ptosis).

The results of the adult population study of *Attebo et al* (39) indicated that, the predominant cause of amblyopia was anisometropia in 50%, followed by strabismus in 19%, mixed in 27% and visual deprivation in 4%.

1.1.4 Neural Correlates

Extensive research has been undertaken mainly on animal models and more recently on humans in order to determine the neural correlates of the amblyopic deficit and the explanation of the pathophysiologic mechanism of amblyopia. The whole visual pathway has been implicated, from retina through to extra-striate cortex although the striate cortex deficit is best understood. *Hubel and Wiesel* (78-80) were the first to conclude that deprivation has a competitive impact in cortical cells amongst the early pioneers in the field of the anatomical and physiological properties of the visual cortical cells in animal models. The authors reached their conclusion by means of single cell recordings from the visual cortex of kittens and monkeys with unilateral visual deprivation. They established that alternating ocular dominance columns of visual cortical cells reacted selectively to the stimulus of the opened or the occluded eye.

Animal models of amblyopia were used to investigate the neuronal correlates in the visual cortex of animals with experimentally induced strabismus or anisometropia. These animal models revealed changes in the properties of the striate visual cortex (V1), the extent of which seems to depend upon the depth of amblyopia, whilst cortical binocularity appears to depend upon the type of amblyopia (76, 81). In particular, it has been shown that severe amblyopia can cause a change in eye dominance away from the affected eye. However in moderate amblyopia there seems to be a shift in eye dominance only for higher spatial frequencies, with ocular dominance being more balanced for low spatial frequencies particularly with anisometropic amblyopia. Furthermore, animals with strabismic amblyopia seemed to have a reduced number of binocularly activated neurones, compared to the cortex of anisometropic amblyopes. It has also been shown that the site of the amblyopic deficit extends beyond the primary visual cortex, as the neural deficits associated with amblyopia were not confined to the the visual cortex, but extended to include the lateral geniculate nucleus (81, 82).

Functional magnetic resonance imaging techniques (fMRI) have contributed greatly in investigating and illustrating neural changes in humans. The cortical function of humans with strabismic amblyopia was assessed by *Barnes et al* (83) using fMRI techniques and radial sinusoidal grating stimuli of variable spatial frequency. No evidence of normal function in any visual area, including V1 and V2, was seen in any of the subjects, even for stimuli with a spatial frequency within the amblyopic passband (figure 1.1). The authors suggested that V1 was possibly the earliest abnormal site in amblyopia, however it was also argued that feedback from the extra-striate cortex to V1 could also result in a reduced response, with the primary abnormality being found in the extra-striate cortex.

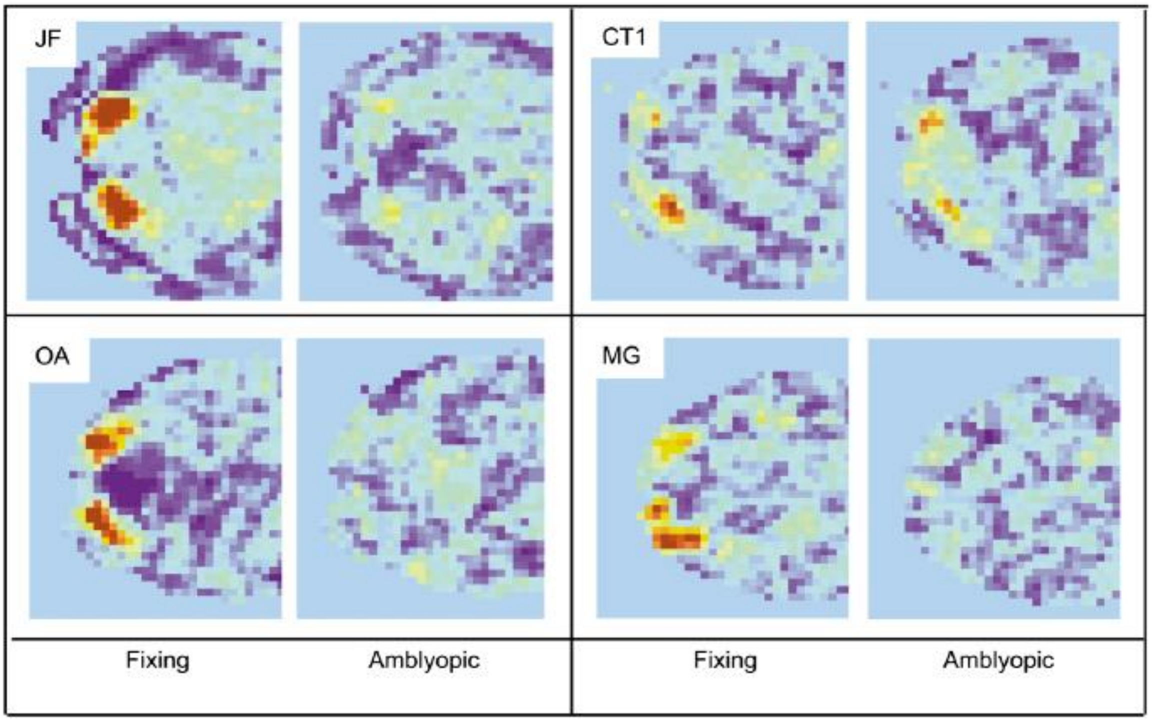


Figure 1.1. *Colour map t-statistic images for four subjects for fixing and amblyopic eye stimulation. Each panel shows the posterior portion of a single functional slice along the calcarine sulcus; typically the activity was located at the occipital pole consistent with the cortical representation of the fovea. Note that in all subjects, except CT1, there was a marked reduction in activity for amblyopic as compared to fixing eye stimulation. (from Barnes et al, 2001, [ref. no.83]).*

Whilst fMRI studies investigating contrast sensitivity by *Goodyear et al* (84) found no difference in the magnitude of the response to identical contrast stimuli in the early visual centres (V1 and V2) of both normal and amblyopic subjects, there appeared to be fewer activated image voxels in the amblyopic subjects. The authors argued that the elevated contrast thresholds found in amblyopia were the result of a reduced number of responsive neurons during stimulation of the amblyopic eye, rather than a reduced neuronal firing rate which seemed to be unaffected in amblyopia. However, it is also believed that neuronal defects in amblyopia might possibly be related to irregular sampling of the visual information by a normal number of neurons, rather than an absolute loss of neurons (85).

1.1.5 Period of critical development

The normal development and right function of the cortical neuronal circuits fundamentally depend on the clarity of the visual image and the equal perception of the visual stimuli with respect to the eyes (74-76, 86). In the stages of early visual development, the response to the visual environment by the cortical neurons is adaptive, in order that the plasticity mechanisms effect a neuronal response commensurate with the visual input (74-76, 86). Moreover, the cortical alterations detected in animal as well as human models with abnormal binocular interaction and/or form vision deprivation become irreversible with time (74-76, 86). Hence, amblyopia mirrors the results of the competition between the input by each eye to visual cortical cells (74-76, 86). The effect of binocular competition on the developing visual system depends on age and the period of plasticity represents the ‘critical’ period of visual development (74-76, 86). Animal models have been employed to investigate the extent and duration of this critical period.

In an attempt to define the critical period of brain plasticity, *Horton et al* (87) investigated the effects of monocular visual deprivation on the development of ocular dominance columns in the macaque cortex. They found that early occlusion had the greatest effects on the developing cortex, regarding the degree of the column shrinkage. In particular, occlusion at 1 week of age seemed to cause the most severe changes resulting in the most severe column shrinkage. When compared to the changes induced by occlusion at 5 weeks of age, the shrinkage was twice as great, whilst occlusion at 12 weeks of age had no effect on the columns. Output from the parvocellular channels of the lateral geniculate body that convey fine spatial information to the visual cortex were affected far more than that of the magnocellular channels which convey motion.

The data from the macaque cortex conflict with that of *Hubel and Wiesel* (88) who investigated the period of susceptibility on a cat model, where monocular occlusion before 4 weeks of age had no effect on visual development. However, there was impaired visual development between 4 and 8 weeks of age, even when the eye was occluded for as little as 3-4 days. This indicated that in the cat the visual system goes through a period where it is too immature to be affected by visual deprivation during the first few weeks of life. *Horton* (87) suggested that the macaque model, rather than the cat model, more closely equated with human visual development and argued that in the neonate, prompt treatment should be considered for all causes of unilateral deprivation.

The findings of these investigations have pinpointed a ‘sensitive period’ in the development of the system of vision, a period when visual deprivation and/or abnormal binocular interaction causes amblyopia (74-76). Furthermore, longitudinal vision screening programmes and evaluations of applied treatment regimens for amblyopia have established that the best approach to managing amblyopia is facilitated by detecting the amblyogenic factors before the age of two and preventing them (89). This is achieved by eliminating the causes for visual deprivation and/or abnormal binocular interaction. If amblyopia is detected in children, we can apply treatment for its reversal, ideally when the subjects are less than 6-7 years old (89). A degree of plasticity, however, has been observed in adults with amblyopia who have improved in visual function in the amblyopic eye after loss of vision in the non-amblyopic eye due to ocular trauma or disease or while undertaking orthoptic treatment during adulthood (90-101). This disputes the maximum age at which treatment of amblyopia can still be effective.

1.1.6 Treatment

In treating amblyopia, the main aim is the management of the primary amblyogenic condition, thus amplifying the visual stimulation of the amblyopic eye and assisting its visual input to the brain (75, 76). This is effected by adequately rectifying the refractive error, improving the clarity of the images and furthermore, by occluding the dominant eye, limiting its cortical input (1, 89, 102-107). Data loggers that monitor patching have been used successfully to demonstrate the effect of occlusion therapy (108-112). In particular, occlusion monitors provide the ability to objectively measure patching therapy and establish the relationship between functional improvement and effective dose of amblyopia treatment. However, occlusion therapy, despite its effectiveness in the treatment of amblyopia, can induce negative behavioral changes in children and adversely affect family life, which may also bear on the compliance with the prescribed therapy (1, 104). Simultaneously, care must be taken in order to avert visual deprivation amblyopia in the occluded eye (86, 103, 113).

1.1.7 Prognosis

The prognosis for visual function, after a systemic course of treatment in amblyopia, is related to the age of detection of the visual impairment, the cause and depth of amblyopia and the compliance with the prescribed treatment regimen (1, 89, 102). The compliance to treatment depends on the patient's age, the level of visual acuity in the non-amblyopic eye, the socio-economic status, the parental perception of the deficit and the credibility of treatment, as well as by the financial cost and psychosocial impact to patient and family (1, 89, 102, 114).

1.1.8 Disability associated with amblyopia

Apart from the impairment of visual acuity, the amblyopic (102, 115-142) and non-amblyopic eye (102, 143-157) in both strabismic and anisometropic amblyopia are characterized by abnormal contour interaction, inaccurate eye movements, reduced contrast perception and positional uncertainty, resulting in an extended functional visual loss. In everyday life, unilateral amblyopia is related to poor binocular vision, limited employment opportunities, as a result of the visual standards requirements posed by specific jobs and an increased risk of visual impairment when trauma or pathology inflict the normal eye (1, 73).

The most frequent functional consequence related to amblyopia, that affects binocular viewing, is reduced stereopsis (77, 86). Reduced depth perception has an adverse effect on many key tasks for pre-school and early-school aged children involving good hand-eye coordination, such as handwriting or scissor dexterity skills and on activities requiring comprehension of compound visual projects (1, 158).

Furthermore, visual function questionnaires employed in a study by *Sabri et al* (159) assessed the subjective-individual impact, visual and psychological, of a weaker eye and evident strabismus in adolescents. The findings of the study established that amblyopia and/or strabismus have negative effects on the subjective visual function and general well-being of teenagers.

Rahi et al (160), in a large population-based study found no significant functional and clinical differences between individuals with amblyopia and normal sighted participants regarding educational attainment, employment opportunities and socioeconomic achievements. Nevertheless, *Chua et al* (161) have pointed out that while amblyopia was not significantly related to lifetime occupations, the number of people suffering from amblyopia who had completed higher university degrees was considerably fewer. Moreover, amblyopia may hinder career choices, as certain jobs pose requirements on the visual standards of applicants (1, 73). This is especially true in the armed forces and the civil service sector.

Tommila and Tarkannen (162), in Finland, have estimated that the incidence of the loss of the healthy eye was 1.75/1000 in 35 adult individuals suffering from amblyopia, over a 20-year period, while the overall blindness rate of children was 0.11/1000 and of adults, aged 15-64 years, 0.66/1000 for the same period. In one population based study in the UK, of 370 individuals with unilateral amblyopia over a 24-months period, *Rahi et al* (163) have concluded that the projected life time risk of serious vision loss (socially significant visual impairment, severe visual impairment, visual impairment or blindness) in the fellow eye, due to ocular trauma or eye disease, was 1.2%-3.3%.

Chua et al (161), investigating 118 adult participants with amblyopia in Australia (Blue Mountains Eye Study), have reported a relative risk of 2.7% for the 5 year risk of bilateral visual impairment (BVI) among individuals with amblyopia. They estimated that the 5 year incidence of visual impairment in the better seeing eye in people at risk of vision loss worse than 6/12, occurred in 9/27 participants with amblyopia (33.3%), compared to 264/2114 without amblyopia (12.5%). *Leeuwen et al*

(164) also confirmed these findings in the Rotterdam study, involving a population-based cohort of 5220 subjects, with a mean age of 67.4 years, including 192 individuals with amblyopia. The authors have concluded that the relative risk of BVI for amblyopes was 2.6% and that the 5-year cumulative incidence of BVI was 1.4% for individuals aged 55-64 years, 4.8% for individuals aged 65-74 years and 13% for those aged 75-84 years. These figures were 0.3%, 1.2% and 5.0% for the non-amblyopic population. For individuals with amblyopia, the lifetime risk for BVI was 18%, whereas they lived on average 7.2 years with the deficit, while for the non-amblyopic individuals, these figures were 10% and 6.7 years, respectively.

Thus, the health cost to patients and the health service associated with visual disability caused by visual loss in the non-amblyopic eye of patients with amblyopia is considerable due to the high prevalence of amblyopia. This means that, the cost-utility of the vision screening programmes among the childhood population, as well as the cost effectiveness of the prescribed treatment regimens, although extensively argued, seem to be justified (165).

1.2 Reading

Reading is an extraordinarily sophisticated task involving a synthesis of a number of different motor, sensory and cognitive functions. In order to achieve reading, these functions combine accurate eye movements, perception of the visual stimuli, and processing of visual information at higher cortical levels, where the derived information is analyzed and integrated in a unique way.

1.2.1 Saccades and Fixations

Reading ability is dependent on macular function and eye movements show a clearly defined strategy during reading (166-168) (figure 1.2). When reading English text, eye movements consist of short and rapid movements called saccades, that typically move the eyes forward about 6-9 character spaces equal to 1-2° (166-168). Saccades take 20-50 ms to complete, depending upon the length of the movement and virtually no visual information is extracted during saccadic eye movements (166-168).

Between saccades, the eyes remain stationary for brief periods of time (typically 200-250 ms) called fixations (166-168). Visual information is only extracted from the printed page during fixations (166-168). Therefore, when reading English text, a series of short saccades and fixations are used to scan text across a line from left to right, followed by a larger leftward saccade to bring the gaze to the beginning of the next line (166-168).

A small number of saccades are in the opposite direction to the reading order of text (i.e. right to left in English reading), where the reader reprocesses a previously read word (166-168). These are called regressions and usually account for about 10-15% of the saccades made (166-168). Regressions are probably caused by problems with linguistic processing as well as oculomotor errors (166-168).

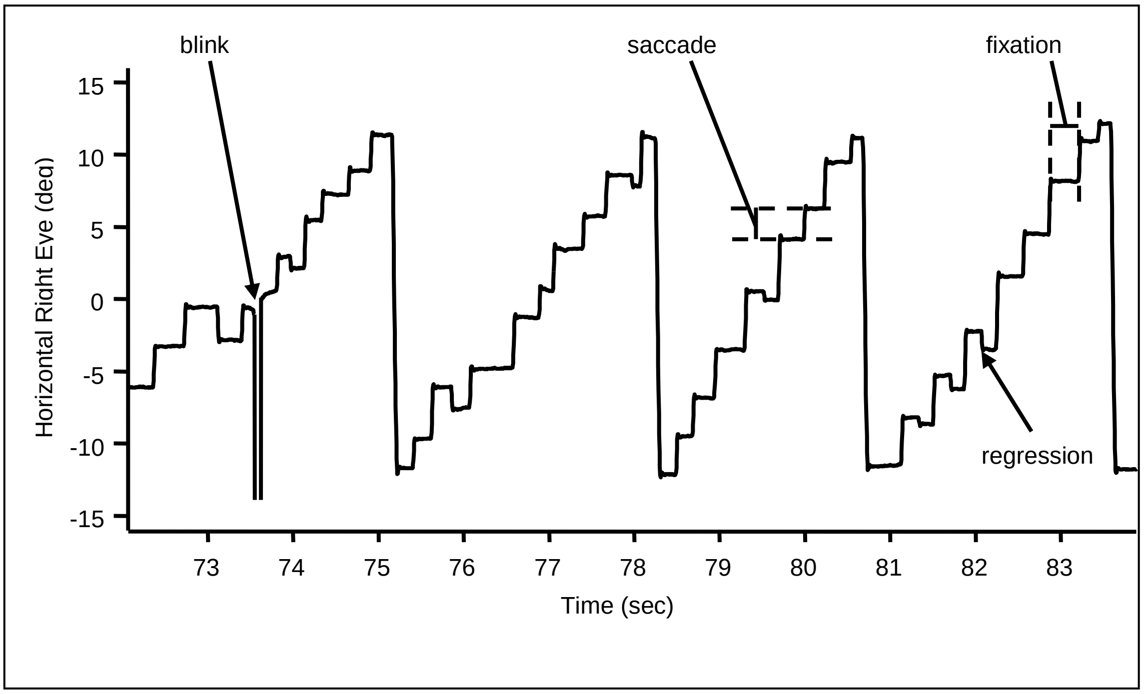


Figure 1.2. *Original recordings of eye-movement patterns of a normally sighted individual observed during reading. The reading parameters, namely saccades, fixations and regressions are highlighted. When reading English text a series of short saccades and fixations are used to scan text across a line from left to right followed by a longer forward saccade to bring the gaze to the beginning of the next line. A small number of saccades called regressions are in the opposite direction to the reading order of the text (i.e. right to left in English reading) where the reader reprocesses a previously read word. A blink as recorded in eye movement patterns derived is also illustrated.*

1.2.2 Visual span, Perceptual span, Uncrowded span.

Since reading ability relates to macular function, the frequency of saccades is attributed to acuity restrictions (166, 167, 169). Visual acuity attains its maximal function at the centre of the retina, sharply decreasing as we move towards the periphery and hence subtle discrimination is only possible in the region of the fovea, or the central 2º of vision (169). Furthermore, there is an inverse relation holding between the capacity for word recognition and the angular disparity between the fovea and the retinal image of the word (170). In practice, this means that a reader needs to fixate most words so that they can be identified (166, 167, 169).

Reading rate is determined by the "visual span", the "perceptual span" and, more recently, the "uncrowded span" has been recognized in relation to amblyopia (171-174). As reading consists of four fixations per second, *Legge et al* (171) suggested that the number of letters acquired in each fixation limits reading. Therefore, they defined the visual span in reading as the number of characters in a line of text that are recognized on each glance and estimated its extent to approximately 10 letters.

Rayner et al (172, 173) have demonstrated the importance of the parafoveal processing on reading rates and defined the perceptual span as the range of characters relative to the current fixation that affect the eye movements at reading. A technique called the eye-contingent display change technique, in which letters outside a window, spanning a given number of character spaces, are replaced with x's has been used to show that the region from which useful information can be encoded can extend as far as 14-15 character spaces to the right and 3-4 character spaces to the left of fixation.

Recently, *Pelli et al* (174) provided evidence for the uncrowded span, determined by the number of character positions in a line of text that are not crowded, spaced apart more than the critical spacing. They defined the critical spacing as the smallest centre-to-centre distance between letters that inhibits crowding. According to the uncrowded span theory, reading rate in healthy individuals and amblyopic subjects is proportional to the uncrowded span.

1.2.3 Eye movement control in reading

There is considerable variability in both saccade length and fixation duration, even in the reading performance of the same individual (166-168). Regarding the saccade length, saccades range from moving the eyes a single character forward to as much as 15-20 characters (166-168). Similarly, regarding the fixation duration, the range varies from shorter than 100ms to longer than 400ms (166-168). Controversy exists as to whether eye movement patterns are determined primarily by oculomotor factors (oculomotor models) or cognitive factors (processing models) or a combination of both (166-168, 175). Eye movement recording techniques have been used extensively to test the models that have been proposed to explain oculomotor control during reading (166-168, 175).

1.3 Background to the project

1.3.1 Amblyopia and Reading

Reading is typically included in assessments of visual function as it is one of the key visual tasks related to daily living. For various visual deficits, including amblyopia, reading speed measurements provide greater sensitivity about a visual impairment than simply recording visual acuity alone (176-180).

In fact, after having examined the reading capacity in fifty cases of ‘cured’ strabismic amblyopia, *Zürcher et al*. (176) concluded that, although linear vision for distance and near was full, reading capacity was markedly impaired. The authors recommended that occlusion treatment should continue until reading ability recovers, rather than just using visual acuity to determine successful outcome.

By using standardized reading charts for the simultaneous determination of reading acuity and speed, *Stifter et al.* (177) recently compared the monocular and binocular reading performance in children with unilateral microstrabismic amblyopia to normally sighted children with full visual acuity in both eyes. They found that, as well as the impaired reading performance with the amblyopic eye, the binocular maximum reading speed in children with microstrabismic amblyopia was significantly reduced compared to the normally sighted children (figure 1.3). No significant differences between the two groups were found, however, with respect to the binocular LogMAR visual acuity and reading acuity. In addition, during monocular reading performance with the amblyopic eye and the sound fellow eye in the amblyopic group, the maximum reading speed was found significantly impaired in the amblyopic eyes compared to the sound fellow eyes. As it was expected, a significant interocular difference in visual acuity and reading acuity was also recorded in the amblyopic group. Since reading speed is known to be closely related to visual function, these findings indicate the presence of a functionally relevant deficit that would be underestimated by acuity measurements only.

Thus, to improve treatment, in addition to visual acuity measurements, the authors also recommended that reading performance should be monitored over time, using standardized reading tests.

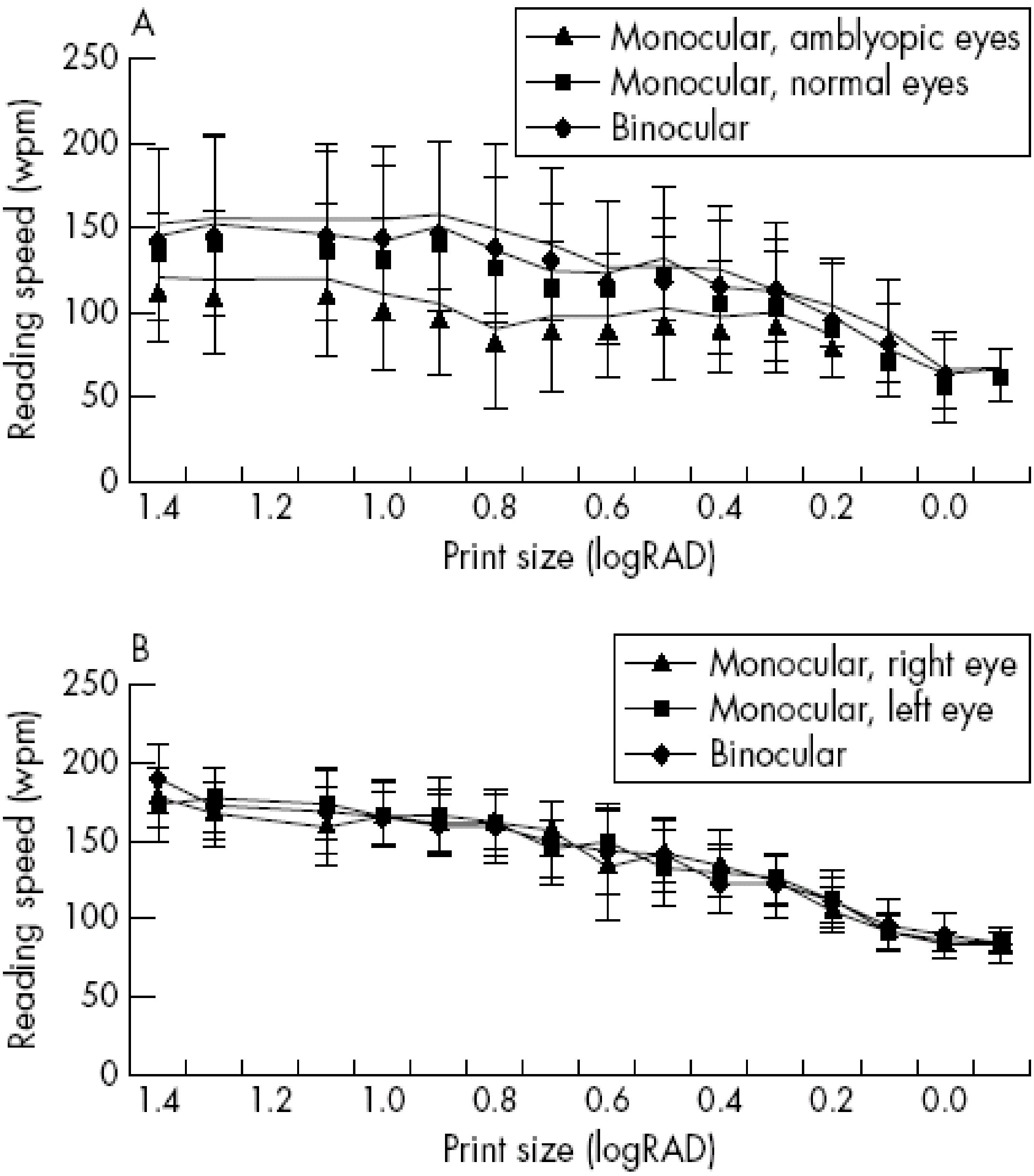


Figure 1.3. *Reading speed (words per minute = wpm) based on print size (logRAD) (A) in children with unilateral microstrabismic amblyopia; (B) in normal sighted controls (n = 40) (from Stifter et al, 2005 [ref. no. 177]).*

Additionally, after evaluating reading acuity and speed in another group of children with microstrabismic amblyopia using the same standardized reading chart system, *Stifter et al* (178) also recorded an impairment with respect to the maximum reading speed when the amblyopic eye was viewing compared to the non-amblyopic eye. Interestingly enough, in this investigation in eight amblyopic children, there was no significant interocular difference in visual acuity. Likewise, comparing the amblyopic with the non-amblyopic eye reading performance, using the abbreviated MNRead chart, *Rice et al* (179) found that the median reading speed was remarkably impaired when the amblyopic eye was viewing.

Patients with anisometropic amblyopia have also been reported to show reading deficits. While investigating the monocular reading performance with the amblyopic and non-amblyopic eye in children with anisometropic amblyopia, *Osarovsky et al* (180) concluded that monocular reading with the amblyopic eye was markedly impaired, compared to the non-amblyopic eye, with respect to the mean and the maximum reading speed. While exploring the relationship between specific reading disability in children and amblyopia, *Koklanis et al.* (181) showed that reading disorders were relatively rare in children with amblyopia. However, amblyopia seemed to be related to a lack of phonological awareness and a difficulty in decoding words. Strabismic amblyopia and the lack of binocular vision functions were particularly linked to poor phonological skills and a deficient speed when naming aloud a sequence of recognizable visual stimuli. This rapid automized naming (RAN) ability, developed by *Denkla and Rudel* (182), was considered a reliable means for predicting future reading ability.

Levi et al (183) recently suggested that “amblyopic reading is crowded”. The authors postulated that the amblyopic deficit during reading performance was mainly due to the increased crowding effect in the amblyopic fovea, rather than to decreased acuity, and speculated that reading rates in amblyopia could be predicted by the uncrowded span theory (174) (figure 1.4). By using the Rapid Serial Visual Presentation technique, they noticed that the critical spacing (i.e. the spacing between the letters required to read at maximum speed) was increased in the amblyopic subjects. It was about five times higher than the normal critical spacing with the amblyopic eye viewing and about twice the normal critical spacing with the non-amblyopic eye viewing. The maximum central reading rate was, therefore, practically equal in the two eyes of the amblyopes, when the centre-to-centre spacing of the letters was adequate to achieve fluent reading, while the maximum peripheral reading rate showed no interocular difference over the whole range of letter spacing tested (figure 1.5).

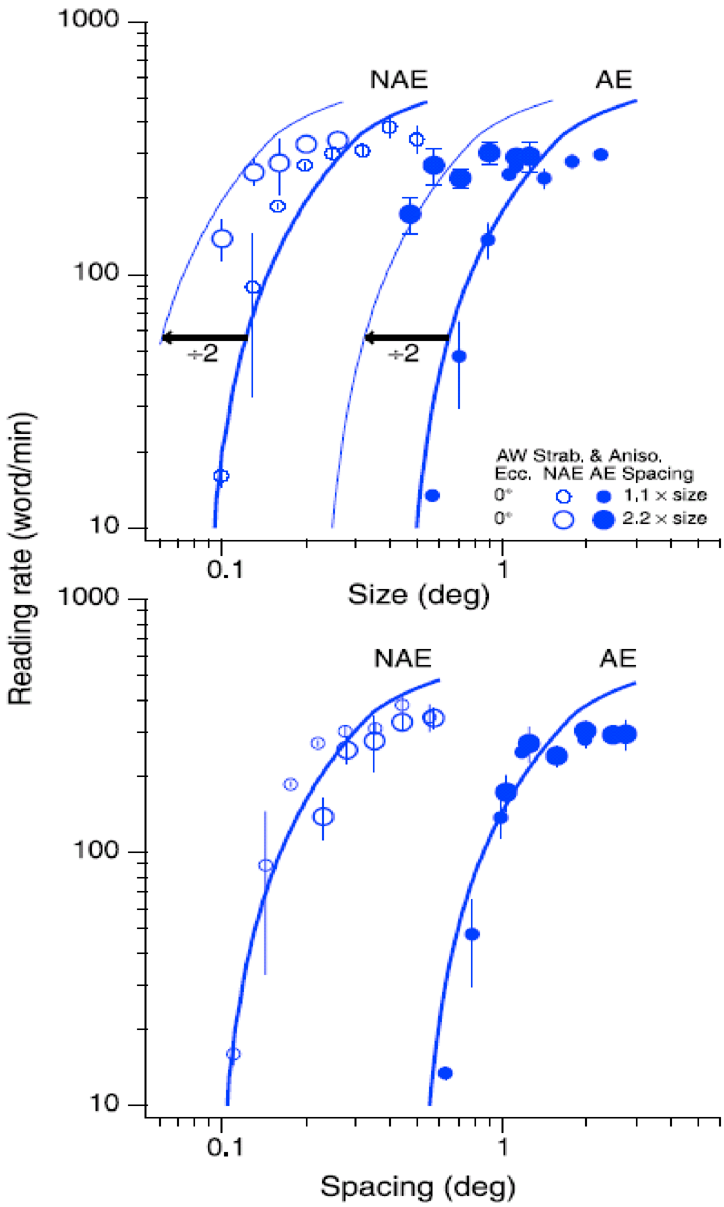


Figure 1.4. *Reading rate versus size (top) and spacing (bottom) for each eye of an amblyope (strabismic and anisometropic). The small symbols are for normal spacing (1.1 x size), and the large symbols are for double spacing (2.2 x size). The thick lines are the best fit of the uncrowded-span model (Pelli et al., 2007) to the normal-spacing data. The thin lines in the top graph are copies, shifted left (arrows) by a factor of 2, to predict the double-spacing data if spacing limits reading. One observer's reading performance was measured with normal and doubled letter spacing (i.e. 1.1 and 2.2 times the letter size). In the size graph (top), doubling the spacing displaces the data a factor of 2 to the left, showing that spacing matters. In the spacing graph (bottom), doubling the size has no effect (both data sets lie on the same curve), showing that size does not matter) (from Levi et al, 2007 [ref. no. 183]).*

Finally, while comparing the amblyopic central vision reading with the normal peripheral vision reading, the authors suggested that amblyopic fovea did not resemble normal periphery. This was based to their observation that, although the required spacing in order to read at maximum speed was increased in the amblyopic central vision, maximum reading rate was preserved and was similar to normal central vision (figure 1.5).

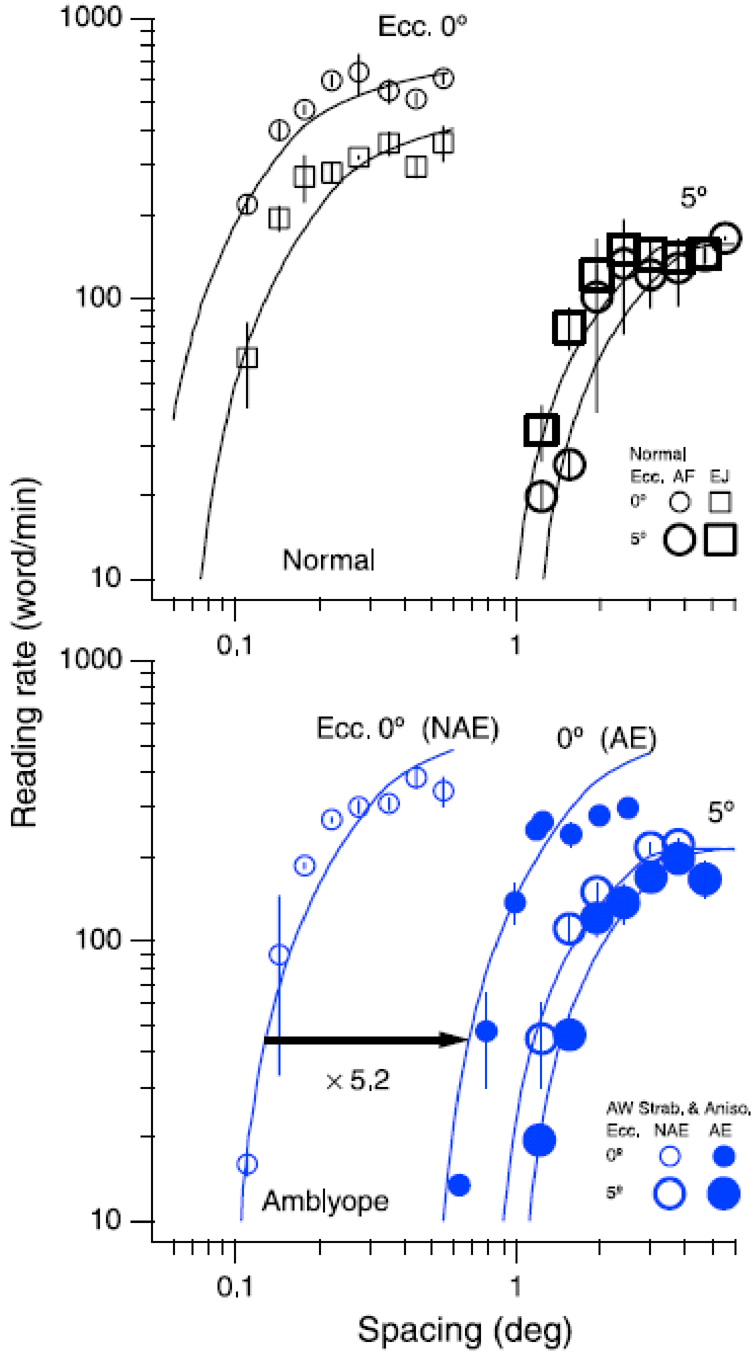


Figure 1.5. *Reading rate versus spacing. (Top) Reading rate for two normal observers viewing centrally (small symbols) or at 5- in the lower visual field (large symbols). (Bottom) Reading rate for each eye of an amblyopic observer (A.W.) with both strabismus and anisometropia: non-amblyopic (open symbols) and amblyopic (solid symbols). The lines are the best fit of the uncrowded-span model (Pelli et al., 2007). The arrow shows the difference between the amblyope's eyes, documenting the shift of the foveal reading curve to the right to larger spacing (ratio of AE to NAE). Reading rate increases rapidly with print size and then, beyond the critical print size, asymptotes to a maximum reading rate. Chung et al. (1998) showed that the curve measured in the*

normal periphery is similar in shape to that measured centrally but is shifted to the right (larger print sizes) and down (slower maximum reading rates). Figure (top) replicates their result in two normal observers. Figure (bottom) compares the amblyopic and non-amblyopic eyes of one amblyope, showing that in amblyopic central vision, as in the normal periphery, the curve is shifted rightward, as indicated by the arrow. However, unlike the peripheral reading rate, the maximum central reading rate is practically the same in the two eyes. For this amblyopic eye, the curve for central vision is shifted to the right by a factor of 5.2, whereas the peripheral curve is hardly affected by amblyopia (from Levi et al, 2007 [ref. no. 183]).

1.3.2 Eye movements and reading with central field loss

Amblyopic fovea has been hypothesized to resemble normal periphery. Specifically, both amblyopic central vision and normal peripheral vision are regarded as degraded visual systems compared to normal central vision. Amblyopic fovea and normal periphery are similar, in many ways, both being characterized by increased crowding and reduced vernier acuity (133, 134, 151, 169, 184-186) compared to normal vision.

In strabismus, in order to eliminate confusion and diplopia during binocular visual function, the visual system adopts suppression (187-189). Furthermore, the locus of fixation has been found to be shifted to an eccentric retinal area in a significant proportion of patients suffering from strabismic amblyopia (190-193). Therefore, it is pertinent to review the outcome of the extensive research that has been undertaken with respect to eye movement adaptations while reading with central field loss.

When the centre of a reader’s visual field is obscured, reading speed declines and oculomotor pattern differs, compared to normal reading (169). The developed reading strategies have been thoroughly investigated in individuals with central field loss either induced artificially or related to eye pathology.

1.3.2.1 Reading performance in normal subjects with simulated foveal scotomas

Rayner et al (166,167, 172) investigated the effects of artificial scotomas on reading performance in normal subjects and highlighted the importance of the foveal vision capabilities during reading. In their foveal masking paradigm, central scotomas were simulated using the eye-contingent display change technique to create foveal masks, subtending between 1 and 17 characters size. The masks moved across the presenting text in synchrony with the reader’s eye movements, which were recorded using the Dual-Purkinje eye-tracking system. The authors noted the strong negative relationship between the number of centrally masked characters and reading rate and concluded that reading speed deteriorates strikingly with increasing mask size. It was interesting to observe that even a single letter size foveal mask caused a reduction in reading speed to one-half its normal value.

Furthermore, increasing the mask size resulted in a change in oculomotor parameters, such as an increase in the mean fixation duration, the number of progressive/forward saccades and the number of regressive/backward saccades. These changes were also associated with difficulties in comprehension of the presented reading material indicated by the dramatic reduction in the number of correctly reported sentences. It should be noted however, that the reading material was presented in a fixed print size, so increasing the mask size would have resulted in a reduced perceptibility of the reading text.

In an attempt to extend Rayner's investigation, *Fine et al* (194) tried to determine whether the number of letters masked or the size of the mask in degrees was the main component resulting in decreased reading rates. By varying the number of letters masked in reading text, across several mask sizes and recording the eye movements using a dual-Purkinje-image eyetracker, the authors found that the number of letters masked was the predominant factor affecting reading behavior until mask size was 7.5° and the number of letters masked more than seven. Thus, an increased font size may adequately compensate for the reduced reading rates observed in patients suffering from central scotomas.

1.3.2.2. Reading performance in patients with foveal scotomas

Extensive research has been undertaken in eye movement characteristics during reading with the use of infrared gazetrackers and more recently, with the employment of the scanning laser ophthalmoscope in patients suffering from central field loss. One of the characteristic features of macular degenerations, such as age-related macular degeneration (AMD) and Stargardt's disease, is the development of an absolute central scotoma (169). In almost all of the affected individuals, the loss of foveal vision is followed by Preferred Retinal Loci (PRL) in order to fixate steadily on objects of interest using one or more extra-foveal areas. A number of studies have highlighted the importance of preferred retinal loci awareness during reading, as well as the number and location of the preferred retinal loci used while performing a reading task.

Crossland et al (195) investigated the significance of preferred retinal locus development during reading in patients with central scotomas due to macular disease. The authors recorded fixational eye movements using a scanning laser ophthalmoscope and infrared gaze-traker and evaluated reading rates using "MN-Read" style sentences as reading material. They concluded that reading speed was not significantly associated with PRL location or the presence of multiple PRLs. However, patients who lack consciousness of employing a non-central retinal area for fixation but still adjust their oculomotor behavior to use consistent repeatable PRLs while reading, actually exhibit higher reading rates.

In order to evaluate the importance of using more than one multiple preferred retinal loci during reading, *Deruaz et al* (196) studied the eye movement patterns in patients with central scotomas and multiple preferred retinal loci. The authors used a scanning laser ophthalmoscope to record fixational eye movements. They concluded that patients with foveal loss tended to use at least two PRLs during reading in order to acquire a global view of the text with the use of the one PRL and to obtain further detail with the use of the other PRL.

The choice of the exact position for the PRL development has not been fully understood yet, especially for tasks requiring fixation such as reading. *Alpeter et al* (197) have shown that, apart from the obstructive aspect of the foveal scotoma and the developed correspondence in binocular visual function, the topographical variations in attentional performance may play a key role.

Sunccess et al (198) investigated the location of the eccentric PRL for fixation, as well as the fixation patterns during reading in patients with central scotomas, due to age-related macular degeneration, using a scanning laser ophthalmoscope. They noted that there was a preference for fixation with the scotoma placed to the right in the majority of the participants, which resulted in faster reading rates, compared to patients who fixated with the scotoma to the left of fixation. In particular, in patients fixating with the scotoma to the right, a reading rate of ≥50 words/min was achieved in 38%-100% of the eyes, depending on the extent of the retinal lesion. In patients who fixated with the scotoma to the left, none of the eyes demonstrated a reading rate of ≥50 words/min. The authors suggested, therefore, that this arrangement of PFL and scotoma might be advantageous for reading because it indicated where the fixation has landed, with respect to the previous word. This would allow readers to integrate the previously acquired information with the currently fixated information and to programme the subsequent saccadic eye movements.

In contrast to this, *Fine et al* (199) monitored eye movement patterns during reading using a dual-Purkinje-image eyetracker in normally sighted individuals with the left or right of their visual field masked from view with simulated hemifield scotomas. They observed that letter identification, word identification and reading rates were improved in the participants fixing with the scotoma to the left, compared to the participants fixing with the scotoma to the right. Consequently, they suggested that when the information to the right visual field was obscured by the scotoma, reading rates decline primarily due to the increased number of saccades performed to successfully read the stimuli.

In addition, *Rayner et al* (166, 167) investigated the importance of the available information to the left and to the right of the fixation in reading with normal vision employing the moving window technique. By varying the size and location of the window that moved across the reading text in synchrony with the reader's fixational eye movements, the authors assessed reading behavior in relation to information available in the parafoveal vision. They concluded that it was the text available to the right of the current fixation, guiding the subsequent eye movements, that was the most important for efficient reading. Therefore, when patients with central field loss use a PRL on the left to place their scotoma to the right of fixation in visual space, the information that has not yet been fixated would be masked from view, resulting in reduced reading rates.

Research has been undertaken regarding the strength of association between fixational stability and reading performance. *Crossland et al* (200) investigated the relationship between reading speed and fixational stability in patients with newly developed macular disease using a scanning laser ophthalmoscope and an infrared gazetracker to evaluate the fixational eye movements. The authors noticed that 54% of the variance in the oculomotor patterns could be attributed to changes in fixational stability, even though stability of fixation was not significantly associated with clinical features such as visual acuity, contrast sensitivity or scotoma size. Therefore, the reading deficit in patients with macular disease may partially be ascribed to impairments in fixational stability.

The findings of *Crossland et al* (200) were in conflict with *Deruaz et al* (201) observations, who also studied the fixation behavior and the oculomotor patterns in patients with central scotomas from age-related macular degeneration (AMD) or Stargardt's disease with the use of a scanning laser ophthalmoscope. The authors attributed the fixational instability observed during eccentric viewing to perceptual fading or Troxler's phenomenon, a condition probably related to the local adaptation effects in the retina. In particular, they suggested that the saccades performed while alternating between PRLs resulted in greater clarity of the perceived image since this prevented the fading of small targets presented in the peripheral visual field. Therefore, intentional changes in fixational eye movements, while attempting to decode letters or words, could facilitate the perception of reading text in individuals with central scotoma and eccentric viewing.

In addition, *Safran et al* (202) investigated the eye movement patterns during reading in a patient with a central scotoma using several preferred retinal loci while text material was projected on his retina with the use of a scanning laser ophthalmoscope. The authors concluded that the observed changes in fixation position and the associated oculomotor adaptations comprising of backward saccades and unexpected line losses could probably improve the perception of the eccentrically fixated text stimulus, even though they resulted in reduced reading rates.

In order to elucidate the efficacy of the residual retina for achieving visually demanding tasks in patients with macular scotomas, *Timberlake et al* (203) examined the eye movement patterns for fixating, inspecting acuity targets, scanning simple text and reading. They also used a scanning laser ophthalmoscope to map retinal lesions resulting from macular scotomas and identify preferred retinal loci. The authors observed a discrepancy between the preferred retinal loci used in each of these tasks, indicating that different PRLs were employed to achieve fixating, inspecting acuity targets, scanning simple, non-sense-syllable text and reading.

The processes related to oculomotor adaptations to eccentric viewing have also been evaluated. *Whittaker et al* (204) studied the characteristics of foveating and non-foveating saccadic response to salient visual targets presented in the peripheral visual field in patients with long-standing macular scotomas using a 2-dimensional search coil. They found that the tested individuals tended to suppress foveating saccadic mechanisms and directed presented peripheral stimuli to the preferred retinal locus used for fixation. However, these fixational eye movements were characterized by longer latencies and lower gains compared to the foveating saccades of normal individuals.

Fornos et al (205) investigated the oculomotor adaptations to eccentric viewing during reading in normally sighted observers using an eye-tracking system to record eye movements. The authors noticed that, in order to achieve effective reading, the participants initially suppressed the reflexive vertical foveating saccades. Subsequently, they tended to adjust the horizontal eye movement patterns by gradually increasing the number of the progressive/forward saccades and minimising the number of the regressive/backward saccades.

1.3.2.3 The effect of font size on reading performance in normal subjects with simulated foveal scotomas and in patients with foveal scotomas

The effect of print size on reading rates and the associated eye movement parameters have been evaluated in individuals with central field loss either induced artificially or related to eye pathology.

Fine et al (206) monitored the reading eye movement patterns in normal subjects with simulated central scotomas using a dual-Purkinje-image eyetracker. The authors noticed that reading rates were reduced in all the print sizes tested compared to normal central reading and suggested that the decreased reading speed was primarily related to an increase in the number of saccades and extended fixation durations. This was considered to be caused by the visual span shrinkage resulting from the simulated central visual field loss.

McMahon et al (207) investigated the strength of the relationship between saccadic frequency and reading rates, in patients with macular degeneration, using an electro-oculogram/saccadic velocity recording instrument. They noticed that there was a strong negative correlation between the eye movement parameters under investigation, with higher saccadic frequencies associated with reduced reading rates. The authors speculated that the increase in the number of saccades resulted from the poor saccadic accuracy observed in patients with central field loss, presumably being related to a reduced visual span.

Bullimore et al (208) investigated reading strategies as a function of print size, in patients with age related maculopathy, with an infrared scleral reflection device. They observed that the reduced reading rates were highly associated with an increased number of saccades and prolonged fixation duration. These oculomotor abnormalities during reading were suggested to be related either to the subjects' inability to obtain the desired information from a fixation or an existing inefficacy to integrate the perceived information across saccades.

In order to determine the contribution of the oculomotor patterns in the reduced reading rates in patients with central field loss, *Rubin et al* (209) evaluated reading performance for rapid serial visual text presentation to conventional text presentation in individuals with and without scotomas in the central part of their visual field. The rapid serial visual presentation technique minimizes the need for eye movements as the visual stimuli are presented sequentially at the same retinal area location. Reading rates with the use of the rapid serial visual presentation paradigm versus static text were increased less in patients with central field loss compared to normal controls. Low vision patients, with a macular scotoma, exhibited an improvement by a factor of 1.5±0.41 with the RSVP while normally sighted observers showed an improvement by a factor of 2.1±0.38 on their maximum reading rates. The results indicate that controlling for the contribution of eye movements in reading performance in patients with central field loss had little effect on the recorded reading rates.

1.3.3 Sensory and Oculomotor abnormalities in strabismic amblyopia

Many studies have implicated the amblyopic eyes (102, 123, 145, 146, 187-193, 210-232) as well as the non-amblyopic eyes viewing (102, 123, 143-146, 183, 187-189, 232, 233) of strabismic amblyopes as exhibiting sensory abnormalities such as crowding and suppression as well as oculomotor abnormalities in respect to stability of fixation and to saccadic, smooth pursuit and optokinetic nystagmus eye movements. Improvement in the generation of visual stimuli using computer-generated images and projection/display systems as well as advances in eye movement recording techniques, including infrared pupil tracking and magnetic search coils, have contributed greatly to our understanding of these sensorimotor abnormalities.

1.3.3.1 Crowding and Suppression

People suffering from amblyopia are in general often noted as suffering from a more severe visual acuity deficit when they are tested using a full line of optotypes, rather than isolated optotypes (86, 102, 210). This is commonly described as "increased contour interaction" or "crowding effect" which refers to the reduced degree of visibility of a visual stimulus in the presence of nearby objects (86, 102, 210). It must be considered seriously when testing the visual acuity of amblyopic patients, since its impact on the visual acuity screening of the amblyopic eye may be significant (86, 102, 210). Crowding occurs in the visual cortical areas, most probably the primary visual cortex V1 (210). One should be cautious of presenting only single optotypes and, thus, ignoring the crowding effect, since this frequently leads to an overestimation of visual acuity. Therefore, it has been widely accepted that a row of visual targets furnishes a more rigorous assessment of visual acuity and improves chances for detecting amblyopia (LogMAR crowded tests, figure 1.6).

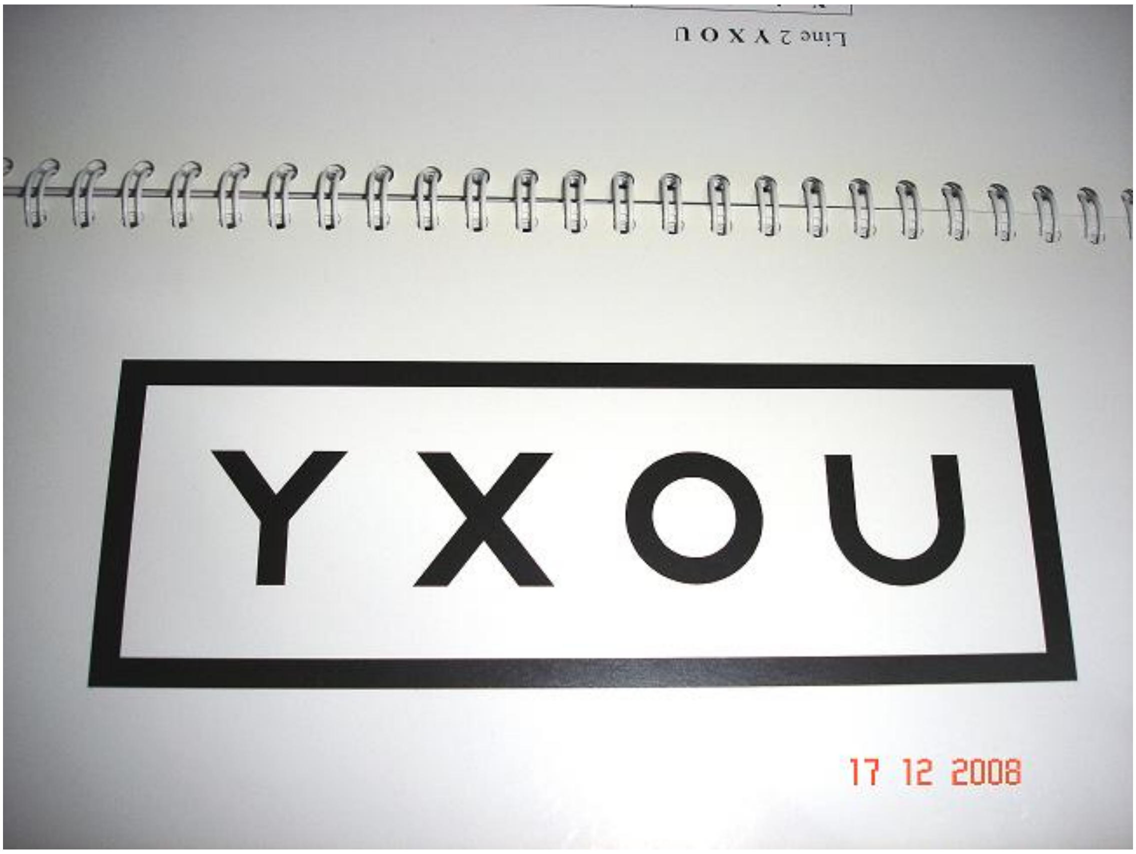


Figure 1.6. *The logMAR crowded test used in our investigation (McGraw et al)*

Suppression is the sensorial adaptation of the visual system during binocular vision after the onset of strabismus in order to eliminate confusion and diplopia (77, 86, 187-189). As the eyes are misaligned, dissimilar images are projected onto the fovea and the corresponding retinal areas beyond the fovea (77, 86). When both eyes are open, the active inhibition by the visual cortex of the visual input of one eye is represented by suppression. In particular, the image from the fovea of the deviating eye is suppressed to avoid confusion while the image from the peripheral retina of the deviating eye is suppressed to avoid diplopia (77). As the input of the fixating eye suppresses the input from the deviating eye, one might hypothesize that the prolonged and asymmetric suppression in the primary visual cortex (V1) ultimately leads to amblyopia in the more frequently suppressed eye (77, 86, 187-189).

1.3.3.2 Fixational Abnormalities

A significant proportion of the patients who suffer from strabismic amblyopia exhibit a shift of the locus of fixation, normally the fovea, to an eccentric retinal area in the amblyopic eye (190-193). One of the early pioneers in this field was *Von Noorden* (190-193), who worked on the fixation characteristics and the pathogenesis of eccentric fixation in strabismic amblyopia. Normally, a fixation reflex is induced by the image of a visual object falling on the peripheral retina of a normal eye, thus causing the eye to move and to shift the image from the periphery to the fovea. The authors observed that in strabismic amblyopia, suppression early in life causes decreased foveal visual acuity in the amblyopic eye, which results in a significant association between an eccentric retinal area and the fixation reflex (190-193).

Unsteady fixation of the amblyopic eyes has been described by many investigators. For example, *Srebro et al* (211) investigated the ability of amblyopic eyes to maintain steady fixation on a small point target in both anisometropic and strabismic amblyopes, by using an infrared reflection technique to measure the horizontal eye position. The authors concluded that the amblyopic eyes drifted more than the non-amblyopic eyes of amblyopic subjects or the normal eyes of normal controls. Likewise, *Schor et al* (212), studied the fixation ability in patients suffering from strabismic amblyopia, and found that the amblyopic eyes of strabismic amblyopes exhibited unsteady fixation. The horizontal components of the recorded unsteady fixation consisted by nasalward slow drifts and abnormally large saccades. In a similar attempt to analyse the components of the fixational eye movements in patients with abnormal binocular interaction, *Ciuffreda et al* (213-215), investigated patients having amblyopia without strabismus, constant strabismus with amblyopia and intermittent strabismus. They used a photoelectric method to record horizontal eye position during monocular and binocular attempts of the participants to fixate a small point target presented on a display screen. They found that, in comparison to the non-amblyopic eyes, the fixational eye movements in the amblyopic eyes, were characterized by increased fixational drifts associated with amblyopia and saccadic intrusions related to strabismus. Manifest nystagmus and latent nystagmus were also included in the fixational abnormalities of the amblyopic eyes. Likewise, by monitoring the fixational behaviour in amblyopic eyes and non amblyopic eyes during monocular viewing on a small target, *Westall et al* (216) also concluded that there was an increased variance on eye position in the amblyopic eyes compared to the non-amblyopic eyes.

While attempting to clarify the possible cause of the unsteady and eccentric fixation with the amblyopic eye viewing, *Siepmann et al* (217) assessed the fixation behaviour in amblyopic eyes in patients suffering from strabismic amblyopia using a scanning laser ophthalmoscope. They noticed that the decreased visual acuity of the amblyopic eyes resulted from an existing defective motor control associated with the impaired fixational reflex. In parallel, *Flom et al* (218) reviewed literature to explore the reasons for the fixation characteristics of amblyopic eyes, and noted that amblyopic eyes frequently attempted to fixate with an eccentric retinal locus having higher acuity than the fovea.

Similar observations were made regarding the fixational eye movements of non-amblyopic eyes. In particular, after having investigated the fixation characteristics of the non-amblyopic eye in amblyopic patients, *Kandel et al* (233) concluded that non-amblyopic eyes exhibited an eccentricity of monocular fixation with an obvious nasal component. Likewise, *Bedell et al* (145) also supported the fact that the non-amblyopic eyes of amblyopic subjects were characterized by unsteady fixation, with minute fixational eccentricity and increased velocity of nasalward drifts.

1.3.3.3 Saccadic Abnormalities

Amblyopic eyes are also characterized by central visual field defects, increased saccadic latencies and deficient saccadic accuracy while attempting to follow target stimuli. In animal models reared with surgically induced strabismus, abnormal early visual experience may result in deficits in the nasal visual field of the affected eye (219, 220). In order to examine whether abnormal binocular interaction produces similar deficits in the human visual field, *Sireteanou et al* (219, 220) investigated the visual field characteristics, the latency of saccades and the accuracy of pointing toward stimuli in humans suffering from strabismic and/or anisometropic amblyopia. They used static and kinetic perimetry for the evaluation of the visual field characteristics and a computer controlled infrared camera system to record fixation and eye movements. The authors concluded that there was reduced light sensitivity in the central part of the visual field, but no systematic deficits in the peripheral visual field of the amblyopic eyes. No asymmetries were found in either the saccadic latency or pointing accuracy between the nasal and temporal hemiretina of the amblyopic subjects.

With respect to the saccadic latencies, discrepancies were observed in the experimental findings of different investigators. Prolonged reaction times resulting in increased saccadic latencies in strabismic amblyopes were described by *Ciuffreda et al* (221, 222), *Hamasaki et al* (223) and *Nuzzi et al* (224). In particular, *Ciuffreda et al* (221, 222) investigated the saccadic latencies in amblyopic subjects with a photoelectric method to record horizontal eye position while attempting to track a small bright spot of light moving with random horizontal step displacements over the central retina. They concluded that in patients suffering from constant strabismus amblyopia, amblyopic eyes were characterized by increased saccadic latencies compared to non-amblyopic eyes and binocular tracking, therefore indicating processing delays of the visual information in the amblyopic eyes.

Similarly, *Hamasaki et al* (223) investigated the reaction time to a spot of light flashed in the centre of a continuously present annulus in patients suffering from strabismic amblyopia in comparison to normally sighted controls. They noticed that the amblyopic eyes exhibited longer reaction times (298±78.0 msec) compared to the non-amblyopic eyes (254.9±45.8 msec) of the amblyopic subjects, as well as the normal eyes of the normal controls. The interocular difference in reaction times in the amblyopic subjects was also significantly increased compared to the normally sighted controls. In addition, *Nuzzi et al* (224) investigated reaction times in strabismic amblyopic patients by evaluating the electrographic trace responses towards visual stimuli in the centre of a monitor screen. They noted that visual reaction times in strabismic amblyopes were significantly extended compared to normal controls. Prolonged reaction times were also observed in the amblyopic eye compared to the non-amblyopic eye.

On the contrary, *Schor et al* (225) found that saccadic initiation in amblyopic eyes was as rapid as in normal eyes (200-300msec) after having investigated the saccadic latencies in strabismic amblyopic subjects. They recorded the horizontal components of the eye movements using a pair of infrared sensitive diodes positioned in a spectacle frame while following a small spot moving in the horizontal meridian. However, the saccades performed when the amblyopic eye was viewing were reduced in amplitude compared to the non-amblyopic eye viewing and exhibited an asymmetry. In particular, saccades corresponding to temporalward target motion were more frequent, smaller in amplitude and less accurate than saccades corresponding to nasalward target motion.

1.3.4 The reading rate curve as a function of font size

The reading rate curve as a function of letter size, as well as the changes in reading strategies for reading text presented at different letter sizes, have been described in individuals with normal central and peripheral vision and in patients with central field loss (169, 170, 207, 208, 234, 235).

Legge et al (234) examined the effect of print size on reading rate in normal central vision using text of varying character sizes presented on a TV monitor. Healthy individuals were instructed to scan the text. The authors found that reading speed increased with increasing print size, up to a critical print size beyond which reading speed remained at a plateau level, termed the maximum reading speed (figure 1.7). Reading speed deteriorated rapidly for very small characters, approaching the acuity limits and declined slower for extremely large print. The rapid decline in reading rates with increasingly smaller characters was associated with acuity limitations while the gentle decline in reading rates with increasingly larger characters might have been related to limitations of visual information available in each fixation.

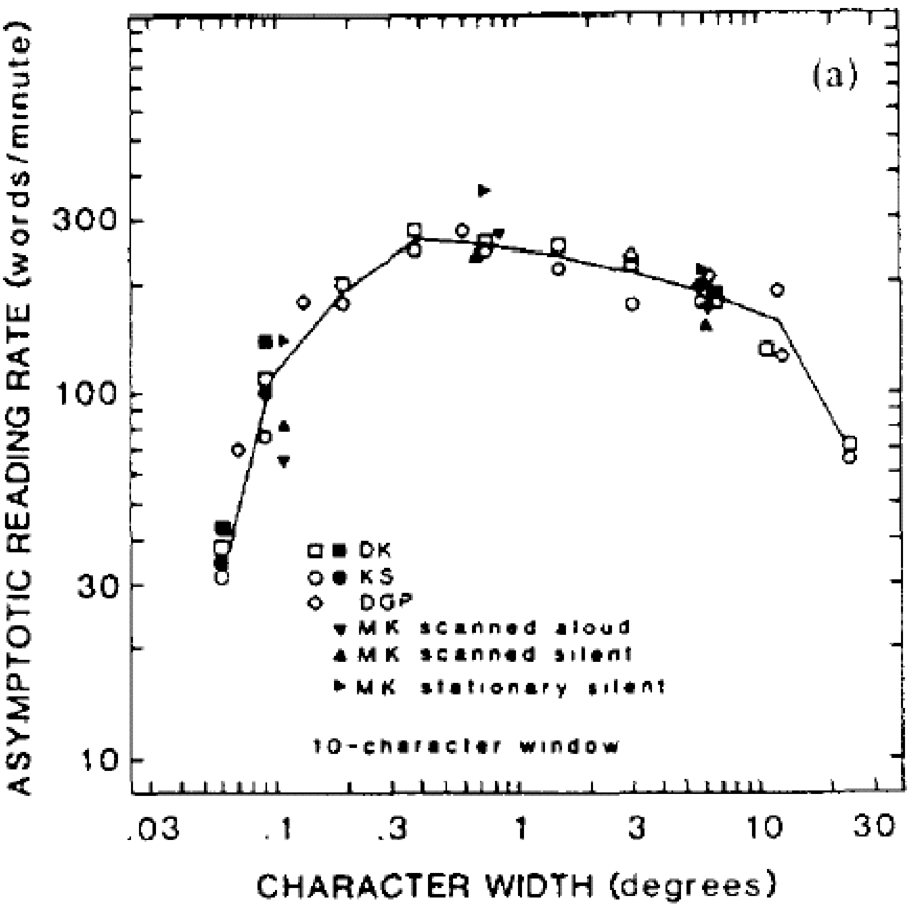


Figure 1.7. *Effects of character size on reading rate. Asymptotic reading rate is plotted as a function of character size for experiments with matrix sampling. Data are shown for four observers and for white-on-black text (open symbols) and black-on-white text (solid symbols). The solid curve connects average asymptotic reading rates at each character size (from Legge et al, 1985, [ref. no. 234]).*

Chung et al (169, 235) investigated the effect of print size on reading speed in normal peripheral vision with the Rapid Serial Visual Presentation Technique. Using this paradigm for different print sizes examined at different eccentricities, the authors confirmed that reading speed also increased with increasing print size up to a "critical print size", beyond which reading speed remained at the maximum reading speed level (figure 1.8). The rate of change in reading speed, as a function of print size, remained invariant in central and peripheral vision. However, maximum reading speed was significantly lower in peripheral vision compared to central vision, despite the increased print size. Furthermore, *Latham et al* (170), with the effects of eye-movements eliminated using the Rapid Serial Visual Presentation paradigm, have similarly shown that, reading rate of meaningful sentences could not be equated across the visual field by simple magnification, even though the word recognition rates could be equated across the visual field by appropriate magnification of the stimulus.

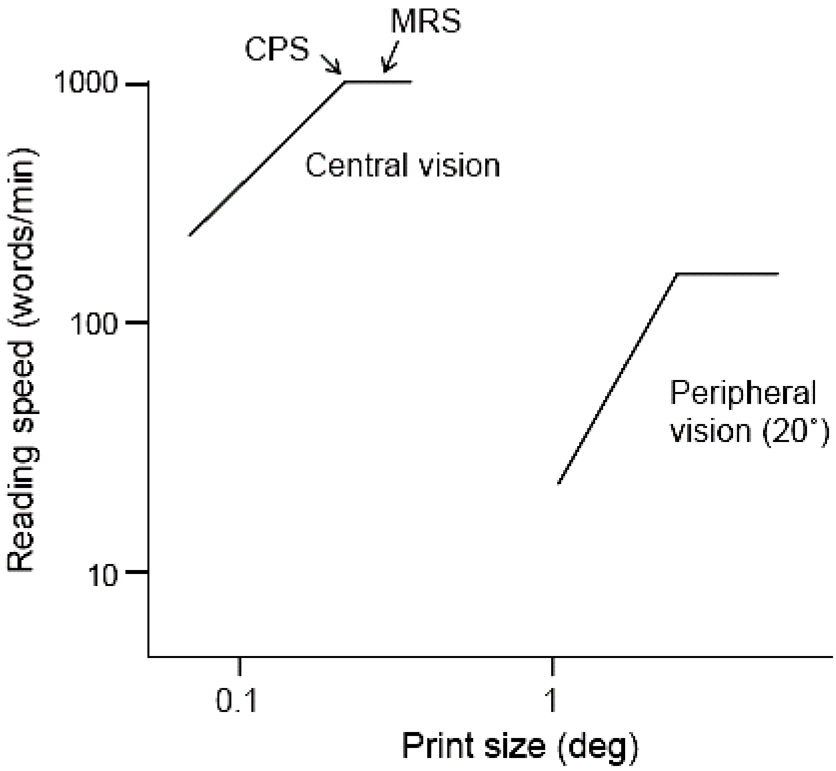


Figure 1.8. *A schematic representation of reading speed in central and peripheral vision as a function of print size, as measured using the RSVP paradigm (modified after Chung, Mansfield and Legge47). For both central and peripheral vision, reading speed increases with larger print size until a critical print size is reached (CPS), after which maximum reading speed (MRS) has been reached. The different print sizes at which CPS is reached for central and peripheral vision reflect the different resolution limits for the two different eccentricities. However, the key difference is that the MRS is lower for the peripheral retina, despite increased print size. The periphery cannot provide reading speed comparable to the fovea (from Battista et al, 2005, [ref. no. 169]).*

Summarizing, despite enlargement of letter size to compensate for decreased acuity with eccentric viewing, peripheral reading speed did not approach that achieved using the fovea in normal vision (169, 207, 208). Similar results were also derived while accounting for the contribution of the eye movements in reading rates using the Rapid Serial Visual Presentation Technique (169, 209, 236) and the crowding effect using reading material presented with increasing letter spacing (169, 237, 238).

1.4 Aims of the study

Reading is an integral part of our lives. Reading tasks are regularly performed in the field of education, information and entertainment. Reading offers immediate access to knowledge. It supplies the reader with constructive ideas. It provides stimulation and promotes the intellectual growth.

Amblyopia is a significant cause of unilateral visual impairment in childhood and is considered as one of the most common causes of persistent unilateral visual loss in adulthood. The impact of amblyopia on vision is significant as well as the dysfunction associated with this visual disorder. Moreover, amblyopia consists of a substantial proportion of workload among paediatric ophthalmologists and orthoptists in everyday clinical practice. However, the cost-effectiveness of the vision screening programmes among the childhood population has been extensively debated and remains controversial. Furthermore, the cost benefits of amblyopia treatment are highly contentious, partly because of the insufficient evidence base underlying occlusion therapy and because the functional outcomes of amblyopia treatment are poorly understood. Finally, the health cost to patients and the health service associated with visual disability caused by visual loss in the non-amblyopic eye due to ocular trauma or pathology, which is more prevalent than previously thought, is also considerable due to the high occurrence of amblyopia.

Reading is important in the fields of education, information and entertainment. Considering the high prevalence of amblyopia in both childhood and adult population, reading performance in patients suffering from amblyopia has been poorly investigated.

Moreover, eye movement recording techniques have been used extensively to test the models that have been proposed to explain oculomotor control during reading (166-168, 175). To my knowledge, no study has yet been done to assess functional reading ability and investigate eye movement patterns associated with amblyopia with the use of the eye movement recording equipment.

In my study I aim to: (i) corroborate previous findings in which deficits in reading ability resulting from amblyopia have been described, (ii) evaluate for the first time the oculomotor characteristics associated with impaired reading performance in adult strabismic amblyopia, (iii) investigate underlying abnormalities in fixational and saccadic eye movements and how they are associated with reading in adult strabismic amblyopes, and (iv) assess the effect of print size on reading rates in adult strabismic amblyopia and how it effects the oculomotor characteristics.

These findings will be discussed and, in particular, reading strategies in amblyopia will be compared to other diseases where mechanisms are better understood, such as in age-related macular degeneration. A more detailed elaboration of these aims with the specific hypotheses tested is included at the commencement of each investigation.

2. Experiment 1: Reading strategies in strabismic amblyopia

2.1 Aims of the study

A wealth of literature exists concerning the eye movement strategies used during reading, which has greatly extended our knowledge about the reading processes at higher and lower levels (166-168, 175). With the development of eye movement recording systems allowing a large amount of accurate drift free data to be easily collected, a surge in eye movement investigations in reading commenced in the mid 1970 which still continues today (166-167). Earlier studies using eye movement recordings were impeded by the technological limitations of the equipment available. Electro-oculograms (EOG) initially employed to record eye movements, while performing a reading task used electrodes on the skin adjacent to the orbit which create eyelid artefact and therefore, gave rise to recording errors and inaccurate measurements. More recent development of infrared pupil tracking techniques and magnetic search coil techniques has reduced recording error and artefact. Generation of target stimuli has also improved over the years and, with the development of computers, stimuli could be produced more simply and conveniently on a computer monitor or projection screen. Eye movement recordings have also been used to investigate reading, following pathology, influencing the visual system (195, 200, 204-205, 207-208), as well as with aging (239). However, these techniques have never been applied to studying reading in amblyopia.

Strabismic amblyopia is associated with profound visual pathway changes, which have been previously described (74-76). Adult strabismic amblyopes were chosen to participate in my study as they compose a uniform group of patients.

2.2 Hypotheses Tested

Amblyopia is associated with foveal suppression scotomas. Reading performance in normal individuals with simulated scotomas as well as in patients with central scotomas is characterized by reduced reading rates significantly associated with increased saccades number and prolonged fixation duration. Therefore, I hypothesize that reading speed in adult strabismic amblyopes during monocular reading with the amblyopic eye is significantly slower compared to normal controls monocular reading with the non-dominant eye. Taking into consideration the oculomotor parameters observed during reading with central field loss, I also hypothesize that reading in adult strabismic amblyopes is significantly associated with increased number of saccades and prolonged fixation duration.

Additionally, in certain visual deficits caused by amblyopia changes have been shown to occur in the non-amblyopic eye as well as the amblyopic eye. It is important to ascertain whether similar deficits exist in the non-amblyopic eyes of adult strabismic amblyopes and even binocularly for reading.

2.3 Methods

2.3.1 Subjects

Twenty patients were recruited from the Ocular Motility Clinic, Department of Ophthalmology at Leicester Royal Infirmary, University Hospitals of Leicester NHS Trust. They were aged 24 to 64 years old (mean 44.9 ± 10.7 years); eight were male and twelve were female (table 2.1). All the tested subjects were diagnosed with unilateral amblyopia caused by strabismus, defined as a minimal two line interocular difference in distance visual acuity. Distance visual acuity in the amblyopic eye ranged from 0.580 to 0.130 LogMAR (mean visual acuity=0.332 LogMAR, SD=O.153) and in the fellow normal eye from 0 to -0.180 LogMAR (mean visual acuity=-0.061 LogMAR, SD=0.053). With respect to the severity of amblyopia, mild amblyopia was defined as visual acuity in the amblyopic eye better than or equal to 0.300 LogMAR and moderate amblyopia was defined as visual acuity in the amblyopic eye ranged from 0.300 to 0.735 LogMAR. Ten participants had mild amblyopia and ten had moderate amblyopia. Thirteen of the tested subjects were diagnosed with exotropia (eight with secondary exotropia) and seven with esotropia. None of the tested subjects demonstrated binocular vision and stereovision and all of them had undertaken treatment for amblyopia (occlusion therapy or surgery) in the past (eleven underwent both occlusion therapy and surgery, three occlusion therapy only and six surgery only). Four of the subjects showed eccentric and sixteen central fixation pattern, determined by the exact localization of their fovea, in direct ophthalmoscopic examination, while attempting to fixate monocularly the fixation target of the direct ophthalmoscope.

A healthy control group of twenty volunteers recruited from primarily non-academic staff of the University of Leicester and the Leicester Royal Infirmary also participated in the clinical study (table 2.2). All participants had fully corrected visual acuity and did not suffer from any neurological or psychiatric disease or any other ocular comorbidity. The two study groups were comparable in age, sex and educational-intelligence level matched using the National Adult Reading Test (NART) (240). The NART provides a reliable estimate of intelligence quotient (IQ) by evaluating the ability to pronounce a list of non-phonetic words of increasing complexity correctly - an intellectual ability that is preserved despite any form of brain damage. Amblyopic subjects and normal controls participating in the study were at least high school graduates and had a full-scale NART score of 90 or above (p=0.312). Overall, the full scale NART score of the participants was within the average range with a mean of 108.90 (SD=6.31). No one scored more than 2SDs below average.

All the participants were native English speakers, naïve to eye movement experiments and unaware of the questions under study. The study followed the tenets of the Declaration of Helsinki and was approved by the local ethical committee. Written informed consent was obtained from all subjects prior to their participation.

Amblyopic subjects	Age	Gender	NART	Orthoptic Status	Visual Acuity in Amblyopic Eye	Visual Acuity in non-Amblyopic Eye	Visual Acuity in Both Eyes	Fixation	Treatment
1	47	M	105	R exo	0.475	0	0	eccentric	surgery
2	43	F	105	R eso	0.325	0	0	central	surgery
3	48	F	106	L eso	0.475	0	0	central	patching/surgery
4	38	M	114	R eso	0.125	-0.15	-0.15	central	patching
5	64	F	106	L exo	0.2	-0.075	-0.075	central	patching/surgery
6	58	F	109	R eso	0.25	0	0	central	surgery
7	45	F	105	L eso	0.575	0	0	eccentric	patching
8	24	F	103	L eso	0.175	-0.075	-0.075	central	patcing/surgery
9	49	F	112	L exo	0.175	-0.075	-0.075	central	patching/surgery
10	30	F	109	R exo	0.175	-0.075	-0.075	central	surgery
11	51	M	114	L exo	0.2	-0.05	-0.05	central	surgery
12	51	M	117	R exo	0.475	-0.175	-0.175	central	patching
13	58	F	104	R eso	0.3	0	0	central	patching/surgery
14	48	F	122	L exo	0.475	-0.075	-0.075	central	patching/surgery
15	54	M	103	L exo	0.5	-0.1	-0.1	central	patching/surgery
16	36	F	102	L exo	0.325	-0.1	-0.1	central	patching/surgery
17	25	F	105	L exo	0.575	-0.1	-0.1	eccentric	patching/surgery
18	40	M	107	R exo	0.175	0	0	central	surgery
19	38	M	106	R exo	0.2	-0.1	-0.1	central	patching/surgery
20	51	M	124	R exo	0.475	-0.075	-0.075	eccentric	patching/surgery

Table 2.1. *Clinical details of strabismic patients participating in the study*

Normal controls	Age	Gender	NART	Orthoptic Status	Visual Acuity in non-Dominant Eye	Visual Acuity in Dominant Eye	Visual Acuity in Both Eyes	Fixation	Treatment
1	47	F	113	orthotropia	-0.025	0	0	Central	-
2	32	M	107	orthotropia	-0.1	-0.1	-0.1	Central	-
3	24	F	105	orthotropia	0	0.025	0	Central	-
4	27	M	103	orthotropia	-0.05	-0.05	-0.05	Central	-
5	50	F	105	orthotropia	-0.025	-0.05	-0.05	Central	-
6	47	M	117	orthotropia	-0.025	-0.025	-0.05	Central	-
7	50	F	114	orthotropia	-0.05	-0.025	-0.025	Central	-
8	46	M	117	orthotropia	0	-0.025	-0.025	Central	-
9	26	M	106	orthotropia	-0.05	-0.05	-0.05	Central	-
10	40	M	121	orthotropia	0	-0.025	-0.025	Central	-
11	60	F	119	orthotropia	-0.025	0	-0.025	Central	-
12	50	M	118	orthotropia	0	-0.05	-0.05	Central	-
13	33	M	115	orthotropia	0	0	0	Central	-
14	30	M	105	orthotropia	-0.05	-0.25	-0.05	Central	-
15	54	F	108	orthotropia	-0.075	-0.1	-0.1	Central	-
16	58	F	107	orthotropia	0	-0.05	-0.05	Central	-
17	52	F	110	orthotropia	-0.05	-0.025	-0.05	Central	-
18	36	F	111	orthotropia	-0.025	-0.025	-0.025	Central	-
19	45	F	113	orthotropia	-0.075	-0.025	-0.05	Central	-
20	49	F	103	orthotropia	-0.05	-0.05	-0.075	Central	-

Table 2.2. *Clinical details of normal controls participating in the study.*

2.3.2 Vision assessment

A full ophthalmic examination including assessment of distance visual acuity (LogMAR crowded acuity tests), binocular function (Bagolini striated glasses test), stereopsis/stereoacuity (Titmus stereo fly test and TNO test), ocular motility examination, cover/uncover and alternate cover test, split lamp examination and direct ophthalmoscopy was performed in all subjects. Each subject was optimally corrected for all clinical vision tests and reading trials.

2.3.3 Reading assessment

Tested subjects were requested to read paragraphs of continuous text presented on a screen (figure 2.1). Instead of opting for arbitrary words or sentences lacking contextual coherence, a story consisting of a sequence of apprehensible sentences was employed as reading material, since this was considered more representative of a usual reading context.

The reading material used in the study comprised nine text paragraphs, with the text of 'Tom Thumb' taken from the English translations of the Brothers Grimm fairy tales, as used in the N8 pages of the Moorfields Bar Reading Book (241). The difficulty of the text used was lower than the reading abilities of the subjects, in order to guarantee that their performance would not be hindered by the difficulty of the reading material used.

> There was once a poor woodman sitting by the fire in his cottage, and his wife sat by his side spinning. 'How lonely it is,' said he, 'for you and me to sit here by ourselves without any children to play about and amuse us, while other people seem so happy and merry with their children!' 'What you say is very true,' said the wife, sighing and turning round her wheel, 'how happy should I be if I had but one child! and if it were ever so small, nay, if it were no bigger than my thumb, I should be very happy, and love it dearly.' Now it came to pass that this good woman's wish was fulfilled just as she desired; for, some time afterwards, she had a little boy who was quite healthy and strong, but not much bigger than my thumb. So they said, 'Well, we cannot say we have not got what we wished for, and, little as he is, we all love him dearly;' and they called him Tom Thumb.

Figure 2.1. *Example of the text paragraph used as reading material in the 1st experimental reading task as displayed on the projection screen.*

The size of each text paragraph was a standard reading format, with a text width of 775mm and height of 466mm, subtending a horizontal visual angle of approximately 35.8º width and 22.0º height.

The text was presented as black letters on a white background. The luminance of the letters was 0.88cd/m² and the background luminance was 14.3cd/m², resulting in a letter contrast of 93.84%. Only the left hand side of each line was justified. The text was displayed in Courier New font, 9-point size, without splitting words and was centred on the screen both horizontally and vertically. Instead of the more common proportional width fonts like Times New Roman, a fixed-width font (monospaced) was used, as equal character width was advantageous for reading speed calculations. The print size was defined as the angular subtense of the print on the retina and, therefore, the print size used was measured as the height of a lower-case ‘x’. The corresponding LogMAR size was calculated from the equation $\log_{10}$ [(angle subtended by x-height)/(5 arc min)] following the design of print sizes used in MNREAD acuity charts (242) which are continuous-text reading-acuity charts suitable for measuring reading acuity and reading speed of normal and low-vision patients.

In most cases, the size of fonts must be larger than the acuity limit, in order for people to attain fluent reading without weariness. The enlarged print size, the acuity reserve or critical font size is a factor of 2 or more over acuity letters (243, 244). Thus, the print size selected for the study corresponded to a visual acuity of 0.735 in LogMAR optotype. Since the amblyopic subjects that participated suffered from mild to moderate amblyopia (visual acuity 0.575-0.130), the minimum acuity reserve for fluent reading was two times threshold acuity size.

Each text paragraph had approximately the same layout, consisting of 13.11 lines (SD 0.39), 178.6 words (SD 8.72) and 900.66 characters with spaces (SD 28.7) with 1.5 interline spacing. These were equal to 13.62 words per line (SD 0.37) and

68.75 characters with spaces per line (SD 0.83). Each line of the text subtended a horizontal visual angle of approximately 35.8º width and 1.5º height and each separate letter subtended a visual angle of approximately 1.5º. Subjects were seated at a viewing distance of 1.20m in front of the stimulus display screen with their primary gaze position to correspond to the centre of the screen. Their head was stabilized using a forehead and chin rest to minimize head movements and they were observed continuously throughout the experiment to ensure that as static a position as possible was maintained.

Carver (245) has coined the term 'rauding' to refer to the reading for understanding involved in normal reading. Word recognition, the comprehension and integration of sentences are all part of rauding, which assesses the subject's natural viewing strategy. Therefore, participants were instructed to read at a normal rate to obtain meaning from the text for all reading assessments, and silently, rather than aloud, as jaw movements introduce artifacts in eye movement data, by causing vibration of the head mounted eye tracker. After the end of each paragraph, subjects had to report to the experimenter the end of the trial. The next trial with a new paragraph began whenever the subjects were ready.

Comprehension was checked after the participant reported reaching the end of each paragraph, by requesting an answer to two multiple-choice questions relevant to the previously read text. All subjects answered the questions correctly and thus demonstrated a good level of understanding of the passages they read.

The order of performing trials of monocular reading with either eye and binocularly was randomized. During monocular reading, the contralateral eye was occluded using an occluder attached on the corresponding eye camera, while recordings were still maintained. The whole duration of the test was approximately 1 hour.

2.3.4 Eye movement recordings

Eye position was measured during trials with an infrared video based eye-tracking system (EyeLink eye tracker, SensoMotoric Instruments Gmbh, Berlin, Germany) using Eyelink software (version 2.04) (246) (figure 2.2).

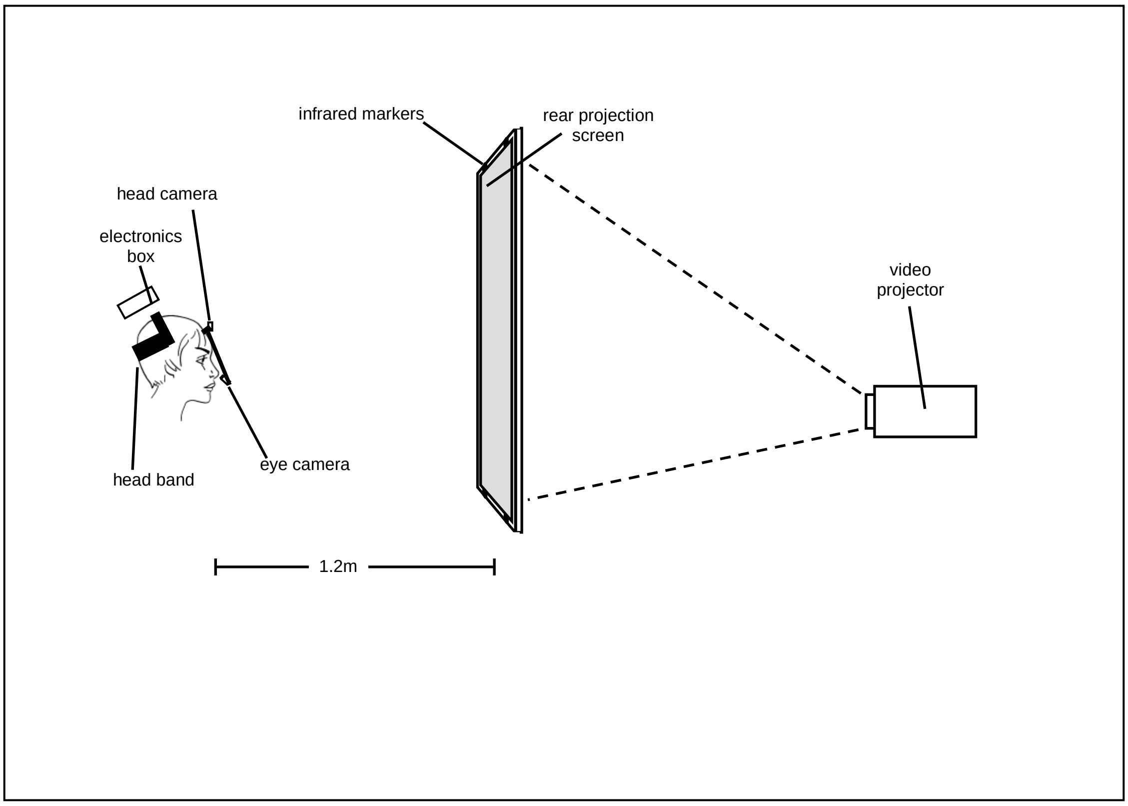


Figure 2.2. *The experimental set-up used in our investigation for recording eye movements and generating visual tasks.*

The SMI EyeLink gaze tracking system comprises a headband mounted measuring unit and two computers. The headband mounted measuring unit consists of two ultra-miniature high-speed custom-built cameras that simultaneously take 250 images per second. Both eyes are recorded to provide binocular eye-tracking while a third camera tracks 4 infrared markers mounted on the visual stimulus display for head motion compensation and true gaze position tracking.

The whole head-mounted apparatus weighs approximately 600 g. The pupil-and head-tracking cameras are mounted on a headband and are positioned in the extreme peripheral visual field offering no obstruction to the subjects' effective field of view.

The EyeLink eye tracker has a resolution of 0.005° and a spatial noise level of less than 0.01°/RMS, allowing a velocity noise level of less than 2°/RMS to be achieved. The 250 sampling rate gives high temporal resolution of 4 msec. The accuracy of the recordings for the gaze data was determined through a verification process performed by the eye tracker before each recording.

On the whole, the EyeLink software measures the centre of the largest area of infrared light below a threshold set by the user, equivalent to pupil centre. Eye tracker recordings were converted into neurophysiological software system files (Spike2, Cambridge Electronic Design, Cambridge, UK).

As all eye movement research requires information on the subject's point of gaze on a display of visual information, such as a screen of text, there is a need to determine the correspondence between pupil position in the eye-camera image and gaze position on the subject display. In the particular experiment, the pupil to gaze calibration was performed with a series of nine fixation points, projected onto a rear projection screen of 1.75m width and 1.17m height, using a projection system (VisLab; SensoMotoric Instruments GmbH) and a video projector (resolution: 1024 x 768; CP-X958 LCD; Hitachi, Ltd., Tokyo, Japan). The nine fixation points were projected individually in the shape of a 3x3 grid, 40° wide and 35° high. The calibration was repeated if the error for any point was more than 1°, or the average error for all points was greater than 0.5°. Only trials where the calibration was categorised as good were included and good calibration was achieved when the ratio of gains was less than 1.5:1 horizontally and 3:1 vertically. During the right eye calibration procedure, the left eye was occluded and during the left eye calibration procedure, the right eye was occluded while eye movement recordings of both eyes were still maintained. Monocular calibrations were important because they assure eye fixation position based on the visual input from that eye alone under monocular viewing conditions.

There was no drift in the EyeLink system, except for some slight movement of the headband that can take a few seconds to settle into position because of the viscoelastic properties of the skin. To compensate for this, a drift correction before each trial was performed which consisted of the subject's fixating a single calibration target (a black spot) displayed at the centre of the screen. The reported gaze position was used to correct for any drift in system accuracy. The linearity of the eye data was corrected by the calibration.

After the system was set up and calibrated, gaze position was monitored in real time and recorded for later analysis.

Specifically, the EyeLink eye tracker used an automatic saccadic detection algorithm based on a velocity threshold of 35°/s and an acceleration threshold of $9500°/s^2$. The Euclidean sum of horizontal and vertical components of the velocity and acceleration was used, resulting in magnitude but no directional information. A measure of two samples was used to derive velocity and a weighted sum of three samples to determine acceleration. The velocity threshold was raised by an average velocity computed for a period of 30ms to prevent false triggering during smooth pursuit. The saccade detector becomes active if either the velocity or acceleration exceeds threshold.

As mentioned above, the basis of eye event detection is the saccade detection from the saccade detector in the EyeLink tracker. Thus, a saccade was defined as a period when the saccade detector was active for two or more samples in sequence and continued until the start of a period of saccades detector inactivity for at least five samples. A blink was defined as a period of missing pupil surrounded by a period of artifactual saccade caused by the sweep of the eyelids across the pupil and corresponded to a period of saccade-detector activity with the pupil missing for 3 or more samples in sequence. Blinks were replaced with a linear sequence of data connecting the points before and after the blink and the presence of a blink in the data was indicated with markers to prevent incorrect analysis. Finally, a fixation event was defined as any period that was neither a saccade nor a blink.

The eye movement data were recorded in an EDF file for later analysis or viewing. An EDF file consists of one or more blocks of eye-movement data, each containing data samples and events. Samples are used to record instantaneous eye position data, up to 250 per second produced from the EyeLink operator PC and include records of eye position and pupil size. Events are used to record important occurrences, either from the experimental application or from changes in the eye-data and include eye-movement records such as saccades, fixations and blinks. Both streams of data are time-synchronized for easy analysis.

2.3.5 Data Analysis

Eye movements were analyzed using customized computer programmes (written in Spike2 neurophysiological software, Cambridge Electronic Design Ltd, Cambridge, UK). For the reading test, the text paragraphs were analyzed line by line. Overall, 13 lines per screen were analyzed. Reading lines were identified from the large return saccades, which typically exceeded 250°/s gaze velocity in a leftward direction. Cursors were used in order to select the data corresponding to reading lines (i.e. from the middle of the first fixation to the middle of the last fixation of each line). The time during which subjects were attempting to read stimuli was defined as the reading period. For the text passages, the reading period for each line of text was defined as the time after the last word of the previous line had been read (or the appearance of the page of text in the case of the first line) until the last word on the current line was read. Reading speed was calculated in characters with spaces/second, representing the quotient derived from characters with spaces for each paragraph of text divided by the time taken to read the paragraph.

The measures derived from the eye movement recordings included: (i) Reading speed (in characters with spaces/sec), (ii) Total number of saccades per line, (iii) Number of progressive/forward saccades per line, (iv) Amplitude of progressive/forward saccades (in degrees), (v) Number of regressive/backward saccades per line, and (vi) Fixation duration (time between successive saccades) in (sec). Means were calculated for all subjects.

Eye movement data were collected during monocular viewing with either eye (amblyopic and non-amblyopic) and binocularly in the amblyopic subjects. Similarly, eye movements were recorded during monocular viewing with either eye (non-dominant and dominant) as well as binocularly in the normal controls.

The dominant eye was determined as the one the subjects spontaneously chose for looking through the pinhole in a paper.

2.3.6 Statistical analysis

Descriptive and Inferential Data Analyses were performed using SPSS for Windows, version 14.0. Differences between the amblyopic subjects and the normal controls with respect to the monocular with either eye and binocular mean reading speed, saccades number and fixation duration were analysed using univariate analysis of variance (ANOVA) after the assumption of normality and the assumption of homogeneity of variances was confirmed. Repeated measures ANOVA were conducted to evaluate the differences in the amblyopic subjects during monocular with either eye and binocular viewing conditions. Specifically, differences between monocular with either eye and binocular reading performance in the amblyopic subjects were assessed with paired-samples t-test (or the non-parametric Wilcoxon Signed-Rank Test).

The assumption of normality was tested using the Shapiro-Wilk test of normality and the assumption of the equality of variances was tested by the Levene's t-test for equality of variances. For all analysis a 2-sided $p\text{-value}<0.05$ was considered to indicate statistical significance. Correlations analysis was used to describe the strength and direction of the linear relationship between the variables investigated and as so, Pearson correlation coefficients (or the non-parametric Spearman's Rank Order correlation) were calculated. Standard multiple regression analysis was used to explore the interrelationship among saccades number, fixation duration and reading speed. In particular, standard multiple regression was used to investigate how well saccades number or fixation duration were able to predict reading speed changes; to assess whether saccades number or fixation duration was the best predictor for reading speed changes and finally, to evaluate the extent each of the examined variables was able to predict the outcome while the effects of the other variable were controlled for.

The following comparisons were made (i) monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, (ii) monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and (iii) binocular reading in both the amblyopic subjects and the normal controls. During binocular viewing, the eye movement recordings from the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls were selected for the comparisons made.

Additionally, in the amblyopic subjects, the following comparisons were performed: (i) monocular reading with the amblyopic eye and the non-amblyopic eye (ii) monocular reading with the amblyopic eye and binocularly and, (iii) monocular reading with the non-amblyopic eye and binocularly.

2.4 Results

2.4.1 Comparing the reading performance of the amblyopic subjects and the normal controls

Original eye movement recordings of an amblyopic subject and a normal control are shown in figure 2.3 for each of the viewing conditions. The characteristic staircase pattern of saccades and fixations from left to right can be seen in each condition. An obvious increase in the time taken to read a line when the amblyopic subject was viewing could be seen by the reduced gradient of the left to right stepwise movement.

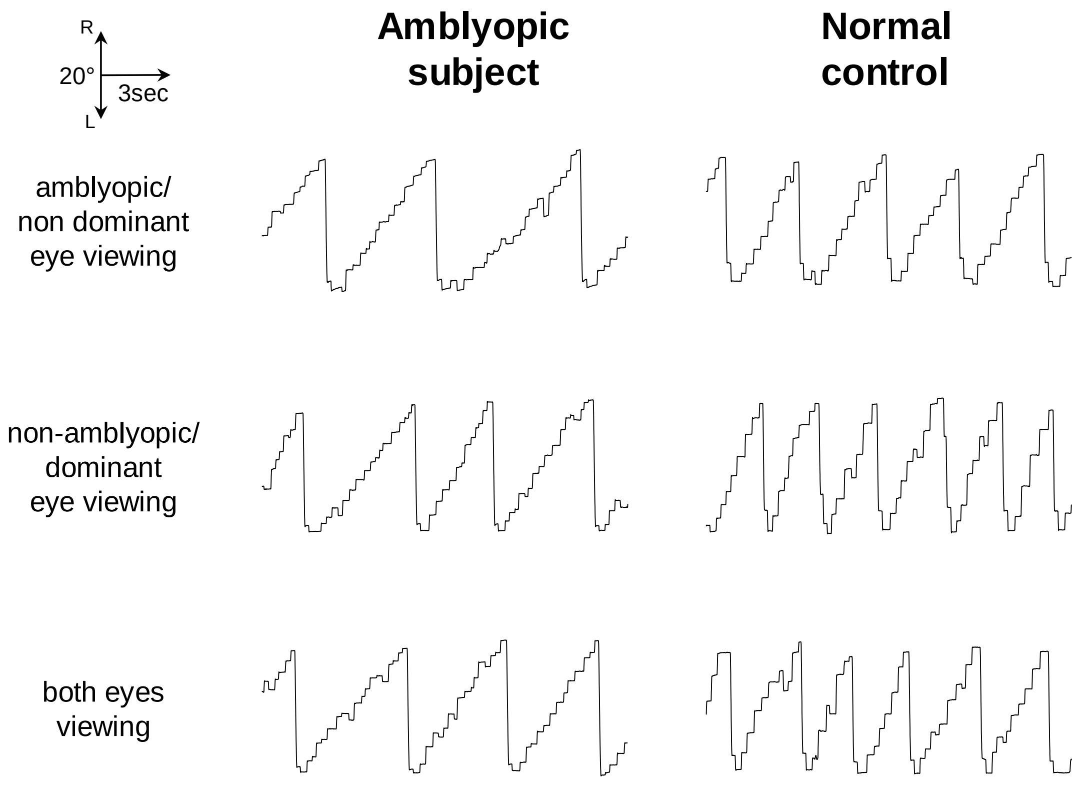


Figure 2.3. *Original recordings of an amblyopic subject and a normal control under monocular viewing with either eye and binocular reading performance. In the selected time period of 3sec, less lines of text were read during monocular viewing with either eye and binocular viewing of the amblyopic subjects compared to normal controls.*

2.4.1.1 Monocular reading (amblyopic eye of the amblyopic subjects and non-dominant eye of the normal controls)

Results of the statistical comparison between the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls viewing for oculomotor parameters are shown in table 2.3. Amblyopic subjects read significantly slower with the amblyopic eye compared to normal controls reading with the non-dominant eye (p<0.0001).

No significant differences were found between the two groups with respect to the total number of saccades per line, the number of progressive/forward saccades per line and their amplitude. On the contrary, amblyopic subjects exhibited significantly more regressive/backward saccades (p=0.003) when reading a line of text and significantly longer fixation durations (p=0.003) compared to normal controls.

Table 2.3. *Comparison of monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Mean measurements of the eye movement parameters, the standard deviations, the derived F-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	**Amblyopic subjects**	**Normal controls**	***F*-statistic *p*-value**
Reading speed (characters with spaces/sec)	13.094 (4.101)	22.188 (5.074)	F=38.848 p<0.0001*
Number of saccades per line	11.971 (4.014)	9.999 (2.513)	F=3.466 p=0.070
Number of progressive/forward saccades per line	9.194 (4.172)	8.433 (1.961)	F=0.546 p=0.465
Amplitude of progressive/forward saccades (deg)	3.823 (1.345)	4.166 (0.825)	F=0.942 p=0.338
Number of regressive/backward saccades per line	2.776 (1.500)	1.566 (0.753)	F=10.391 p=0.003*
Fixation duration (sec)	0.247 (0.028)	0.217 (0.030)	F=10.136 p=0.003*

2.4.1.2 Monocular reading (non-amblyopic eye of the amblyopic subjects and dominant eye of the normal controls)

Results of the statistical comparison between the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls viewing for oculomotor parameters are shown in table 2.4. Amblyopic subjects read significantly slower with the non-amblyopic eye compared to normal controls reading with the dominant eye (p<0.0001). Furthermore, amblyopic subjects exhibited a significantly increased number of saccades per line (p=0.032) compared to normal controls. No significant differences were observed between the two groups with respect to the number of progressive/forward saccades per line, their amplitude and number of the regressive/backwards saccades per line. In addition, fixation duration did not differ significantly between the two groups.

Table 2.4. *Comparison of monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Mean measurements of the eye movement parameters, the standard deviations, the derived F-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	**Amblyopic subjects**	**Normal controls**	***F*-statistic *p*-value**
Reading speed (characters with spaces/sec)	16.241 (3.263)	22.349 (5.710)	F=17.246 p<0.0001*
Number of saccades per line	11.547 (2.524)	9.720 (2.677)	F=4.932 p=0.032*
Number of progressive/forward saccades per line	9.585 (2.285)	8.201 (2.148)	F=3.890 p=0.056
Amplitude of progressive/forward saccades (deg)	3.745 (1.097)	4.281 (0.991)	F=2.631 p=0.113
Number of regressive/backward saccades per line	1.962 (0.787)	1.518 (0.838)	F=2.981 p=0.092
Fixation duration (sec)	0.234 (0.026)	0.217 (0.029)	F=2.230 p=0.144

2.4.1.3 Binocular reading

Results of the statistical comparison between binocular viewing in amblyopic subjects and normal controls for oculomotor parameters are shown in table 2.5. During binocular viewing, amblyopic subjects read significantly slower compared to normal controls ($p<0.0001$). Moreover, amblyopic subjects made significantly more saccades to read a line of text compared to normal controls ($p=0.049$). No significant differences were observed between the two groups with respect to the number of progressive/forward saccades per line and their amplitude. Furthermore, amblyopic subjects exhibited a significantly increased number of regressive/backward saccades per line ($p=0.007$) and a significantly longer fixation duration ($p=0.044$) compared to normal controls.

Table 2.5. *Comparison of binocular reading of the amblyopic subjects and the normal controls. Mean measurements of the eye movement parameters, the standard deviations, the derived F-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	**Amblyopic subjects**	**Normal Controls**	***F*-statistic *p*-value**
Reading speed (characters with spaces/sec)	15.698 (4.034)	23.425 (5.847)	*F*=23.664 *p*=<0.0001*
Number of saccades per line	11.697 (2.853)	9.955 (2.564)	*F*=4.123 *p*=0.049*
Number of progressive/forward saccades per line	9.267 (2.671)	8.354 (2.105)	*F*=1.440 *p*=0.238
Amplitude of progressive/forward saccades (deg)	3.638 (1.069)	4.312 (0.847)	*F*=4.885 *p*=0.053
Number of regressive/backward saccades per line	2.429 (1.019)	1.600 (0.821)	*F*=8.013 *p*=0.007*
Fixation duration (sec)	0.224 (0.028)	0.206 (0.025)	*F*=4.330 *p*=0.044*

In the following pages, six figures are displayed showing values for all three viewing conditions, where:

Figure 2.4. *Reading speed (characters with spaces/sec)*
Figure 2.5. *Total number of saccades per line*
Figure 2.6. *Number of progressive/forward saccades per line*
Figure 2.7. *Amplitudes of progressive/forward saccades per line (deg)*
Figure 2.8. *Number of regressive/backward saccades per line*
Figure 2.9. *Fixation duration (sec)*

The following legend applies to all six figures:

A. Means and standard deviations in amblyopes (n=20) and controls (n=20) in each of the three conditions: *Amblyopic eye of the amblyopic subjects (AE) is compared to non-dominant eye of the normal controls (nDE), non-amblyopic eye of the amblyopic subjects (nAE) is compared to dominant eye of the normal controls (DE) and binocular viewing of the amblyopic subjects is compared to binocular viewing of the normal controls (BE).*

B. Individual mean values for each of the viewing conditions for the amblyopic subjects (n=20): *Amblyopic eye (AE) is compared to non-amblyopic eye (nAE) and binocular viewing (BE).*

C. Individual mean values for each of the viewing conditions for the normal controls (n=20): *Non-dominant eye (NDE) is compared to dominant eye (DE) and binocular viewing (BE).*

Figure 2.4. *Reading speed (characters with spaces/sec)*

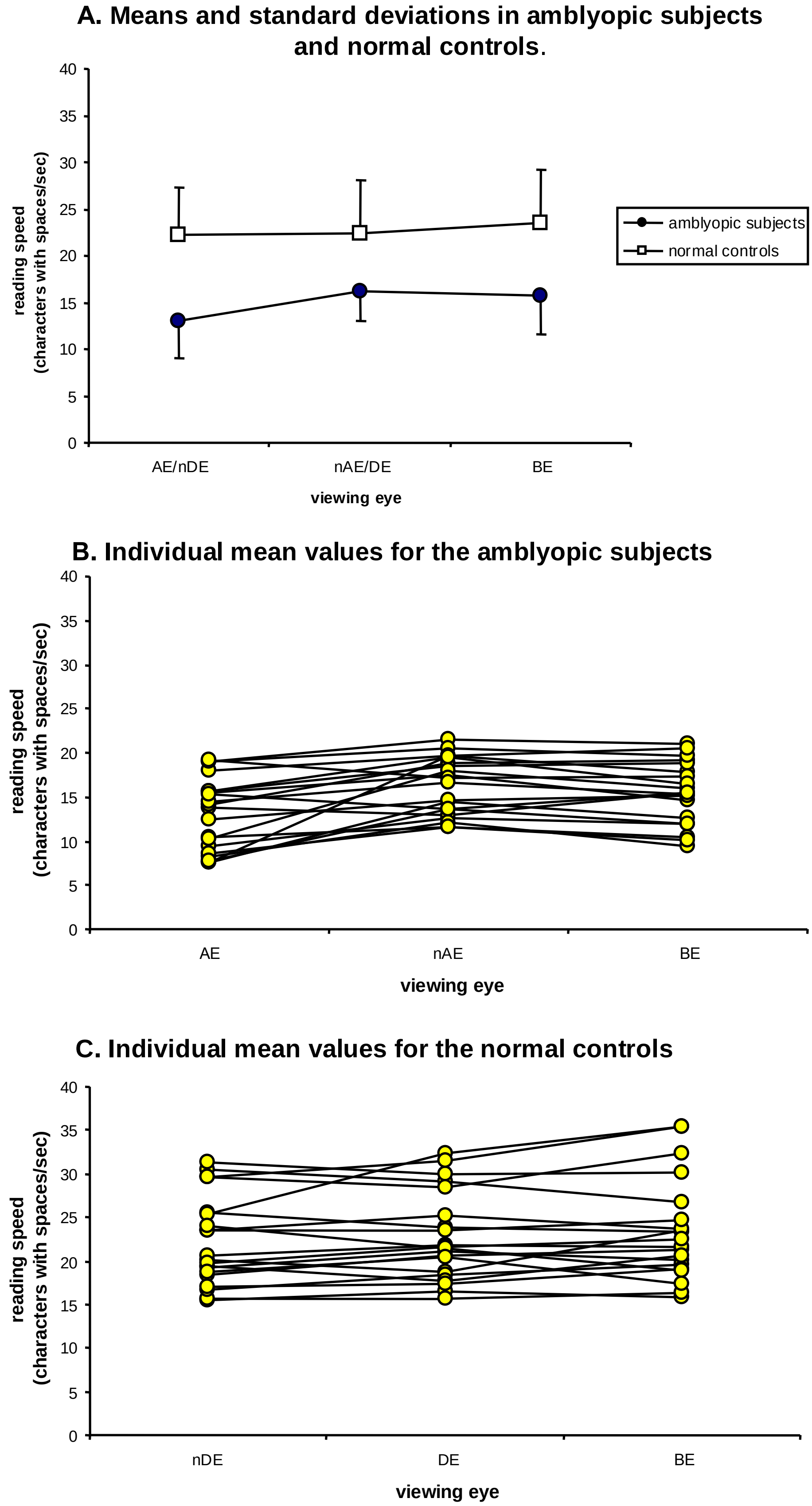
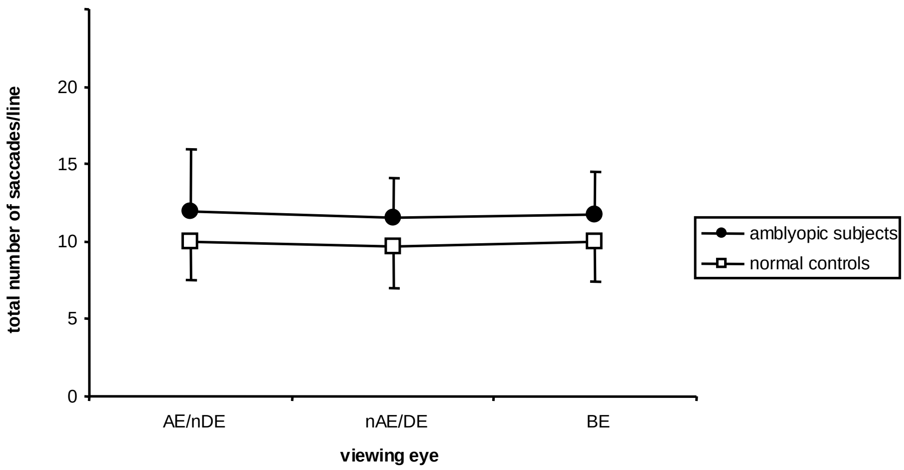
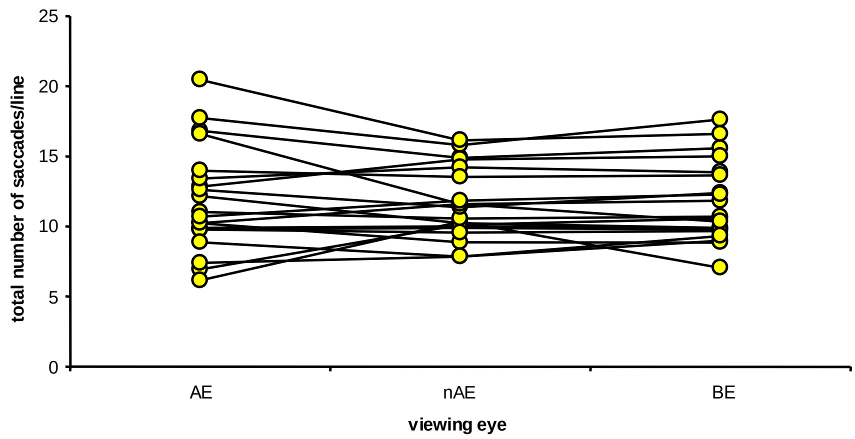


Figure 2.5. *Total number of saccades per line*

A. Means and standard deviations in amblyopic subjects and normal controls.



B. Individual mean values for the amblyopic subjects



C. Individual mean values for the normal controls

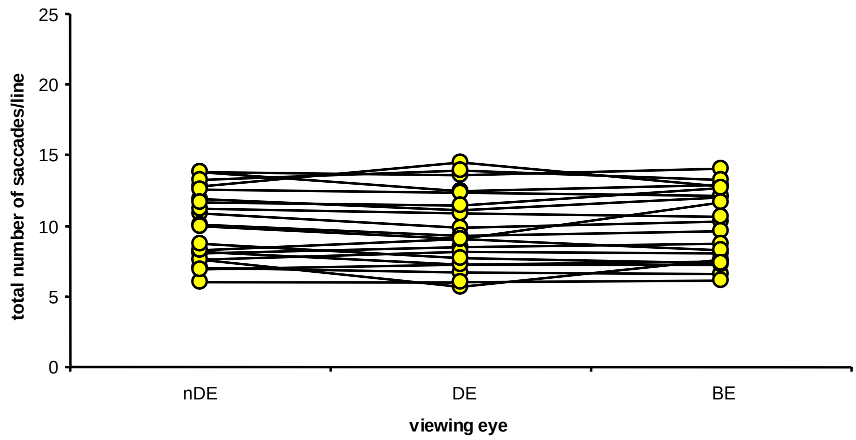
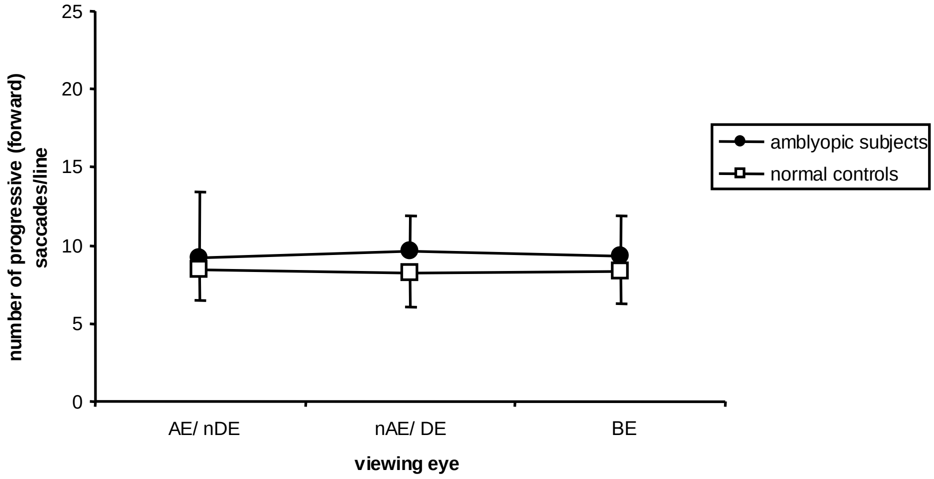
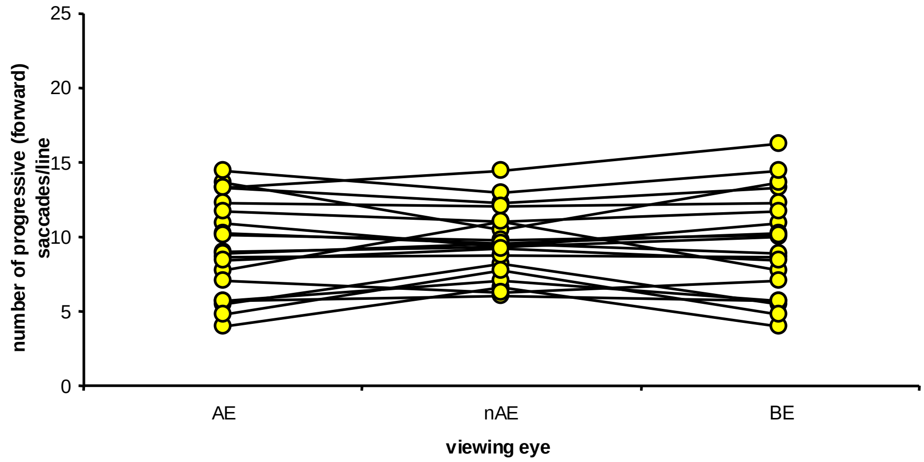


Figure 2.6. *Number of progressive/forward saccades per line*

A. Means and standard deviations in amblyopic subjects and normal controls.



B. Individual mean values for the amblyopic subjects



C. Individual mean values for the normal controls

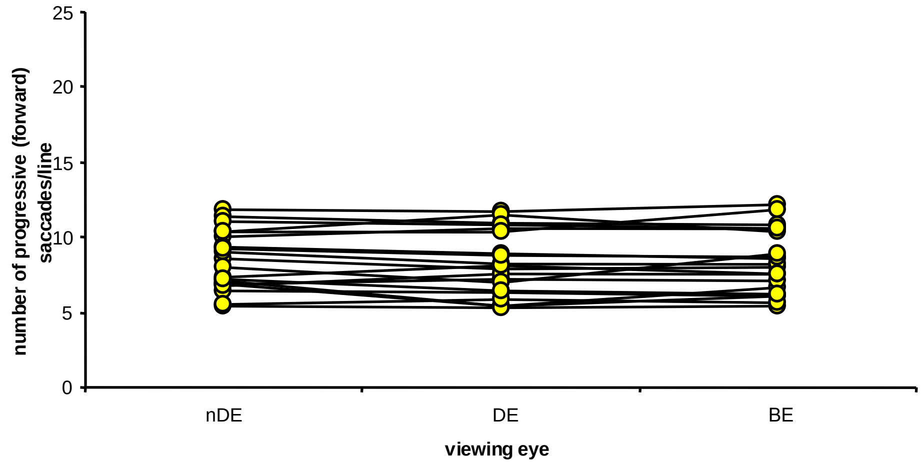


Figure 2.7. *Amplitudes of progressive/forward saccades (deg)*

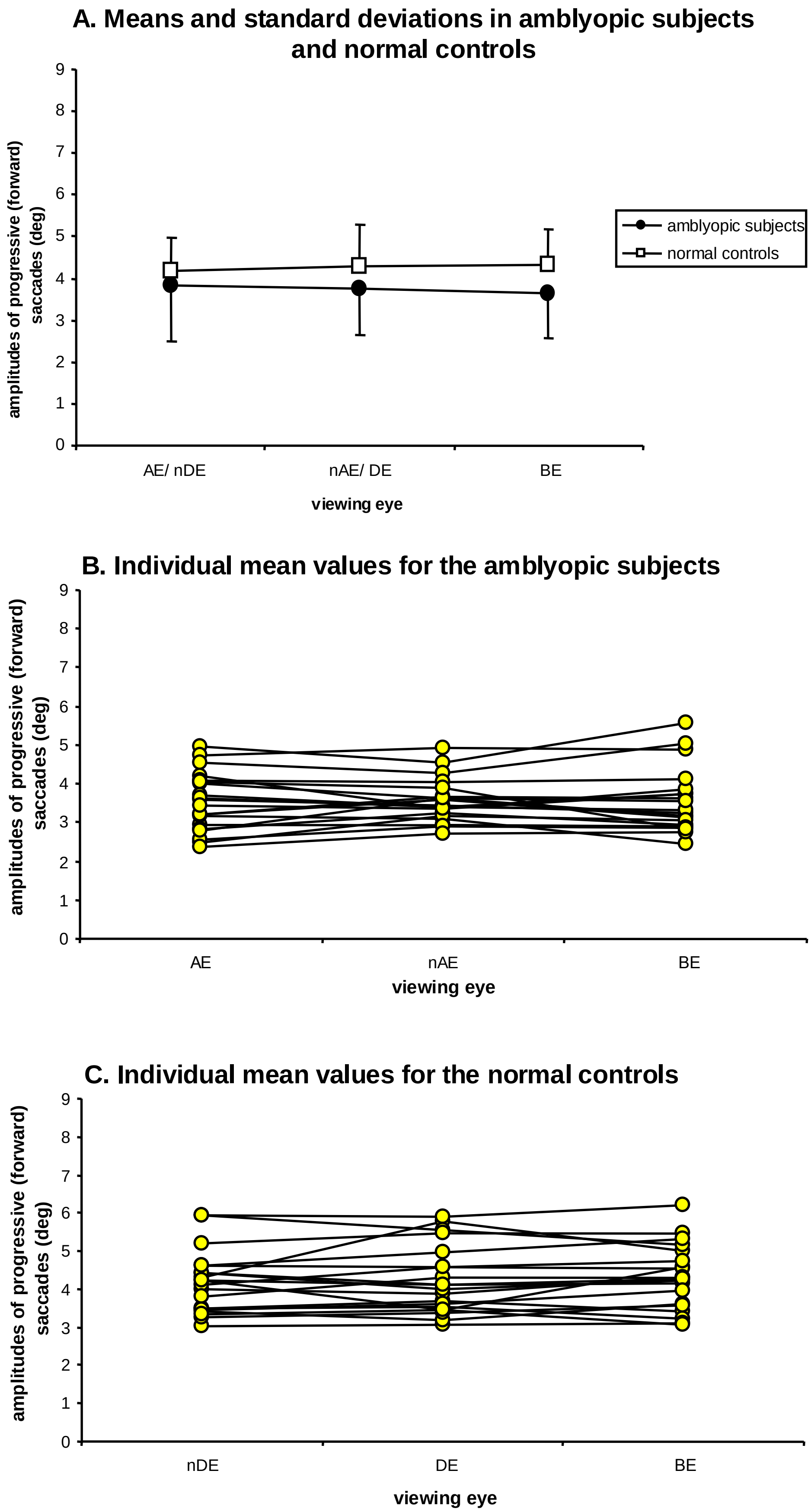


Figure 2.8. *Number of regressive/backwards saccades per line*

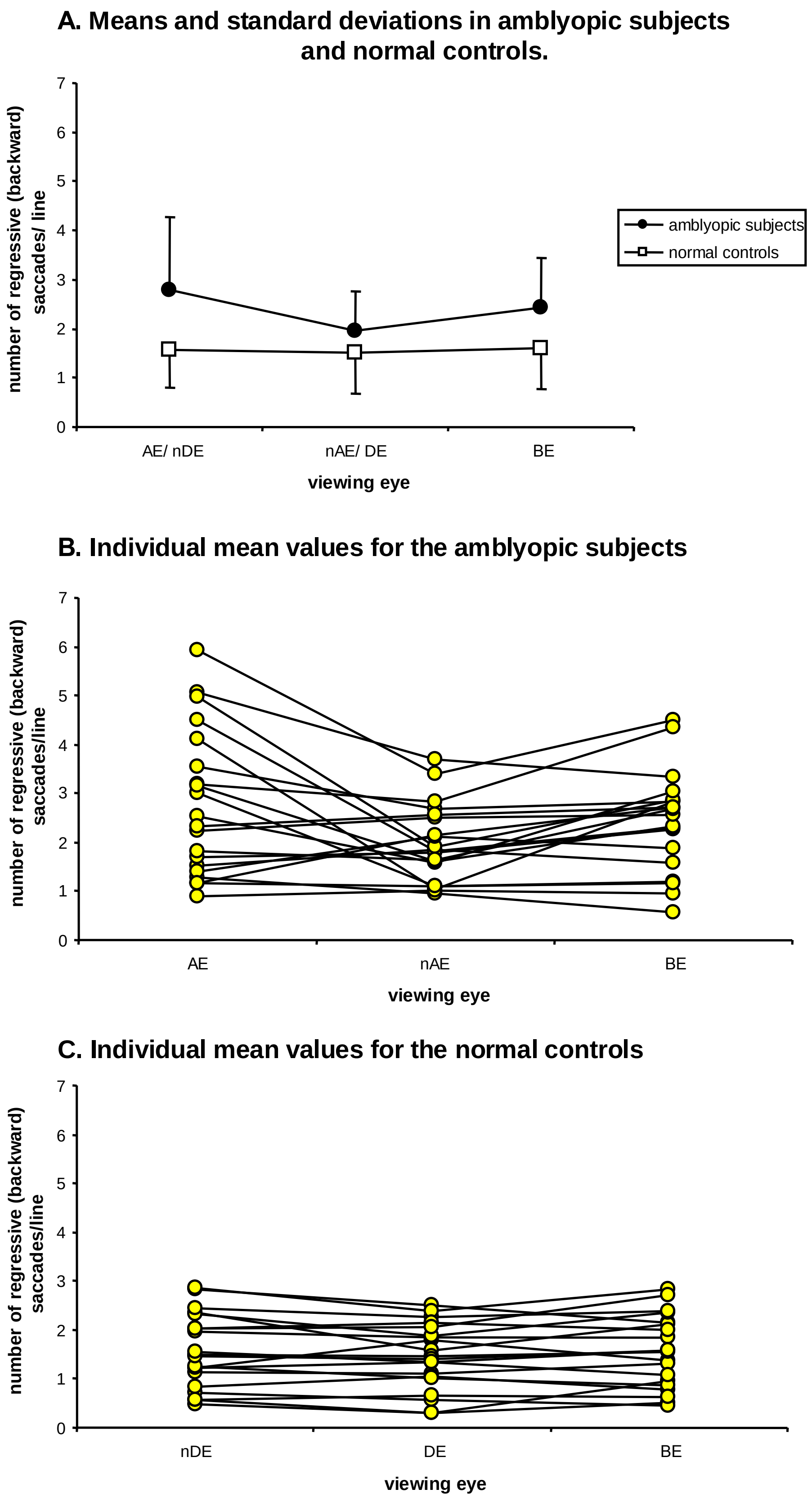
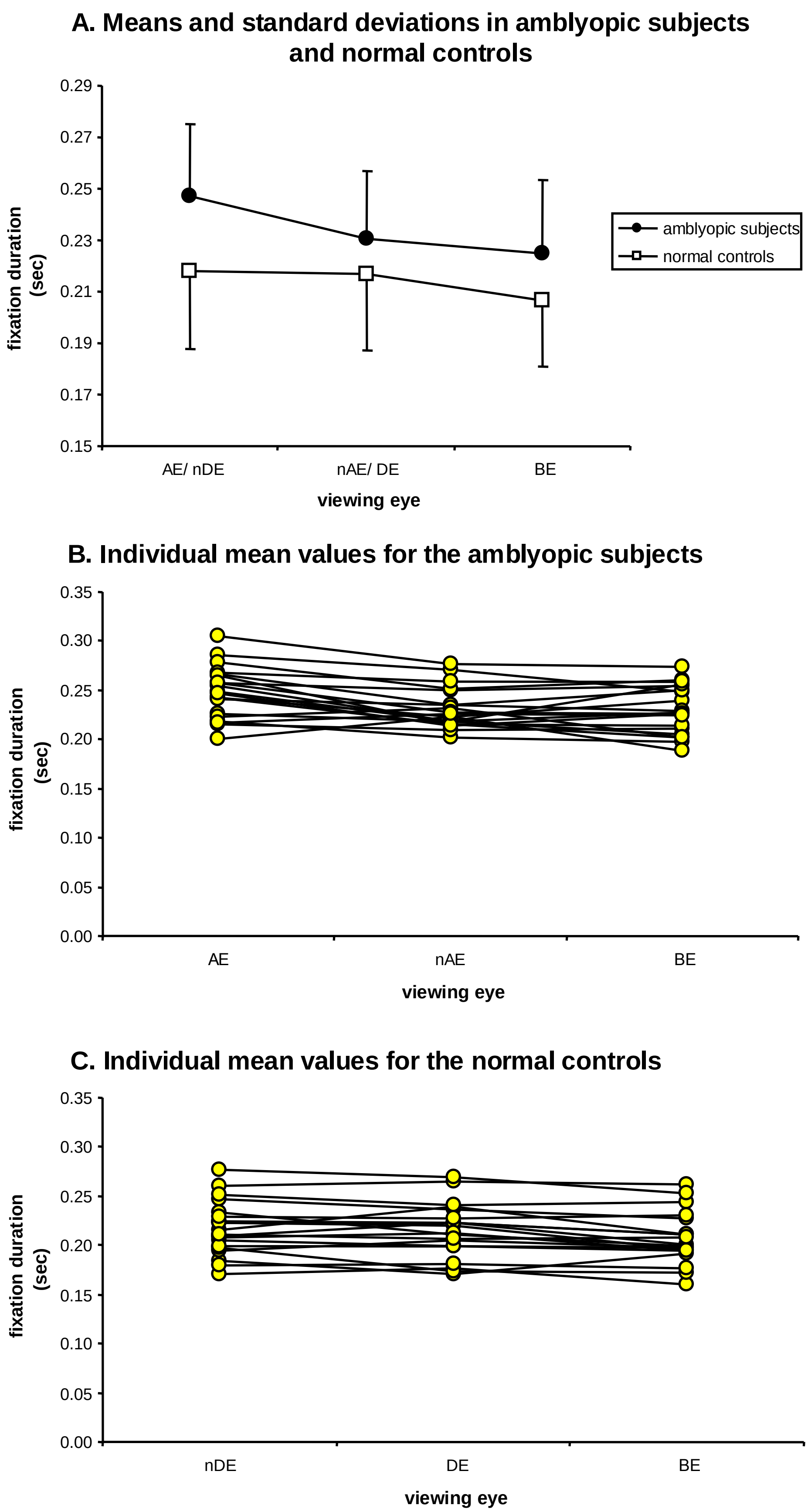


Figure 2.9. *Fixation duration (sec)*



2.4.2 Comparing the monocular with either eye and binocular reading performance of the amblyopic subjects

Reading with the amblyopic and non-amblyopic eye viewing and binocularly in amblyopic subjects was also investigated. There was a significant effect on reading performance regarding the reading speed (Wilks' Lambda=0.470, p=0.001), the number of regressive/backwards saccades per line (Wilks' Lambda=0.603, p=0.010) and the fixation duration (Wilks' Lambda=0.518, p=0.003). No significant differences were found with respect to the total number of saccades (Wilks' Lambda=0.964, p=0.722), the number of progressive/forward saccades per line (Wilks' Lambda=0.937, p=0.558) and the amplitude of the progressive/forward saccades (Wilks' Lambda=0.944, p=0.594) for the three viewing conditions under investigation.

2.4.2.1 Monocular reading with the amblyopic eye and the non-amblyopic eye

Results of the statistical comparison between viewing with the amblyopic and non-amblyopic eye of the amblyopic subjects are shown in table 2.6. Reading speed when reading with the amblyopic eye was significantly decreased compared to reading with the non-amblyopic eye (p<0.0001). No significant differences were observed with respect to the total number of saccades per line, the number of progressive/forward saccades per line and their amplitude. On the contrary, the number of regressive/backward saccades per line was significantly increased (p=0.010) and the fixation duration was significantly longer (p=0.005) during monocular reading with the amblyopic eye compared to monocular reading with the non-amblyopic eye.

Table 2.6. *Comparison of monocular reading with the amblyopic eye and the non-amblyopic eye of the amblyopic subjects. Mean measurements of the eye movement parameters, the standard deviations, the derived t-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	**Amblyopic eye**	**non-Amblyopic eye**	***t*-statistic *p*-value**
Reading speed (characters with spaces/sec)	13.094 (4.101)	16.241 (3.263)	t=-4.264 p<0.0001*
Number of saccades per line	11.971 (4.014)	11.547 (2.524)	t=0.778 p=0.446
Number of progressive/forward saccades per line	9.194 (4.172)	9.585 (2.285)	t=-0.672 p=0.510
Amplitude of progressive/forward saccades (deg)	3.823 (1.345)	3.745 (1.097)	t=0.271 p=0.790
Number of regressive/backward saccades per line	2.776 (1.500)	1.962 (0.787)	t=2.863 p=0.010*
Fixation duration (sec)	0.247 (0.028)	0.230 (0.026)	t=3.203 p=0.005*

2.4.2.2 Monocular reading with the amblyopic eye and binocularly

Results of the statistical comparison between viewing with the amblyopic eye and binocularly for the amblyopic subjects are shown in table 2.7. Reading speed during monocular reading with the amblyopic eye was significantly slower compared to binocular reading (*p*=0.011). No significant differences were observed with respect to the total number of saccades per line, the number of progressive/forward saccades per line and their amplitude as well as the number of regressive/backward saccades per line between the two viewing conditions under investigation. On the contrary, fixation duration during monocular reading with the amblyopic eye was significantly increased compared to binocular reading (*p*<0.0001).

Table 2.7. *Comparison of monocular reading with the amblyopic eye and binocularly of the amblyopic subjects. Mean measurements of the eye movement parameters, the standard deviations, the derived t-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	Amblyopic eye	Both eyes	*t*-statistic *p*-value
Reading speed (characters with spaces/sec)	13.094 (4.101)	15.698 (4.034)	*t*=-2.802 *p*=0.011*
Number of saccades per line	11.971 (4.014)	11.697 (2.853)	*t*=0.567 *p*=0.578
Number of progressive/forward saccades per line	9.194 (4.172)	9.267 (2.671)	*t*=-0.156 *p*=0.878
Amplitude of progressive/forward saccades (deg)	3.823 (1.345)	3.638 (1.069)	*t*=0.585 *p*=0.566
Number of regressive/backward saccades per line	2.776 (1.500)	2.429 (1.019)	*t*=1.378 *p*=0.184
Fixation duration (sec)	0.247 (0.028)	0.224 (0.028)	*t*=4.203 *p*<0.0001*

2.4.2.3 Monocular reading with the non-amblyopic eye and binocularly

Results of the statistical comparison between viewing with the non-ambyopic eye and binocularly for the amblyopic subjects are shown in table 2.8. During monocular reading with the non-amblyopic eye and binocularly, no significant differences were observed with respect to the reading speed, the total number of saccades per line, the number of progressive/forward saccades per line and their amplitude. Amblyopic subjects reading with the non-amblyopic eye, exhibited significantly fewer regressive/backward saccades when reading a line of text compared to binocular reading (p=0.005). No significant differences were observed in fixation duration between the two viewing conditions under investigation.

Table 2.8. *Comparison of monocular reading with the non-amblyopic eye and binocularly of the amblyopic subjects. Mean measurements of the eye movement parameters, the standard deviations, the derived t-statistics and p-values are illustrated. A two sided p-value highlighted with an asterisk is considered to indicate statistical significance.*

Variable	non-Amblyopic eye	Both eyes	*t*-statistic *p*-value
Reading speed (characters with spaces/sec)	16.241 (3.263)	15.698 (4.034)	*t*=1.163 *p*=0.259
Number of saccades per line	11.547 (2.524)	11.697 (2.853)	*t*=-0.634 *p*=0.534
Number of progressive/forward saccades per line	9.585 (2.285)	9.267 (2.671)	*t*=1.128 *p*=0.273
Amplitude of progressive/forward saccades (deg)	3.745 (1.097)	3.638 (1.069)	*t*=1.052 *p*=0.306
Number of regressive/backward saccades per line	1.962 (0.787)	2.429 (1.019)	*t*=-3.177 *p*=0.005*
Fixation duration (sec)	0.230 (0.026)	0.224 (0.028)	*t*=1.528 *p*=0.143

2.4.3 Eye movement patterns during monocular and binocular reading performance in the amblyopic subjects and the normal controls

Reading speed represents the functional outcome of the oculomotor parameters during reading, namely the number of saccades and the fixation duration. The association of each of these parameters with the reading speed variability as well as their predictive value were also assessed.

I found that, during monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, the total number of saccades per line, the number of progressive/forward saccades per line, the number of regressive/backward saccades per line and the fixation duration were **negatively** correlated with the reading speed, while the amplitude of the progressive/forward saccades was **positively** correlated to the reading speed. Similar correlations were observed during monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and during binocular reading in both the amblyopic subjects and the normal controls. A summary of the analysis is presented in tables 2.9 to 2.11.

Table 2.9. *Correlation statistics for each oculomotor parameter against reading speed during monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Pearson correlation coefficients (r) or the non-parametric alternative, Spearman's Rank Order Correlation (rho) are illustrated. Correlations are considered significant at the 0.05 level (two-tailed) highlighted with an asterisk.*

Variable	**Amblyopic eye**	**Non-Dominant eye**
total number of saccades per line vs. reading speed	r=-0.421 p=0.065	r=-0.765 p<0.0001*
number of progressive/forward saccades per line vs. reading speed	r=-0.377 p=0.101	r=-0.716 p<0.0001*
amplitudes of progressive/forward saccades vs. reading speed	r=0.170 p=0.475	r=0.591 p=0.006*
number of regressive/backwards saccades per line vs. reading speed	r=-0.078 p=0.744	r=-0.688 p=0.0001*
fixation duration vs. reading speed	r=-0.638 p=0.002*	r=-0.575 p=0.008*

Table 2.10. *Correlation statistics for each oculomotor parameter against reading speed during monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Pearson correlation coefficients (r) or the non-parametric alternative, Spearman's Rank Order Correlation (rho) are illustrated. Correlations are considered significant at the 0.05 level (two-tailed) highlighted with an asterisk.*

Variable	**Non-Amblyopic eye**	**Dominant eye**
total number of saccades per line vs. reading speed	*r*=-0.585 *p*=0.007*	*r*=-0.547 *p*=0.013*
number of progressive/forward saccades per line vs. reading speed	*r*=-0.498 *p*=0.025*	*r*=-0.458 *p*=0.042*
amplitudes of progressive/forward saccades vs. reading speed	*r*=0.605 *p*=0.005*	*r*=0.567 *p*=0.009*
number of regressive/backwards saccades per line vs. reading speed	*r*=-0.430 *p*=0.058	*r*=-0.574 *p*=0.008*
fixation duration vs. reading speed	*r*=-0.735 *p*<0.0001*	*r*=-0.613 *p*=0.004*

Table 2.11. *Correlation statistics for each oculomotor parameter against reading speed during binocular reading of the amblyopic subjects and the normal controls. Pearson correlation coefficients (r) or the non-parametric alternative, Spearman's Rank Order Correlation (rho) are illustrated. Correlations are considered significant at the 0.05 level (two-tailed) highlighted with an asterisk.*

Variable	**Both eyes amblyopic subjects**	**Both eyes normal controls**
total number of saccades per line vs. reading speed	r=-0.443 p=0.051	r=-0.611 p=0.004*
number of progressive/forward saccades per line vs. reading speed	r=-0.345 p=0.137	r=-0.529 p=0.016*
amplitudes of progressive/forward saccades vs. reading speed	r=0.684 p=0.001*	r=0.456 p=0.044*
number of regressive/backwards saccades per line vs. reading speed	r=-0.336 p=0.147	r=-0.551 p=0.012*
fixation duration vs. reading speed	r=-0.825 p<0.0001*	r=-0.597 p=0.005*

Figures 2.10 to 2.14 illustrate the relationship between the total number of saccades per line, the number of progressive/forward saccades per line, the amplitude of the progressive/forward saccades, the number of the regressive/backward saccades per line, the fixation duration and the reading speed during monocular reading with either eye and binocularly in both the amblyopic subjects and the normal controls.

A similar distribution of the data is evident when any combination of the eyes is viewing for both the amblyopic subjects and the normal controls. Furthermore, in amblyopia, as reading speed is slower, the whole range for both the saccades number and fixation duration is shifted to the right compared to normal controls.

Interestingly, during monocular reading with the amblyopic eye in the amblyopic subjects, the total number of saccades shows a greater spread of the data along the X-axis with reduced reading speed. This is mainly due to both progressive/forward and regressive/backward saccades per line where the same pattern is observed. For fixation duration, the spread of the data is more even along the X-axis for changing reading speed.

The following five figures show the correlation between each of the oculomotor parameters and reading speed where:

Figure 2.10. *Total number of saccades per line vs. Reading speed*
Figure 2.11. *Number of progressive/forward saccades per line vs. Reading speed*
Figure 2.12. *Amplitudes of progressive/forward saccades vs. Reading speed*
Figure 2.13. *Number of regressive/reverse saccades per line vs. Reading speed*
Figure 2.14. *Fixation duration vs. Reading speed*

The following legend applies to all five figures:

Means (individual values) are illustrated for each amblyopic subject and normal control. For each figure:
A. Monocular reading with the amblyopic eye of the amblyopic subjects (n=20) compared to monocular reading with non-dominant eye of the normal controls (n=20).
B. Monocular reading with the non-amblyopic eye of the amblyopic subjects (n=20) compared to monocular reading with the dominant eye of the normal controls (n=20).
C. Binocular reading of the amblyopic subjects (n=20) compared to binocular reading of the normal controls (n=20).

Figure 2.10. *Total number of saccades per line vs. Reading speed*

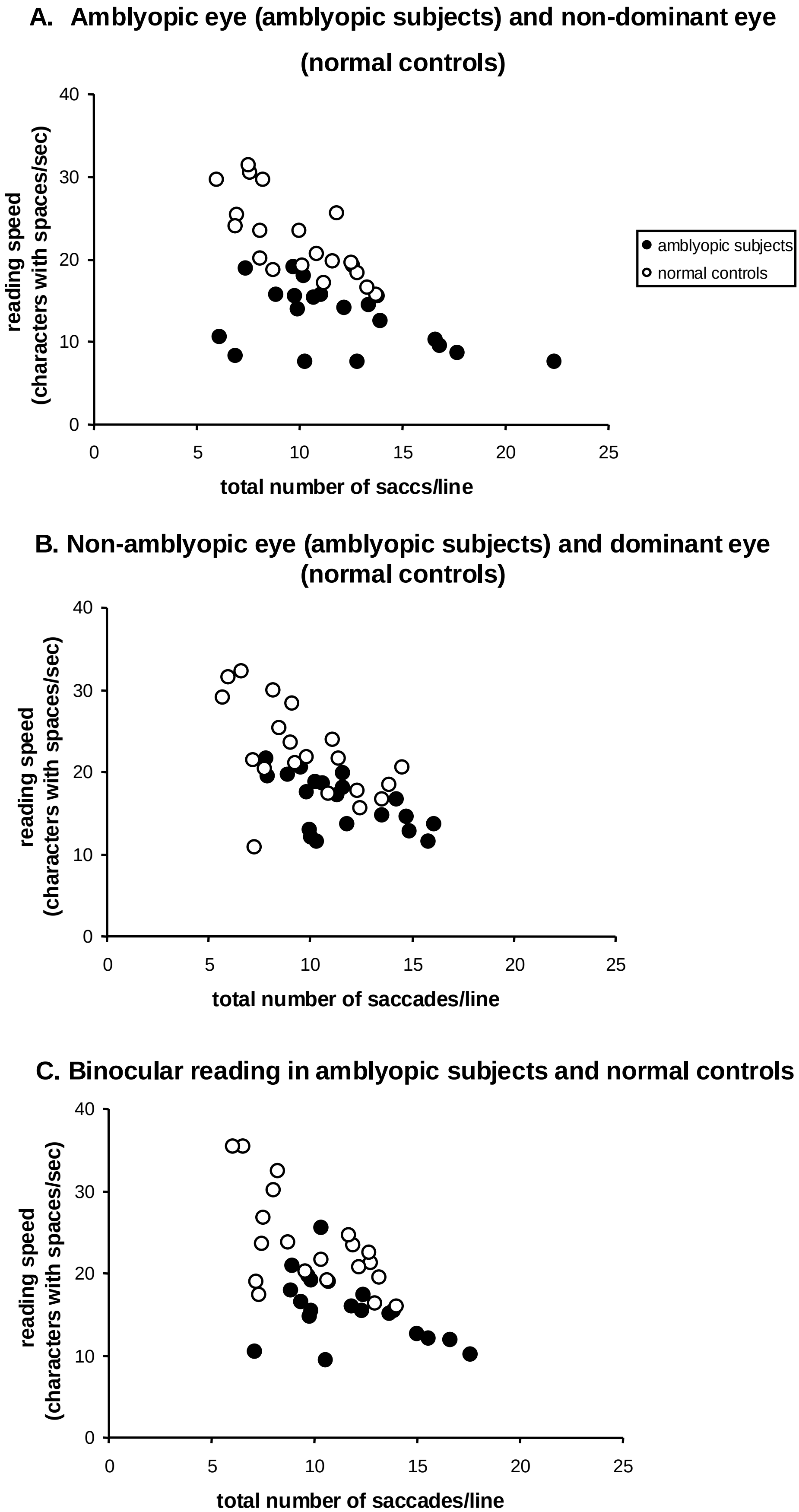


Figure 2.11. *Number of progressive/forward saccades per line vs. Reading speed*

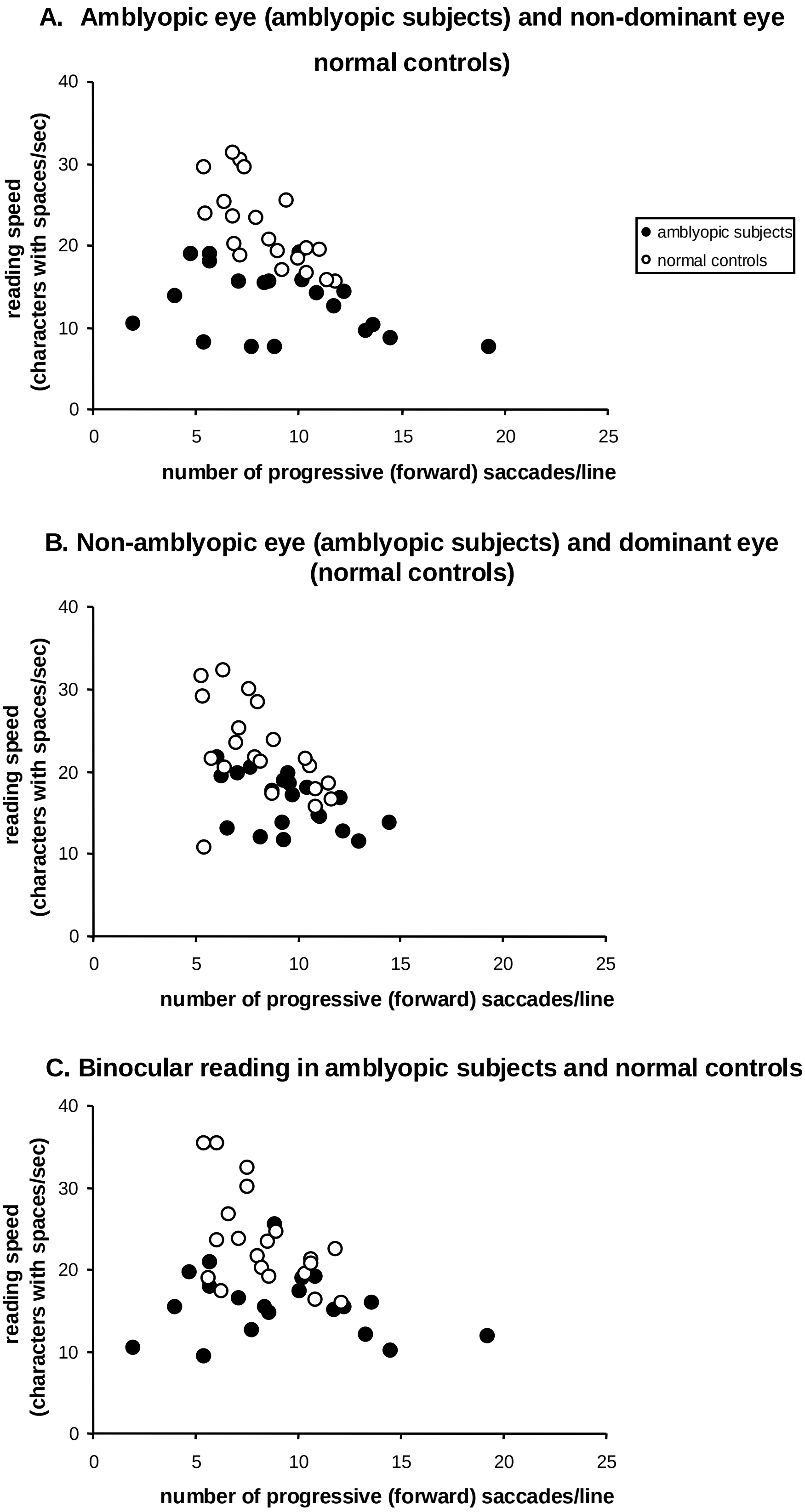
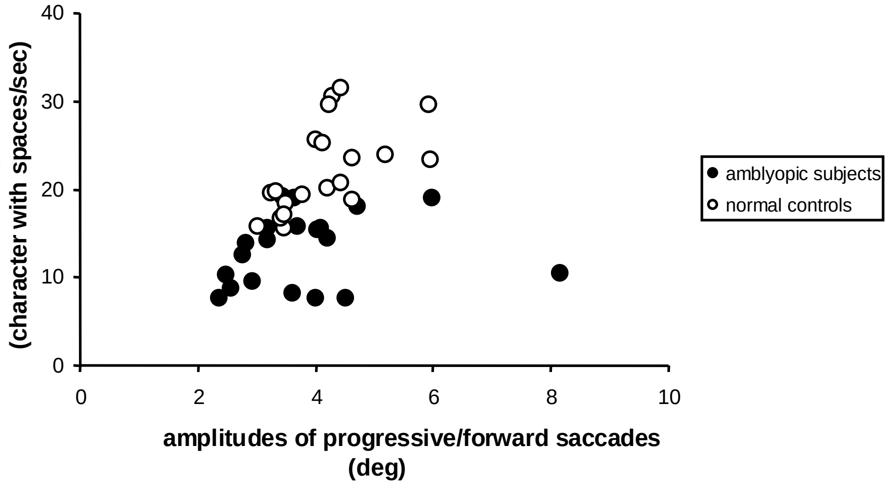
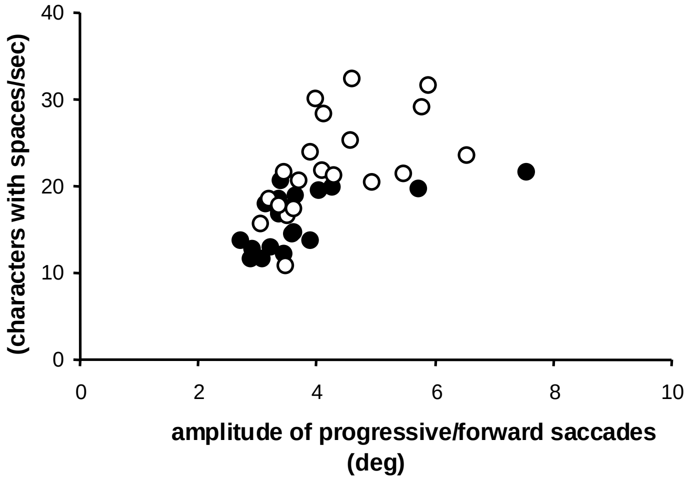


Figure 2.12. *Amplitude of progressive/forward saccades vs. Reading speed*

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

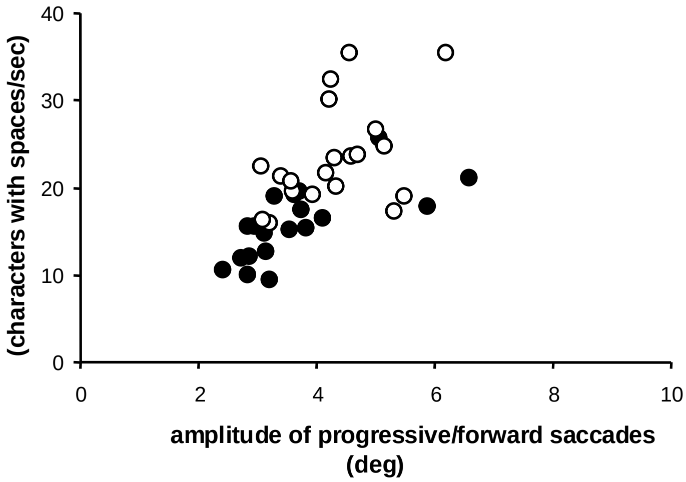


Figure 2.13. *Number of regressive/backward saccades per line vs. Reading speed*

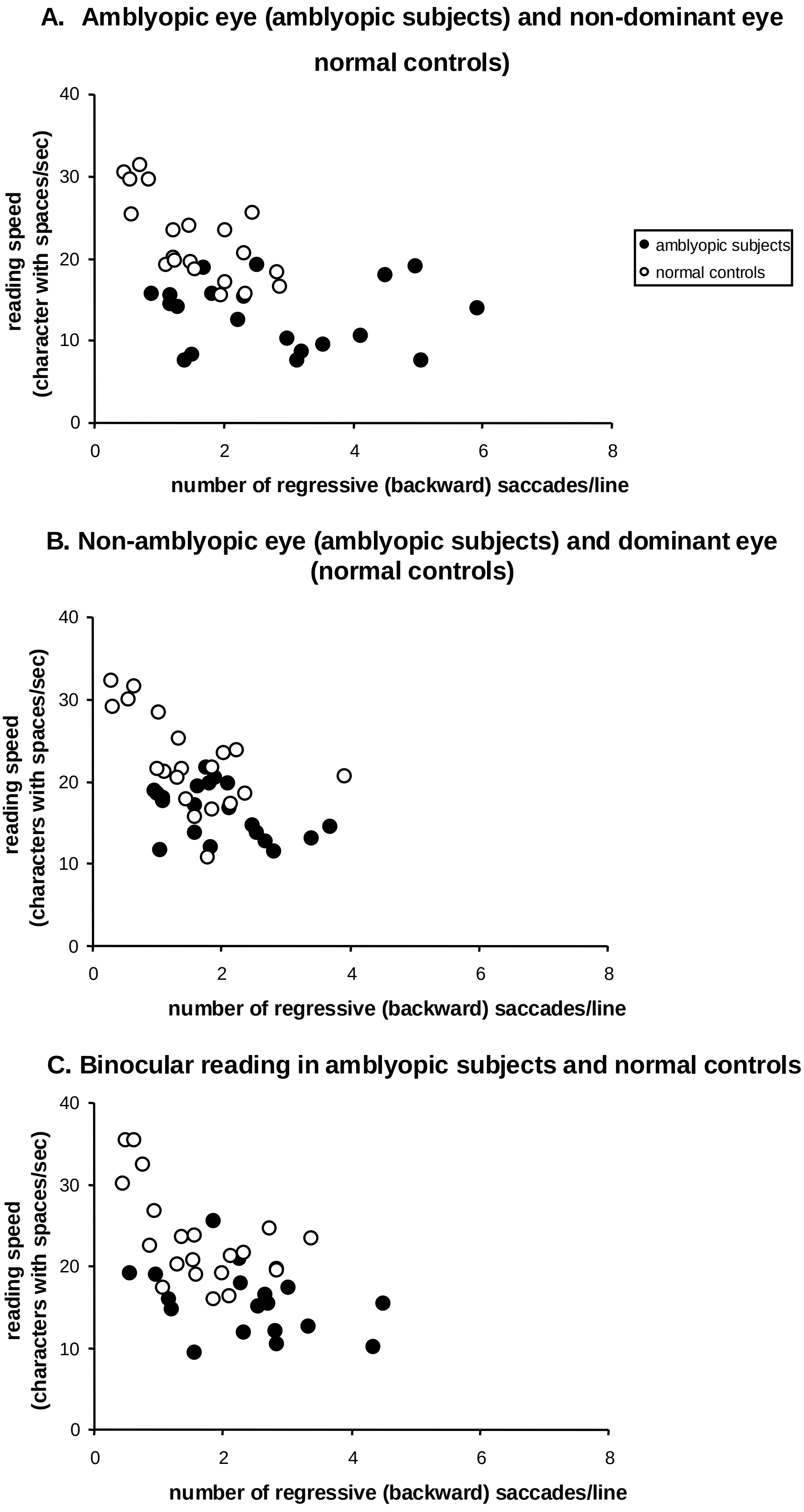
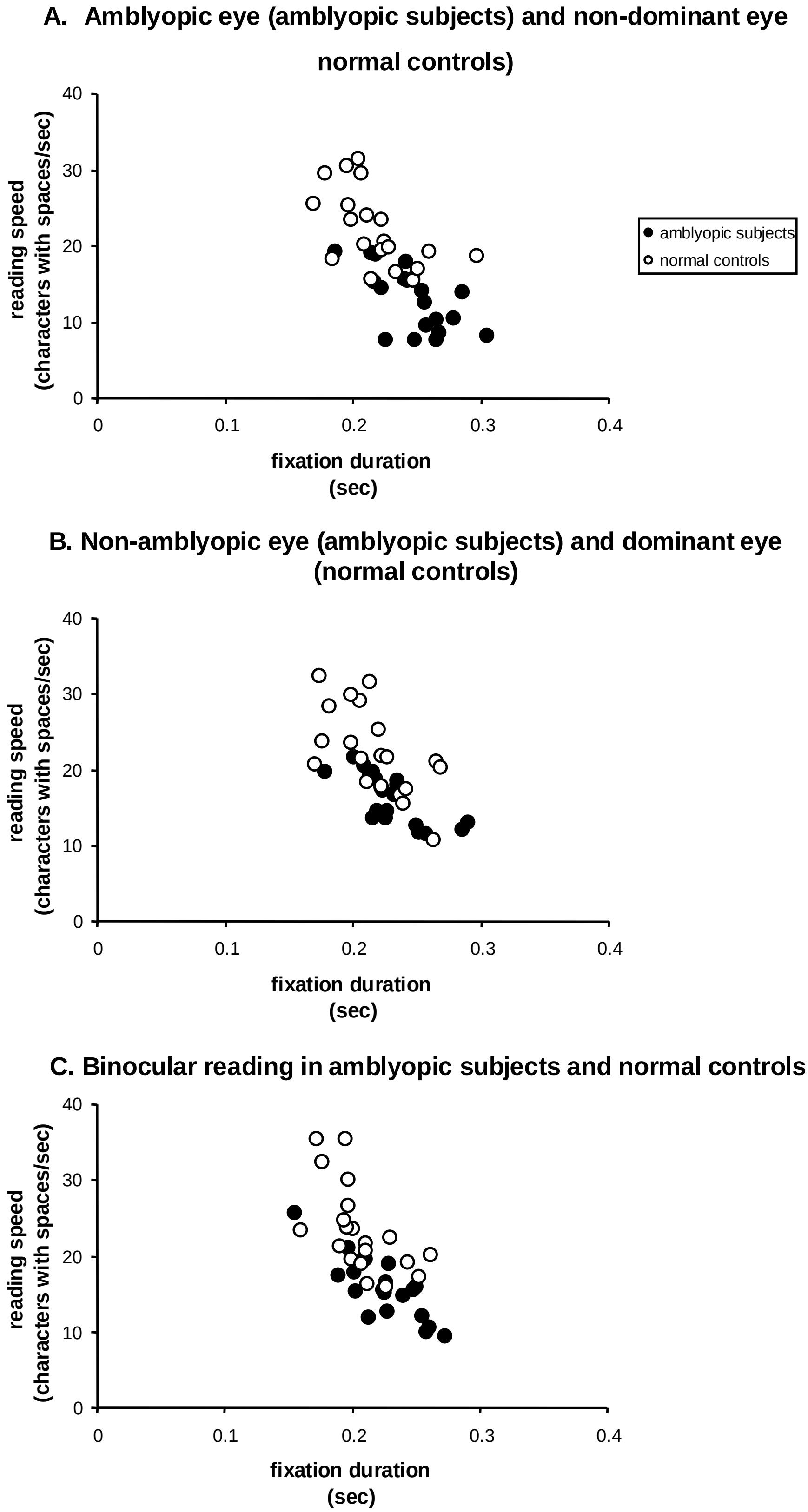


Figure 2.14. *Fixation duration vs. Reading speed*



2.4.4 The predictive ability of saccades number and fixation duration in reading speed changes during monocular and binocular reading performance in the amblyopic subjects and the normal controls - A multiple regression analysis

2.4.4.1. Reading performance in the amblyopic subjects

2.4.4.1.1. Monocular reading with the amblyopic eye

During monocular reading with the amblyopic eye, 51.1% of the variance in reading speed was explained by the number of saccades per line and the fixation duration, reaching statistical significance (p=0.001). Both the number of saccades per line and the fixation duration made a significant contribution to the prediction of the reading speed (p=0.025 and p=0.001 respectively). Fixation duration made the strongest unique contribution to explaining the reading speed changes when the variance explained by the number of saccades was controlled for (beta coefficient -0.621). Saccades number contributed less to reading speed changes (beta coefficient -0.394).

2.4.4.1.2 Monocular reading with the non-amblyopic eye

During monocular reading with the non-amblyopic eye, 79.7% of the variance in reading speed was significantly caused by the number of saccades per line and the fixation duration (p<0.0001). The number of saccades per line as well as the fixation duration contributed significantly to the prediction of the reading speed (p<0.0001 and p<0.0001 respectively) with fixation duration to account more for the reading speed changes (beta coefficient -0.678) compared to the number of saccades per line (beta coefficient -0.510).

2.4.4.1.3 Binocular reading

During binocular reading, 77% of the variance in reading speed was attributed to the number of saccades per line and the fixation duration ($p<0.0001$). Both the eye movement parameters made a significant contribution to the reading speed changes ($p=0.007$ and $p<0.0001$ respectively). Similarly, to monocular reading with the amblyopic and the non-amblyopic eye, fixation duration seemed to justify more of the variance in reading speed (beta coefficient -0.780) compared to the number of saccades per line (beta coefficient -0.340).

2.4.4.2. Reading performance in the normal controls

2.4.4.2.1 Monocular reading with the non-dominant eye

During monocular reading with the non-dominant eye, 76.8% of reading speed changes were attributed to the number of saccades per line and fixation duration ($p<0.0001$). Both the number of saccades per line and the fixation duration made a significant contribution ($p<0.0001$ and $p=0.001$ respectively) with the number of saccades per line to mainly account for the reading speed variations (beta coefficient-0.689) compared to fixation duration (beta coefficient -0.461).

2.4.4.2.2 Monocular reading with the dominant eye

During monocular reading with the dominant eye, 70.4% of the variance in reading speed was explained by the number of saccades per line and the fixation duration ($p<0.0001$). While the contribution of one of the eye movement parameters was controlled for, reading speed changes were caused mainly by fixation duration changes (beta coefficient -0.637, $p<0.0001$) compared to the number of saccades variations (beta coefficient -0.574, $p<0.0001$).

2.4.4.2.3 Binocular reading

During binocular reading, 61.1% of the reading speed variance was attributed to the number of saccades per line and fixation duration ($p<0.0001$). Both of the eye movement parameters contributed significantly to the reading speed alternations ($p=0.001$ and $p=0.002$) with the number of saccades to make much of a contribution (beta coefficient -0.548) compared to fixation duration (beta coefficient -0.513).

2.4.5 Results summary

In summary, during monocular and binocular reading performance, significant differences could be found between the amblyopic subjects and the normal controls particularly with respect to the mean reading speed. Reading speed was found significantly slower in the amblyopic subjects during monocular reading with the amblyopic eye, the non-amblyopic eye and binocularly compared to the normal controls reading with the non-dominant eye, the dominant eye and binocularly respectively. Reading speed during reading with the amblyopic eye was also significantly slower compared to the non-amblyopic eye and binocular reading in the amblyopic group. During reading with the amblyopic eye, the number of regressive/backwards saccades per line and the fixation duration were significantly increased in the amblyopic subjects compared to normal controls reading with the non-dominant eye. During reading with the non-amblyopic eye, the total number of saccades per line in the amblyopic subjects was significantly larger than in dominant eyes of the normal controls. During binocular reading, the total number of saccades per line, the number of regressive/backward saccades per line and the fixation duration differed significantly between the two groups. It was interesting to observe that, the reading eye movements between the two groups showed similar patterns with the amblyopic subjects to exhibit an increased number of saccades per line and prolonged fixation duration compared to the normal controls. In all viewing conditions, in the amblyopic subjects, fixation duration made the strongest unique contribution to explain the reading speed changes while in the normal controls both saccades number and fixation duration seemed to account for the reading speed variations.

3. Experiment 2: Fixational stability and Saccadic Performance - Correlation with the Reading Measurements

3.1 Aims of the study

In patients with strabismic amblyopia, the amblyopic eye, as well as the non-amblyopic eye are characterized by a spectrum of oculomotor abnormalities regarding the fixational stability and the saccadic performance (102, 145, 190-193, 211-225, 233). I sought to investigate whether these abnormalities (namely unsteady fixation, increased saccadic latency and decreased saccadic accuracy) occurred in the amblyopic subjects that participated in my study. I also sought to determine whether these oculomotor abnormalities were related to the reading speed changes that the amblyopic subjects exhibit during monocular reading with either eye and binocularly compared to the normal controls.

A number of standard eye movement tests were performed therefore, under monocular viewing with either eye and binocular viewing, in order to assess the stability of fixation and saccadic performance.

3.2. Hypotheses tested

In strabismic amblyopia, amblyopic eyes are characterized by deficient fixation stability and exhibit increased saccadic latencies and reduced saccadic gains while viewing a moving target stimulus. Therefore, I tested the hypothesis that fixation stability measured with BCEA is significantly impaired in the amblyopic eye of the amblyopic subjects compared to the non-dominant eye of the normal controls. Furthermore, amblyopic eyes of the amblyopic subjects are expected to manifest increased saccadic latencies and reduced saccadic gains compared to non-dominant eyes of the normal controls.

Fixation instability of non amblyopic eyes has been described by many investigators. Furthermore, in my reading experiment a number of oculomotor abnormalities have been found to be related to the reduced reading rates during monocular viewing with the non-amblyopic eye. Therefore, I hypothesized that the non-amblyopic eye of the amblyopic subjects is characterized by larger BCEAs and exhibited shorter and less accurate saccades while viewing a target stimulus compared to the dominant eye of the normal controls. Binocular viewing performance might be similarly affected.

Previous literature has suggested that fixation instability is significantly associated with reduced reading rates. I hypothesized that BCEA during monocular viewing with either eye and binocularly in the amblyopic subjects is significantly correlated to reading speed and fixation duration measurements derived from my reading task. In addition, for the saccadic task, I hypothesized that the latency, the gain and the number of saccades to reach the target during monocular and binocular viewing conditions in the amblyopic subjects are significantly correlated to the fixation duration, the amplitude of the progressive/forward saccades and the total number of saccades during reading.

3.3 Methods

3.3.1 Eye movement recordings

Eye position was measured using the same eye tracker (EyeLink I) and projection system as described in chapter 2.

All investigations were performed while eye movements were recorded during monocular viewing with either eye and binocularly in both the amblyopic subjects and the normal controls with the order randomized. During monocular viewing, the contralateral eye was occluded using an occluder while the eye movement recordings were still maintained. The whole test duration was approximately 25 minutes.

3.3.2. Fixational stability

Stability of fixation in primary gaze position was evaluated. Periods of saccade free fixation of between 1 and 3 seconds were selected from data, when subjects were fixating a spot at primary position, under monocular and binocular viewing. The stability of fixation in minarc^2 during these periods was measured using the bivariate contour ellipse area (BCEA) after data had been removed during blinks and saccades. The bivariate contour ellipse area (BCEA) is a measure of the area of an ellipse which contains 68% of the data during fixation (1 standard deviation). Smaller bivariate contour ellipse area (BCEA) values correspond to steadier fixation.

3.3.3. Saccadic performance

A horizontal and vertical saccadic task was performed, consisting of target jumps, horizontally and vertically every 1.0sec, made randomly between the following positions: -20°, -10°, 10° and 20° (where negative values indicate leftwards), and returning to 0° after each target shift. The target was a black spot (0.88cd/m²) of 1° visual angle on a white background (14.3cd/m²) and was projected onto the rear projection screen using the set-up described earlier. The whole task lasted approximately 70sec. Analysis was performed separately for 10° and 20° amplitude target shifts because previous literature suggests that small distances are often overestimated, while large distances are frequently underestimated (247, 248). Thirty two random target jumps occurred with each one followed by a return to centre.

Data were only analysed for unpredictable target movement, which is when the target was moving from the central position, so as to evaluate the eye movement parameters from the reflexively driven saccades. For the data analysis, cursors were placed semi-automatically at points 500ms before and 1000ms after each target jump. The points could be moved manually to avoid analysing a blink or if the eye movement was not stable at that point. Measurements were calculated for each target jump, as the difference between the values measured at the two points compared to the target corresponding values. On the whole, the measurements derived from the eye movements recordings between the cursors were: (i) The latency of the initial/ primary saccade (in sec), (ii) The gain of the initial/ primary saccade, and (iii) The number of saccades per target shift. *The gain of the initial/ primary saccade* was calculated from the amplitude of the initial/primary saccade (in deg) divided by the target shift. The amplitude of the initial/primary saccade was calculated from the Euclidian sum distance travelled during the initial/primary saccade. Means were calculated for all eye movement parameters under investigation.

3.3.4 Data analysis

For data analysis, the same equipment and calibration procedures were used as in experiment 1. In particular, eye data were calibrated under monocular and binocular viewing prior to each investigation using a series of nine fixation points, projected individually in the shape of a 3x3 grid, ±20° wide and ±17.5° high. The calibrated data were then analysed using customised computer programmes (written in Spike 2 neurophysiological software, Cambridge Electronic Design Ltd, Cambridge), which removed artefact such as blinks from the traces before all data were analysed by one investigator.

3.3.5. Statistical analysis

Descriptive and Inferential Data Analyses were performed using SPSS for Windows, version 14.0. Differences between the amblyopic subjects and the normal controls, regarding the oculomotor parameters for each target direction and amplitude shift, were evaluated by independent samples t-test. Differences between the amblyopic , the non-amblyopic eye and binocular viewing of the amblyopic subjects were assessed by paired samples t-test.

The assumption of normality was tested using the Shapiro-Wilk test of normality and the assumption of the equality of variances was tested by the Levene's t-test for equality of variances. For data that did not meet the assumptions of the parametric techniques (assumption of normality and equality of variances), the non-parametric Mann-Whitney U test or the Wilcoxon Signed Rank test were used. For all analysis a 2-sided p-value<0.05 was considered to indicate statistical significance. For the correlations analysis, Pearson correlation coefficients (or the non-parametric Spearman's Rank Order correlation) were calculated.

For the statistical analysis, the BCEA data values were converted into their logarithms so as to more closely approximate to a normal distribution. In addition, regarding the saccades data, the averages of the derived measurements for each direction of the target stimulus separately for the 20° and 10° amplitude target shifts were used to describe the differences observed between the amblyopic subjects and the normal controls.

All investigations were performed while comparing: (i) monocular viewing with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, (ii) monocular viewing of the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and, (iii) binocular viewing in both the amblyopic subjects and the normal controls. During binocular viewing, the measurements derived from the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls were selected for the analysis.

3.4 Results

3.4.1 Fixational stability

Original data (as X-Y plots) are shown in figure 3.1 for an amblyopic subject and a normal control while aiming to maintain fixation on one spot.

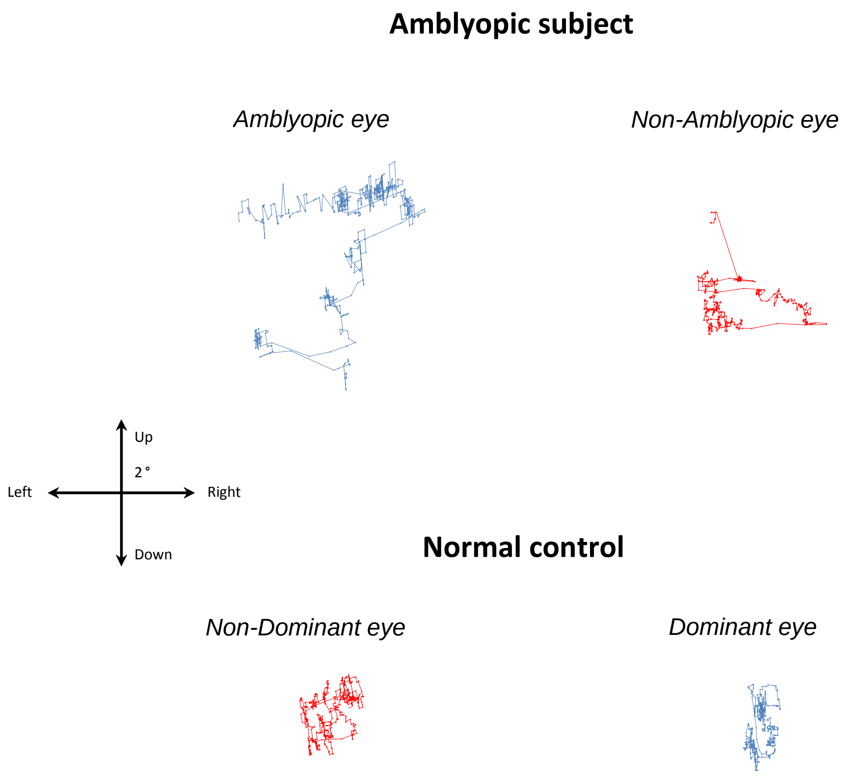


Figure 3.1. *Original recordings of how the eyes drift around (as if the gaze position was a pen) during the time range selected during monocular viewing with either eye of the amblyopic subjects and the normal controls. It is interesting to observe the increased fixation instability during monocular viewing with the amblyopic eye of the amblyopic subjects indicated by the extended areas corresponding to the gaze position traces compared to the non-amblyopic eye, as well as either eye of the normal controls.*

Fixation stability of the amblyopic eye of the amblyopic subjects was significantly impaired compared to the non-dominant eye ($p<0.0001$) of the normal controls. BCEAs recorded during monocular fixation with the non-amblyopic eye of the amblyopic subjects were similar to those recorded during monocular fixation with the dominant eye of the normal controls. No significant differences were observed between the two groups while evaluating fixational stability during binocular viewing (table 3.1). In addition, fixation stability of the amblyopic eye was also significantly impaired compared to the non-amblyopic eye ($t=2.030$, $p=0.037$) and binocular viewing ($t=3.401$, $p=0.003$) in the amblyopic subjects. The nasalward drift observed in some of the amblyopic subjects during monocular viewing with the amblyopic eye might possibly be related to the impaired fixational stability of the amblyopic eye indicated by the extended BCEA.

Table 3.1. *Comparison of fixational stability (minarc^2) between the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, between the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and between both eyes of the two groups. Mean BCEA values, standard deviations, t-statistics and p-values are included in the table. A two-sided p-value<0.05 was used to indicate statistical significance indicated with an asterisk.*

Variable	**Amblyopic eye**	**non-Dominant eye**	***t*-statistic *p*-value**
Fixation Stability (minarc^2)	2.193 (0.435)	1.690 (0.244)	*t*=4.505 *p*<0.0001*
Variable	**non-Amblyopic eye**	**Dominant eye**	***t*-statistic *p*-value**
Fixation Stability (minarc^2)	1.933 (0.512)	1.796 (0.138)	*t*=1.152 *p*=0.262
Variable	**Both eyes Amblyopic subjects**	**Both eyes Normal controls**	***t*-statistic *p*-value**
Fixation Stability (minarc^2)	1.841 (0.319)	1.713 (0.185)	*t*=1.543 *p*=0.131

3.4.2 Saccadic performance

Original eye movement recordings are shown for a typical amblyopic subject and normal control in figure 3.2. No obvious differences between the amblyopic subject and the normal control are apparent in the original recordings.

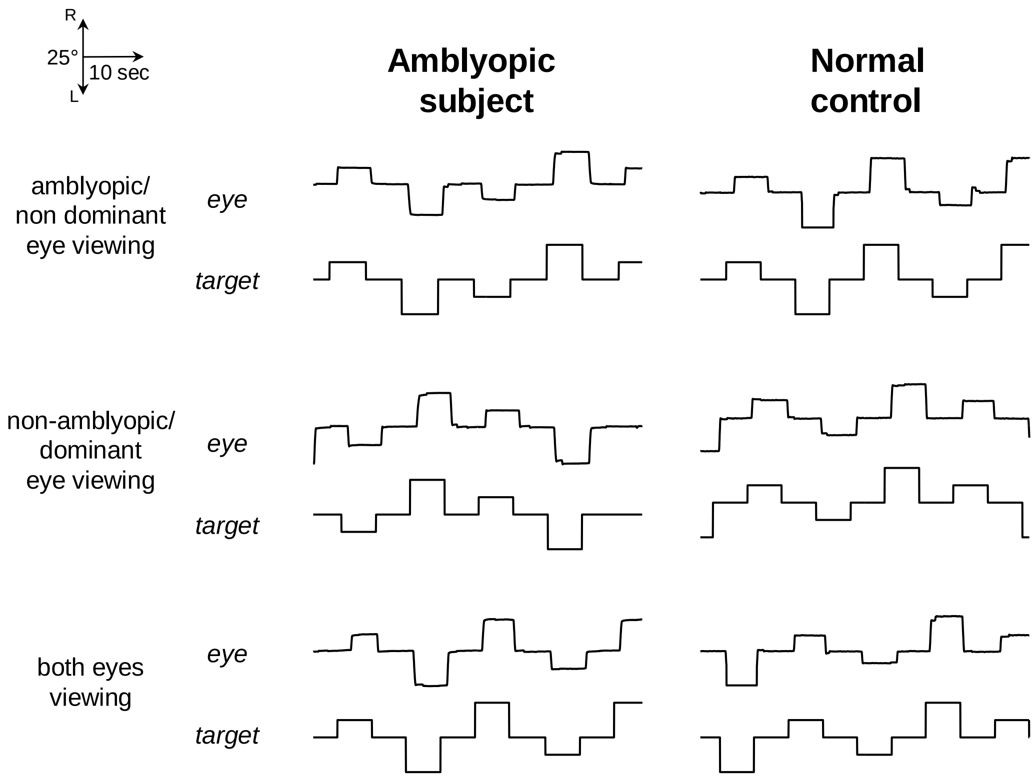


Figure 3.2. *Original recordings during the saccadic task of an amblyopic subject and a normal control under monocular with either eye and binocular viewing. For each viewing condition and comparison made, the original traces corresponding to the relevant target jumps are illustrated. From the original data, it appears that amblyopic subjects make fast and accurate movements with no obvious differences compared to normal controls.*

3.4.2.1 Monocular saccadic performance with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls

While following the 20° amplitude target shifts, amblyopic subjects exhibited significantly increased saccadic latencies (p=0.028) and significantly reduced saccadic gains (p=0.048) compared to normal controls. No significant differences were found between the two groups regarding the number of saccades performed in order to reach the moving target stimulus (table 3.2).

Table 3.2. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	***t/z*-statistic *p*-value**
LATENCY (sec)	0.223 (0.038)	0.199 (0.026)	t=2.290 p=0.028*
GAIN	0.697 (0.137)	0.782 (0.136)	z=-2.031 p=0.042*
NUMBER OF SACCADES	1.539 (0.264)	1.641 (0.264)	z=-1.421 p=0.155

While following the 10° amplitude target shifts, amblyopic subjects were characterised by significantly increased saccadic latencies (*p*=0.001) and significantly lower saccadic gains (*p*=0.027) compared to normal controls. No significant differences were recorded between the two groups with respect to the saccades number (table 3.3).

Table 3.3. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	**t/z-statistic p-value**
LATENCY (sec)	0.222 (0.026)	0.192 (0.024)	t=3.673 p=0.001*
GAIN	0.744 (0.173)	0.843 (0.135)	z=-2.211 p=0.027*
NUMBER OF SACCADES	1.440 (0.257)	1.526 (0.229)	z=-1.394 p=0.163

3.4.2.2 Monocular saccadic performance with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls.

While following the 20° amplitude target shifts, saccadic latency was significantly prolonged (*p*=0.014) and saccadic gain was significantly reduced (*p*=0.049) in the amblyopic subjects compared to the normal controls. No significant differences were observed regarding the saccades number between the two groups (table 3.4).

Table 3.4. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	**t/z-statistic p-value**
LATENCY (sec)	0.218 (0.032)	0.194 (0.027)	z=-2.452 p=0.014*
GAIN	0.681 (0.190)	0.793 (0.153)	z=-1.965 p=0.049*
NUMBER OF SACCADES	1.553 (0.200)	1.652 (0.163)	t=-1.720 p=0.094

While following the 10° amplitude target shifts, amblyopic subjects exhibited significantly increased saccadic latencies (p=0.047) and significantly lower gains (p=0.025) compared to normal controls. No significant differences were found between the two groups with respect to the saccades number (table 3.5).

Table 3.5. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	**t/z-statistic p-value**
LATENCY (sec)	0.201 (0.028)	0.189 (0.020)	z=-1.382 p=0.047*
GAIN	0.734 (0.122)	0.838 (0.128)	z=-2.238 p=0.025*
NUMBER OF SACCADES	1.559 (0.191)	1.473 (0.219)	t=1.323 p=0.194

3.4.2.3 Binocular saccadic performance in the amblyopic subjects and the normal controls

While following the 20° amplitude target shifts, amblyopic subjects were found to exhibit significantly reduced saccadic gains (*p*=0.037) compared to normal controls. No differences were found regarding the saccadic latency and the saccadic number between the two groups (table 3.6).

Table 3.6. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with both eyes of the amblyopic subjects and the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	**t/z-statistic p-value**
LATENCY (sec)	0.220 (0.058)	0.195 (0.024)	z=-1.206 p=0.228
GAIN	0.752 (0.134)	0.828 (0.105)	z=-2.086 p=0.037*
NUMBER OF SACCADES	1.523 (0.295)	1.576 (0.180)	t=-0.684 p=0.499

While following the 10° amplitude target shifts, amblyopic subjects showed a significantly reduced number of saccades (p=0.038) compared to normal controls. No significant differences were found between amblyopic subjects and normal controls regarding the saccadic latency and the saccadic gain (table 3.7).

Table 3.7. *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with the both eyes of the amblyopic subjects and the normal controls. Standard deviations are included in the brackets. T-statistic for parametric data, z-statistic for non-parametric data and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

Variable	**Amblyopic subjects**	**Normal controls**	**t/z-statistic p-value**
LATENCY (sec)	0.208 (0.045)	0.189 (0.013)	z=-1.560 p=0.119
GAIN	0.789 (0.166)	0.862 (0.072)	z=-1.602 p=0.109
NUMBER OF SACCADES	1.370 (0.161)	1.448 (0.127)	z=-2.072 p=0.038*

3.4.3 Correlation of fixational stability and saccadic performance with the reading measurements

I correlated the bivariate contour ellipse areas (BCEA) measurements with the reading speed and fixation duration measurements derived from the reading task performed while evaluating reading strategies under monocular with either eye and binocular viewing conditions. Fixation duration was selected from the eye movement parameters during reading as being the parameter mostly likely to be influenced by the fixation stability characteristics. In all the comparisons made, no significant correlations were observed. In particular, the derived correlation coefficients and their significance for the comparisons made are illustrated in the table 3.8.

Table 3.8. *Pearson correlation coefficients (r) and their significance (two-sided p-value) while correlating the BCEA values with the reading speed and fixation duration measurements derived from the reading task for either eye (amblyopic and non-amblyopic) and binocularly of the amblyopic subjects and either eye (non-dominant eye, dominant eye) and binocularly of the normal controls. For all the correlations, mean values of the derived measurements were used.*

Variable	**Amblyopic eye**	**non-Amblyopic eye**	**Both eyes Amblyopic subjects**
BCEA vs. Reading speed	r=0.116 (p=0.626)	r=0.027 (p=0.909)	r=-0.037 (p=0.878)
BCEA vs. Fixation duration	r=-0.145 (p=0.543)	r=-0.024 (p=0.920)	r=-0.016 (p=0.921)
Variable	**non-Dominant eye**	**Dominant eye**	**Both eyes Normal controls**
BCEA vs. Reading speed	r=-0.050 (p=0.834)	r=0.106 (p=0.656)	r=-0.147 (p=0.537)
BCEA vs. Fixation duration	r=0.213 (p=0.368)	r=-0.023 (p=0.924)	r=-0.108 (p=0.507)

In addition, I correlated the averages of the horizontal components of the saccadic eye movements (latency, gain and number of saccades to reach the target) to fixation duration, amplitude of the forward saccades and total number of saccades during reading. No significant correlations were observed for all the viewing conditions under investigation. The derived correlation coefficients and their significance for the comparisons made are illustrated in the tables 3.9 and 3.10.

Table 3.9. *The correlation coefficients (r for parametric data and rho for non parametric data) and their significance (two sided p-value) while correlating the horizontal components of the saccadic task (latency, gain and number of saccades to reach the target) to the relevant eye movement parameters during reading (fixation duration, amplitude of the progressive/forward saccades and total number of saccades) for either eye of the amblyopic subjects (amblyopic and non-amblyopic) and normal controls (non-dominant and dominant) and binocularly. The saccadic measurements as in response to* ***20° amplitude target shifts.***

Variable	**Amblyopic eye**	**non-Amblyopic eye**	**Both eyes Amblyopic subjects**
Latency vs. Fixation duration	*rho*=0.287 (*p*=0.221)	*rho*=0.229 (*p*=0.332)	*rho*=0.431 (*p*=0.058)
Gain vs. Amplitude	*rho*=0.079 (*p*=0.740)	*rho*=-0.152 (*p*=0.522)	*rho*=-0.036 (*p*=0.879)
Saccades number vs. Saccades number	*rho*=0.043 (*p*=0.858)	*rho*=0.256 (*p*=0.276)	*r*=0.218 (*p*=0.356)
Variable	**non-Dominant eye**	**Dominant eye**	**Both eyes Normal controls**
Latency vs. Fixation duration	*r*=0.176 (*p*=0.459)	*rho*=0.038 (*p*=0.873)	*rho*=-0.416 (*p*=0.068)
Gain vs. Amplitude	*rho*=-0.152 (*p*=0.522)	*rho*=-0.444 (*p*=0.050)	*rho*=-0.255 (*p*=0.278)
Saccades number vs. Saccades number	*r*=-0.043 (*p*=0.857)	*r*=-0.115 (*p*=0.630)	*r*=0.153 (*p*=0.520)

Table 3.10. *The derived correlation coefficients (r for parametric data and rho for non parametric data) and their significance (two sided p-value) while correlating the horizontal components of the saccadic task (latency, gain and number of saccades to reach the target) to the relevant eye movement parameters during reading (fixation duration, amplitude of the progressive/forward saccades and total number of saccades) for either eye of the amblyopic subjects (amblyopic and non-amblyopic) and normal controls (non-dominant and dominant) and binocularly. The saccadic measurements as in response to* ***10° amplitude target shifts.***

Variable	**Amblyopic eye**	**non-Amblyopic eye**	**Both eyes Amblyopic subjects**
Latency vs. Fixation duration	*r*=-0.194 (*p*=0.413)	*r*=0.210 (*p*=0.375)	*rho*=0.403 (*p*=0.078)
Gain vs. Amplitude	*rho*=-0.082 (*p*=0.732)	*rho*=-0.165 (*p*=0.488)	*rho*=0.037 (*p*=0.877)
Saccades number vs. Saccades number	*rho*=-0.048 (*p*=0.841)	*r*=-0.081 (*p*=0.734)	*r*=0.007 (*p*=0.976)
Variable	**non-Dominant eye**	**Dominant eye**	**Both eyes Normal controls**
Latency vs. Fixation duration	*rho*=0.103 (*p*=0.667)	*rho*=0.040 (*p*=0.866)	*r*=-0.358 (*p*=0.121)
Gain vs. Amplitude	*rho*=-0.088 (*p*=0.713)	*rho*=-0.121 (*p*=0.613)	*rho*=-0.329 (*p*=0.156)
Saccades number vs. Saccades number	*r*=-0.018 (*p*=0.941)	*rho*=0.171 (*p*=0.471)	*r*=-0.007 (*p*=0.977)

3.4.4 Results summary

In summary, stability of fixation was found to be significantly impaired in the amblyopic eye of the amblyopic subjects compared to the non-dominant eye of the normal controls, as well as with the non-amblyopic eye. Significant differences were also observed between amblyopic subjects and normal controls with respect to the saccadic latency, the gain of the primary saccade and the number of saccades while performing the saccadic task in all viewing conditions under investigation. No significant correlations were observed with the reading speed measurements or the eye movement parameters derived from the previous study.

4. Experiment 3: The effect of font size on reading performance in strabismic amblyopia

4.1 Aims of the study

The classic reading rate curves are all plotted as a function of letter size (174, 234, 235). In view of this observation, it is important to evaluate changes in reading rates when amblyopic subjects read text presented at different font sizes.

While studying the reading performance using text presented in a fixed font size, my previous investigations have shown that in strabismic amblyopia reading was impaired not only under monocular viewing with the amblyopic eye but also with the non-amblyopic eye with normal visual acuity and with both eyes. Furthermore, my findings highlighted the oculomotor abnormalities that might be associated with the reduced reading speed that amblyopic subjects exhibited under monocular with either eye and binocular viewing, namely the increased number of saccades and the prolonged fixation duration. Therefore, it might be interesting to investigate whether the oculomotor patterns differ when reading in amblyopic subjects compared to normal controls by looking at the effect of font size on oculomotor characteristics.

With this research I aim to: (i) plot the reading rate curve as a function of font size in strabismic amblyopia and, (ii) determine the oculomotor patterns associated with the reading speed changes as a function of font size. These findings will be discussed in relation to the reading rate curves described in normal central and peripheral vision, as well as to the reading strategies associated with other diseases where mechanisms are better understood, such as in age-related macular degeneration.

4.2 Hypotheses tested

Based on the observations of my first reading experiment, I could postulate that reading speed in adult strabismic amblyopes during monocular reading with the amblyopic and the non-amblyopic eye and binocularly is expected to be significantly slower for all the font sizes tested compared to healthy controls reading with the non-dominant eye, the dominant eye and binocularly respectively. In addition, I could expect the changes in oculomotor parameters observed during monocular and binocular reading i.e. the total number of saccades per line, the number of progressive/forward saccades per line, the amplitude of the progressive/forward saccades, the number of regressive/backward saccades per line and the fixation duration to differ significantly between the two groups. In particular, I expect the amblyopic subjects to exhibit increased saccades number and prolonged fixation durations in all the font sizes tested compared to normal controls.

4.3 Methods

4.3.1 Subjects

Fifteen patients were recruited from the ocular motility clinics at Leicester Royal Infirmary, UK (table 4.1). They were aged between 26 and 58 years old (mean 44.60 ± 8.78 years); six were male and nine were female. All the tested subjects were diagnosed with unilateral amblyopia caused by strabismus, defined as a minimal two line interocular difference in distance visual acuity. Distance visual acuity in the amblyopic eye ranged from 0.800 to 0.125 LogMAR (mean visual acuity=0.358 LogMAR, SD=O.194) and in the fellow normal eye from -0.075 to -0.150 LogMAR (mean visual acuity=-0.433 LogMAR, SD=0.046). None of the tested volunteers demonstrated binocular vision and stereovision and all had undertaken treatment for amblyopia (occlusion therapy or surgery) in the past.

A healthy control group of eighteen volunteers recruited from primarily non-academic staff of the University of Leicester and the Leicester Royal Infirmary also participated in the clinical study (table 4.2). All participants had fully corrected visual acuity and no history of neurological, psychiatric or ophthalmological deficits other than amblyopia. The two study groups were comparable in age (p=0.435), sex and educational-intelligence level, matched using the National Adult Reading Test (NART) score (p=0.971).

The participants read English as a first language and were naïve concerning the intentions of the investigation. The study received local ethics committee approval and was performed in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects prior to their participation.

Amblyopic subjects	Age	Gender	NART	Orthoptic Status	Visual Acuity in Amblyopic Eye	Visual Acuity in non-Amblyopic Eye	Visual Acuity in Both Eyes	Fixation	Treatment
1	38	M	114	R eso	0.125	-0.15	-0.15	central	patching
2	47	F	110	Leso	0.2	-0.075	-0.05	central	patching/surgery
3	58	F	109	R eso	0.25	0	0	central	surgery
4	48	F	102	L eso	0.475	0	0	central	patching/surgery
5	58	F	101	R eso	0.3	0	0	central	patching/surgery
6	26	M	116	Rexo	0.225	0	0	central	patching/surgery
7	42	F	110	Lexo	0.575	-0.025	0	eccentric	patching/surgery
8	40	M	107	R exo	0.175	0	0	central	surgery
9	45	F	101	L eso	0.575	0	0	eccentric	patching
10	36	F	100	L exo	0.325	-0.1	-0.1	central	patching/surgery
11	34	F	109	Reso	0.2	-0.025	0	central	surgery
12	48	F	122	L exo	0.475	-0.075	-0.075	central	patching/surgery
13	51	M	124	R exo	0.475	-0.075	-0.075	eccentric	patching/surgery
14	47	M	124	Lexo	0.8	-0.075	-0.075	eccentric	patching/surgery
15	51	M	114	L exo	0.2	-0.05	-0.05	central	surgery

Table 4.1. *Clinical details of the amblyopic subjects participating in the study.*

Normal controls	Age	Gender	NART	Orthoptic Status	Visual Acuity in non-Dominant Eye	Visual Acuity in Dominant Eye	Visual Acuity in Both Eyes	Fixation	Treatment
1	31	F	115	orthotropia	0	0	0	Central	-
2	54	F	108	orthotropia	-0.075	-0.1	-0.1	Central	-
3	32	F	115	orthotropia	0	0	0	Central	-
4	27	F	103	orthotropia	0.025	-0.05	-0.05	Central	-
5	46	M	117	orthotropia	-0.05	-0.05	-0.05	Central	-
6	49	F	103	orthotropia	0	-0.025	0	Central	-
7	43	M	100	orthotropia	-0.5	-0.5	-0.5	Central	-
8	58	F	107	orthotropia	0	0	0	Central	-
9	52	F	112	orthotropia	-0.025	0	0	Central	-
10	45	F	114	orthotropia	-0.025	-0.025	-0.025	Central	-
11	34	F	112	orthotropia	0	0	-0.025	Central	-
12	44	F	121	orthotropia	0	0	0	Central	-
13	24	M	105	orthotropia	-0.025	-0.05	-0.05	Central	-
14	50	M	114	orthotropia	-0.05	-0.05	-0.05	Central	-
15	50	M	105	orthotropia	-0.025	-0.025	-0.025	Central	-
16	36	F	111	orthotropia	0	-0.025	-0.025	Central	-
17	47	F	117	orthotropia	0	0	0	Central	-
18	34	M	115	orthotropia	-0.025	0.025	0	Central	-

Table 4.2. *Clinical details of the normal controls participating in the study*

4.3.2 Reading Assessment

Tested subjects were asked to read paragraphs of text presented on a screen. The reading material used in the investigation comprises of eighteen paragraphs of text taken from the ‘Oxford First Encyclopedia’ (Oxford University Press) (249). To ensure that reading performance was not limited by text difficulty, the level of difficulty of the text did not exceed the reading abilities of all subjects.

Each paragraph of text was designed to give approximately the same layout consisting of approximately the same number of characters with spaces (mean= 300.33, SD=8.32).

The print sizes that were selected for the presentation of the text corresponded to 1.0, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2 LogMAR equivalent optotype. Thus, for the whole reading material used for my investigation there were six sets of three paragraphs of text that corresponded to the same print size, or three sets of six paragraphs each corresponded to the eight print sizes aforementioned. The content of the text was different in all the eighteen paragraphs.

The text was presented as black letters (luminance 0.45 cd/m^2) on a white background (luminance 12.00 cd/m^2), resulting in a letter contrast of 96.25%. The text was displayed in Courier New fixed-width font (monospaced), without splitting words and was centred on the screen both horizontally and vertically. A PowerPoint presentation was used to generate the reading stimuli that were presented on the rear projection screen, whilst the differences in the luminance observed between the presented paragraphs of text were matched using the photometer and the video projector control. Following the principle of my first reading experiment, the print size was defined as the angular subtense of the print on the retina and the corresponding LogMAR size was calculated from the equation $\log_{10}$ [(angle subtended by x-height)/(5 arc min)] following the design of print sizes used in MNREAD acuity charts (241).

Smaller print sizes were limited by pixelation effects of the projector. Therefore, for the smaller print sizes, the distance between the video projector and the rear projection screen was diminished.

The characteristics of the reading material regarding the font size used in the power-point presentation display, the actual size of the letters on the stimulus display screen, the corresponding visual angle of the letters in deg and the LogMAR optotype equivalent are included in table 4.3.

Table 4.3. *Characteristics of the reading material regarding the font size used in the power-point presentation display, the actual letter size on the stimulus display screen in mm, the corresponding visual angle of the letters in deg and the LogMAR optotype equivalent. Measurements are included for the stimuli generation while the video projector was placed far from the rear projection screen and while the video projector was placed near to the rear projection screen.*

	PROJECTOR FAR FROM SCREEN		**PROJECTOR NEAR SCREEN**					
Font size	32	20	32	24	20	16	12	9
Size on screen (mm)	30	19	15	11.5	9.5	7.5	5.5	4.75
Visual angle (deg)	0.859	0.544	0.429	0.329	0.272	0.214	0.157	0.136
LogMAR equivalent	1.013	0.815	0.712	0.596	0.513	0.411	0.276	0.212

Subjects were seated at a viewing distance of 2m in front of the stimulus display screen (1.75m width and 1.17 m height) with their primary position of gaze to correspond as close as possible to the centre of the screen. Their head was stabilized using a forehead and chin rest to eliminate head movements.

Participants were instructed to read silently at a normal rate to obtain meaning from the passage for all reading assessments. After the end of each paragraph, the subjects had to report to the experimenter the end of the trial. The next trial with a new paragraph began whenever the subjects were ready.

After each paragraph, participants were presented with a single word and they were asked to decide whether the presented word was relevant or not to the previously read text to check attention and comprehension. All subjects answered the questions correctly and thus demonstrated a good level of understanding of the passages they read.

4.3.3 Eye Movement Recordings

Eye position was measured during trials with an infrared video based eye-tracking system (EyeLink eye tracker, SensoMotoric Instruments GmbH, Berlin, Germany) using Eyelink software (version 2.04), whilst targets were projected onto a rear projection screen using a projection system (VisLab; SensoMotoric Instruments GmbH) and a video projector (XEA resolution: 1024 x 768; EPSON EMP703).

Eye movement recordings were performed during monocular reading with either eye viewing and binocularly, in both the amblyopic subjects and the normal controls, with the order randomized. During monocular reading, the contralateral eye was occluded using an occluder while the eye movement recordings were still maintained. The whole test lasted for approximately 1 hour.

4.3.4 Data analysis

Eye movement data were converted to Spike2 software files (Cambridge Electronic Design, Cambridge, UK), where the eye movement recordings were analysed using custom written scripts. Means were calculated for all amblyopic subjects and normal controls. The measures derived from eye movement data included:(i) Reading speed (in character with spaces/sec), (ii) Total number of saccades per line, (iii) Number of progressive/forward saccades per line, (iv) Amplitude of progressive/forward saccades (in degrees), (v) Number of regressive/backward saccades per line, and (vi) Fixation duration (in sec).

4.3.5 Statistical Analysis

Descriptive and inferential data analysis was performed using SPSS for Windows (version 14.0). A mixed between-within subjects analysis of variance (Repeated measures ANOVA) was conducted to evaluate the differences between the amblyopic subjects and the normal controls with respect to the monocular and binocular mean reading speed, total number of saccades per line, number of progressive/forward saccades per line, amplitudes of progressive/forward saccades, number of regressive/backward saccades per line and fixation duration. In particular, with the mixed between-within subjects analysis of variance, it was feasible to determine: (i) whether the differences in the eye movement parameters between the amblyopic subjects and the normal controls were significant (main effect for group), (ii) whether the change in the eye movement parameters over the tested print sizes was the same for the two groups (interaction effect) and, finally, (iii) whether there was a change in the eye movement parameters across the different print sizes for each of the tested groups (main effect for print size).

Prior to each investigation, the normality of the residuals was checked (Shapiko-Wilk test of normality).

Only amblyopes who managed to read the presented font sizes with their amblyopic eye were included in the analysis while evaluating monocular reading with the amblyopic eye. In particular, for the statistical analysis, the ‘‘Exclude case pairwise option’’ was used, which excludes the cases (persons) if they are missing the data required for the specific analysis. These cases are still included in any of the analyses for which they have the necessary information (i.e. monocular reading with the non-amblyopic eye and binocular reading).

The following comparisons were made: (i) monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, (ii) monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls, and (iii) binocular reading in both the amblyopic subjects and the normal controls. For the binocular viewing condition, the recordings from the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls were selected for the analysis.

To determine the dominant eye, the subject was asked to look through a pinhole in a paper. The eye spontaneously chosen by the subject for looking through the pinhole was considered to be the dominant eye.

4.4 Results

Original eye movement recordings are shown for an amblyopic subject and normal control for all 8 different font sizes in the following three figures where

Figure 4.1. *Monocular reading with the amblyopic eye of an amblyopic subject and the non-dominant eye of a normal control.*
Figure 4.2. *Monocular reading with the non-amblyopic eye of an amblyopic subject and the dominant eye of a normal control.*
Figure 4.3. *Binocular reading in an amblyopic subject and a normal control.*

An increase in the time taken to read a line when the amblyopic subject was viewing compared to normal control can be seen in the reduced gradient on the left to right staircase movement. For smaller font sizes for both the amblyopic subject and the normal control, the typical staircase eye movement pattern during reading is distorted (probably due to acuity limitations).

Figure 4.1. *Monocular reading with the amblyopic eye of an amblyopic subject and the non-dominant eye of a normal control.*

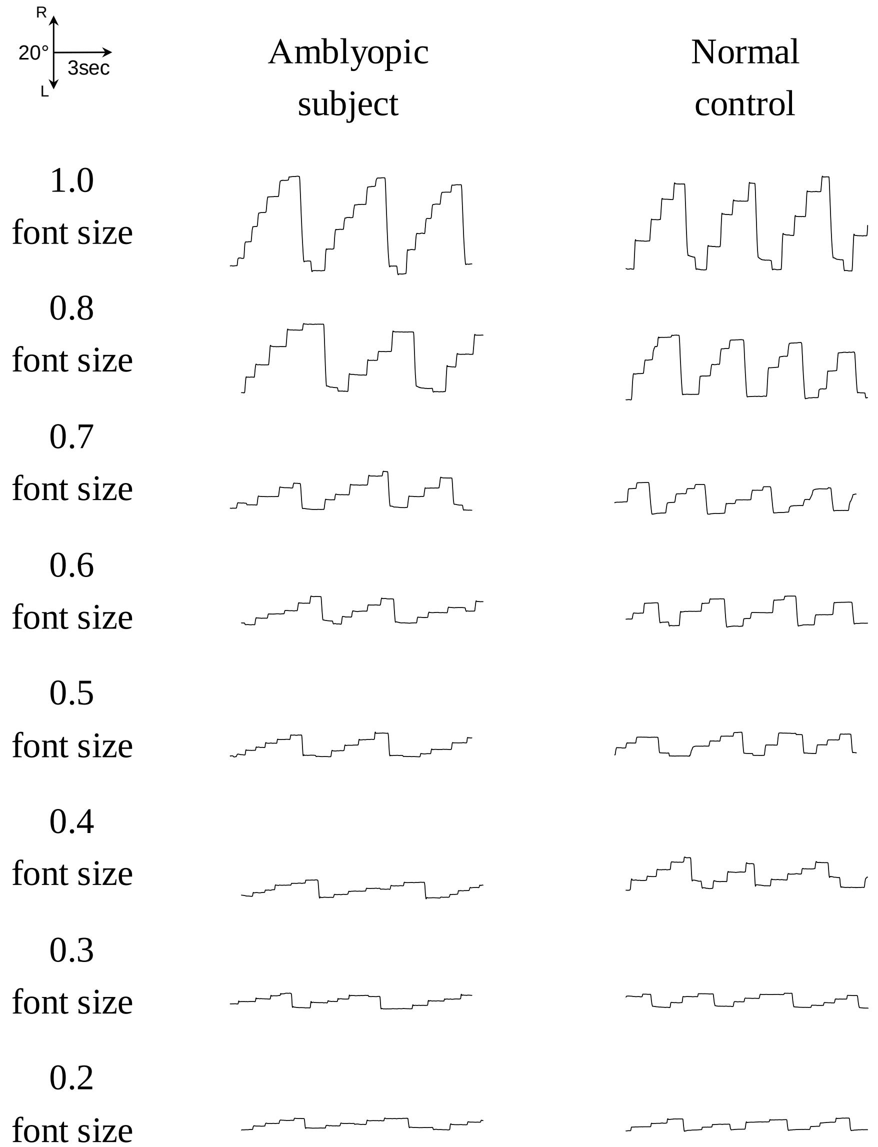


Figure 4.2. *Monocular reading with the non-amblyopic eye of an amblyopic subject and the dominant eye of a normal control.*

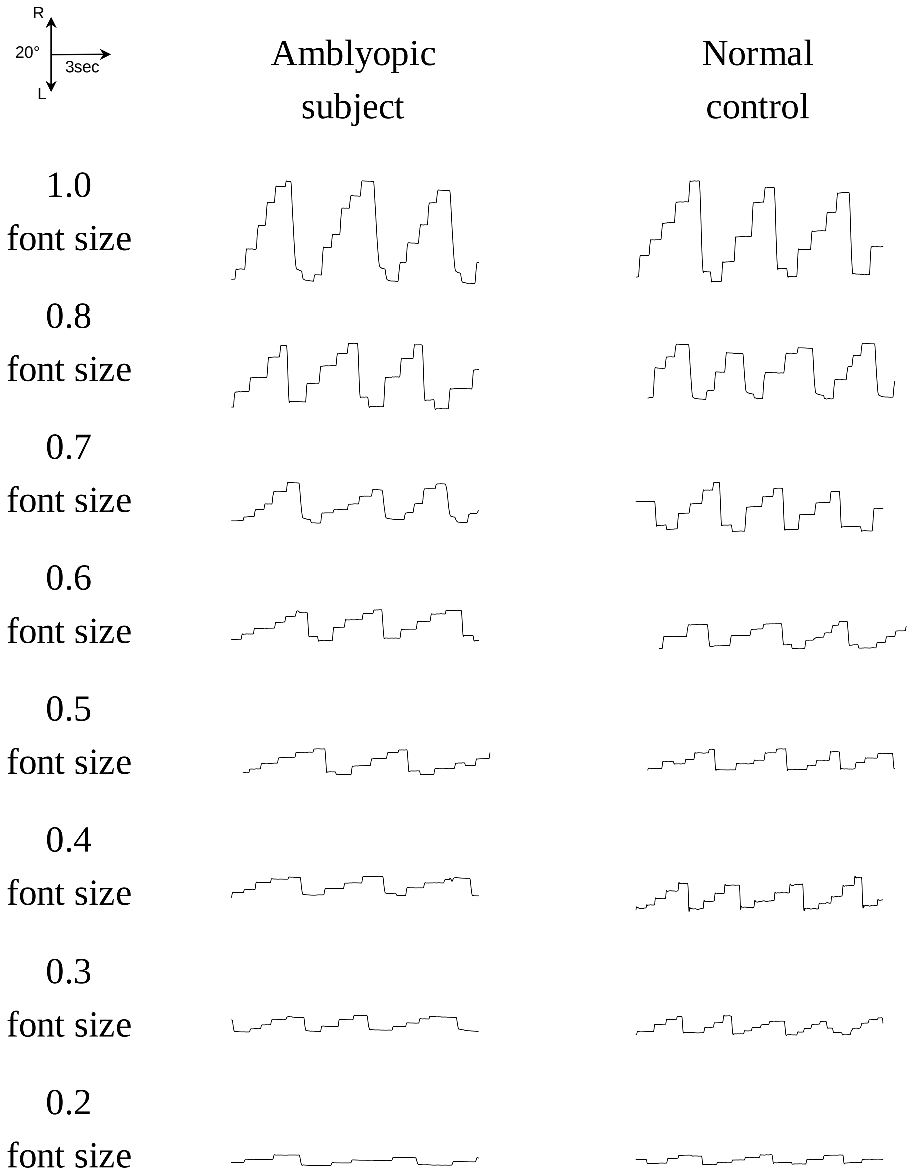


Figure 4.3. *Binocular reading in an amblyopic subject and a normal control*

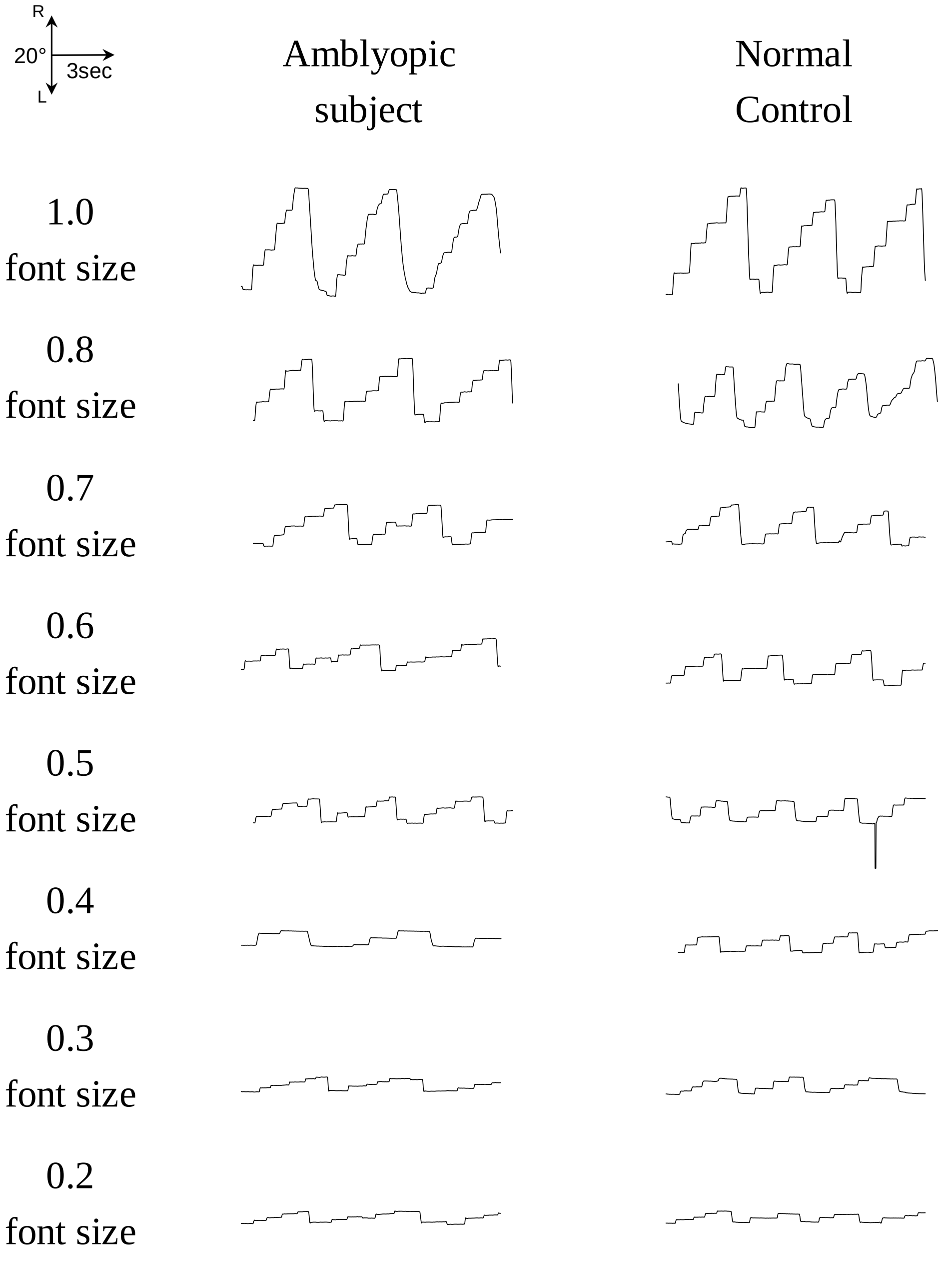


Figure 4.4 illustrates the number of the amblyopic subjects included in my analysis during monocular reading performance with the amblyopic eye in each of the tested font sizes. In amblyopia, due to acuity limitations, reading with the amblyopic eye was achieved only for paragraphs of text presented in font sizes larger than the threshold acuity size of each individual. In particular, thirteen amblyopic subjects managed to read the 1.0 LogMAR equivalent font size with their amblyopic eye, eleven the 0.8 and 0.7 font size, ten the 0.6, 0.5, 0.4 font size, nine the 0.3 font size and six the 0.2 font size. For monocular reading with the non-amblyopic eye and binocularly all the amblyopic subjects (fifteen) were included in the analysis.

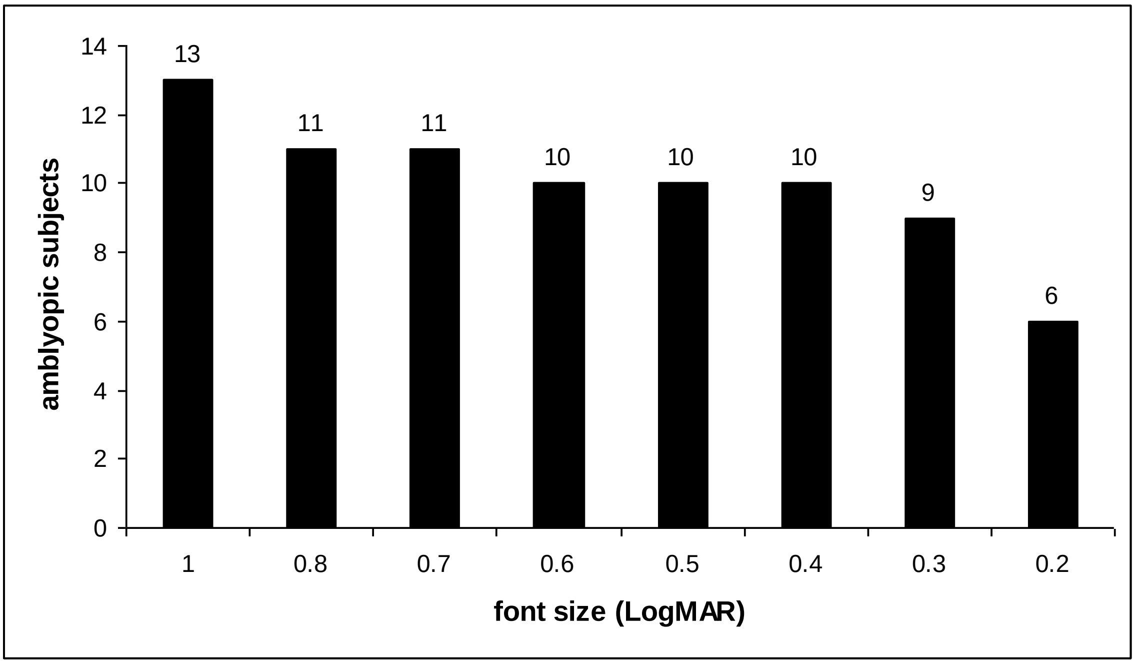


Figure 4.4. *Amblyopic subjects included in my analysis during monocular reading with the amblyopic eye in each of the tested font sizes used in my experimental set-up.*

4.4.1 Reading speed

The reading speed during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.5.

A significant difference in reading speed over the tested print sizes was observed for the two groups with the amblyopic subjects reading significantly slower compared to the normal controls while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls (F=10.681, p=0.004), monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls (F=4.367, p=0.045) and binocular reading in both the amblyopic subjects and the normal controls (F=4.722, p=0.038).

However, the change in reading speed over the tested print sizes was the same for the two groups under either viewing conditions (*Wilks' Lambda*=0.514, p=0.119 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.732, p=0.314 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.642, p=0.112 while comparing binocular reading in both the amblyopic subjects and normal controls). Reading rate curves showed a quadratic curve peaking at about 0.6 LogMAR equivalent font size, with amblyopia causing a shift downwards across the whole curve. It was interesting to observe that in the amblyopic subjects during monocular reading with the amblyopic eye large font sizes were also affected while during monocular reading with the non-amblyopic eye and binocularly smaller font sizes were mainly affected.

A significant change in reading speed was observed across the different print sizes for both the amblyopic subjects and the normal controls (*Wilks' Lambda*=0.179, p<0.0001 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.155,

$p<0.0001$ while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.242, $p<0.0001$ while comparing binocular reading in both the amblyopic subjects and the normal controls); there was a minimal drop in reading speed as print size diminished to a threshold beyond which reading speed dramatically worsens with diminishing print size.

4.4.2 Total number of Saccades per line

The total number of saccades per line during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.6.

The total number of saccades in all the print sizes tested differed significantly between the two groups (F=6.790, p=0.017 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, F=17.797, p<0.0001 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and F=15.869, p<0.0001 while comparing binocular reading in both the amblyopic subjects and the normal controls) with the amblyopic subjects to exhibit significantly more saccades when reading a line of text compared to the normal controls.

However, the change in the number of saccades over the tested print sizes was the same for the two groups under either viewing conditions (*Wilks' Lambda*=0.683, p=0.473 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.725, p=0.293 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.725, p=0.293 while comparing binocular reading in both the amblyopic subjects and the normal controls). In particular, the total number of saccades per line performed by both the amblyopic subjects and the normal controls exhibited a more constant but slight linear change with the print size.

No significant difference in the number of saccades was found across the different print sizes for each of the tested groups under either viewing conditions (*Wilks' Lambda*=0.807, p=0.811 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.693, *p*=0.210 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.616, *p*=0.078 while comparing binocular reading in both the amblyopic subjects and the normal controls).

4.4.3. Number of progressive/forward saccades per line

The number of progressive/forward saccades per line during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.7.

No significant difference in the number of progressive/forward saccades per line over the tested print sizes was found between the two groups while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls (F=4.140, p=0.055), monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls (F=4.177, p=0.050) and binocular reading in both the amblyopic subjects and the normal controls (F=6.271, p=0.058).

Furthermore, there was a similar change in the number of progressive/forward saccades across the different print sizes for both the amblyopic subjects and the normal controls under either viewing conditions (*Wilks' Lambda*=0.581, p=0.227 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.649, p=0.122 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.773, p=0.450 while comparing binocular reading in both the amblyopic subjects and the normal controls), showing a more constant but slight linear change with the print size.

However, significant changes in the number of progressive/forward saccades across the different print sizes were observed for each of the tested groups (*Wilks' Lambda*=0.435, p=0.046 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.547, p=0.026 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks'*

Lambda=0.522, *p*=0.017 while comparing binocular reading in both the amblyopic subjects and the normal controls).

4.4.4 Amplitude of progressive/forward saccades

The amplitude of progressive/forward saccades per line during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.8.

No significant difference in saccadic amplitudes over the tested print sizes was observed between the two groups under either viewing conditions (F=2.418, p=0.135 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, F=0.160, p=0.692 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and F=1.345, p=0.255 while comparing binocular reading in both the amblyopic subjects and the normal controls).

Moreover, the change of the saccadic amplitudes over the tested print sizes was the same for both the amblyopic subjects and the normal controls (*Wilks' Lambda*=0.544, p=0.162 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.804, p=0.568 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.860, p=0.781 while comparing binocular reading in both the amblyopic subjects and the normal controls), showing a linear change with the print size.

However, there was a significant change in saccadic amplitudes across the different print sizes for each of the tested groups (*Wilks' Lambda* =0.060, p<0.0001 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.042, p<0.0001 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.037,

$p<0.0001$ while comparing binocular reading in both the amblyopic subjects and the normal controls).

4.4.5 Number of Regressive/Backward Saccades per line

The number of regressive/backward saccades per line during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.9.

There was no significant difference in the number of regressive/backward saccades per line in all the tested print sizes between the two groups while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls (F=0.733, p=0.402), monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls (F=1.462, p=0.236) and binocular reading in both the amblyopic subjects and the normal controls (F=0.646, p=0.428). However, the large standard deviations in the number of regressive/ backward saccadic measurements in the amblyopic subjects indicated a large intersubject variability in the recorded reading strategies.

Furthermore, the change in the number of regressive/backward saccades over the print sizes tested was the same for both the amblyopic subjects and the normal controls under either viewing conditions (*Wilks' Lambda*=0.481, p=0.082 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.879, p=0.845 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls, *Wilks' Lambda*=0.759, p=0.400 while comparing binocular reading in both the amblyopic subjects and the normal controls), showing a more constant change with the print size.

In addition, no significant change in the number of regressive/backward saccades was observed across the different print sizes for each of the tested groups (*Wilks' Lambda*=0.653, p=0.392 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.774, *p*=0.456 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.502, *p*=0.051 while comparing binocular reading in both the amblyopic subjects and the normal controls).

4.4.6 Fixation duration

The fixation duration during monocular reading with either eye and binocular reading in the amblyopic subjects and the normal controls is illustrated in Figure 4.10.

The fixation duration over the tested print sizes was significantly different between the two groups while comparing monocular reading with the amblyopic eye of the amblyopic subjects with the non-dominant eye of the normal controls (F=7.806, p=0.011), with the amblyopic subjects to perform significantly longer fixation durations in all the print sizes tested (particularly for the smaller ones) compared to the normal controls. No significant difference in fixation duration over the tested print sizes was observed between the two groups while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls (F=0.031, p=0.861) and while comparing binocular reading in both the amblyopic subjects and the normal controls (F=0.257, p=0.616).

However, the change in fixation duration over the tested print sizes was the same for both the amblyopic subjects and the normal controls under either viewing conditions (*Wilks' Lambda*=0.367, p=0.162 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.856, p=0.798 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.686, p=0.192 while comparing binocular reading in both the amblyopic subjects and the normal controls), showing a more constant but slight linear change with the print size.

There was a significant change in the fixation duration across the different print sizes for each of the tested groups (*Wilks' Lambda*=0.103, p<0.0001 while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, *Wilks' Lambda*=0.135, p<0.0001 while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls and *Wilks' Lambda*=0.104, $p<0.0001$ while comparing binocular reading in both the amblyopic subjects and the normal controls), with a significant increase in the fixation duration values, as the print size was getting smaller.

In the following pages, six figures are displayed showing values across different font sizes for all three viewing conditions, where:

Figure 4.5. *Reading speed (characters with spaces/sec) during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

Figure 4.6. *Total number of saccades per line during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

Figure 4.7. *Number of progressive/forward saccades per line during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

Figure 4.8. *Amplitude of progressive/forward saccades per line during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

Figure 4.9. *Number of regressive/backwards saccades per line during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

Figure 4.10. *Fixation duration during monocular with either eye and binocular reading in the amblyopic subjects (n=15) and the normal controls (n=18).*

The following legend applies to all six figures:

A. Monocular reading with the amblyopic eye of the amblyopic subjects (n=15) and the non-dominant eye of the normal controls (n=18).

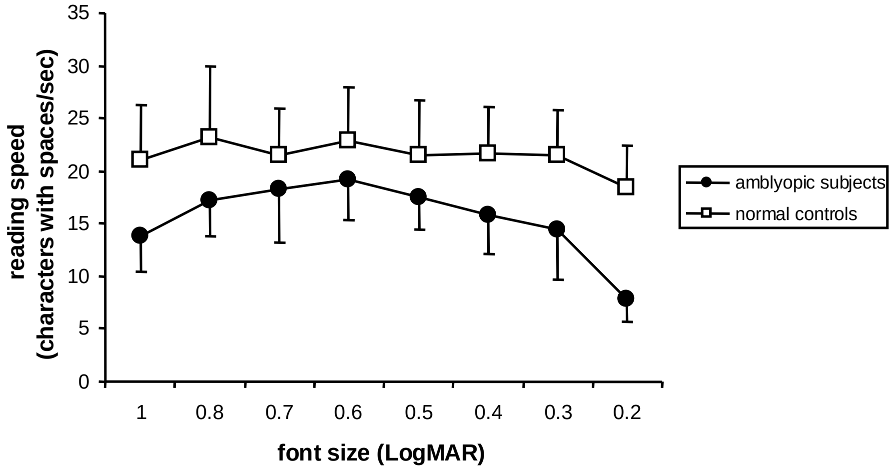
B. Monocular reading with the non-amblyopic eye of the amblyopic subjects (n=15) and the dominant eye of the normal controls (n=18).

C. Binocular reading in both the amblyopic subjects (n=15) and the normal controls (n=18).

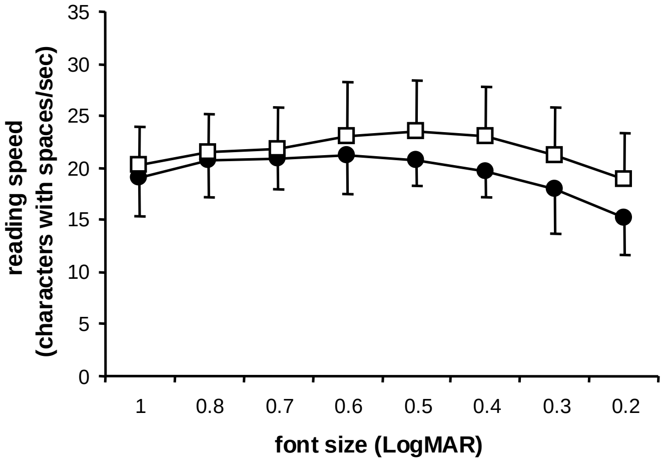
Mean values and standard deviations are illustrated.

__Figure 4.5.__ Reading speed (characters with spaces/sec).

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

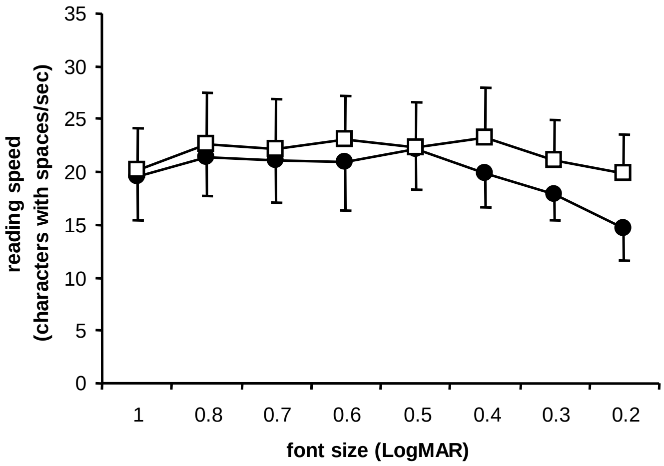
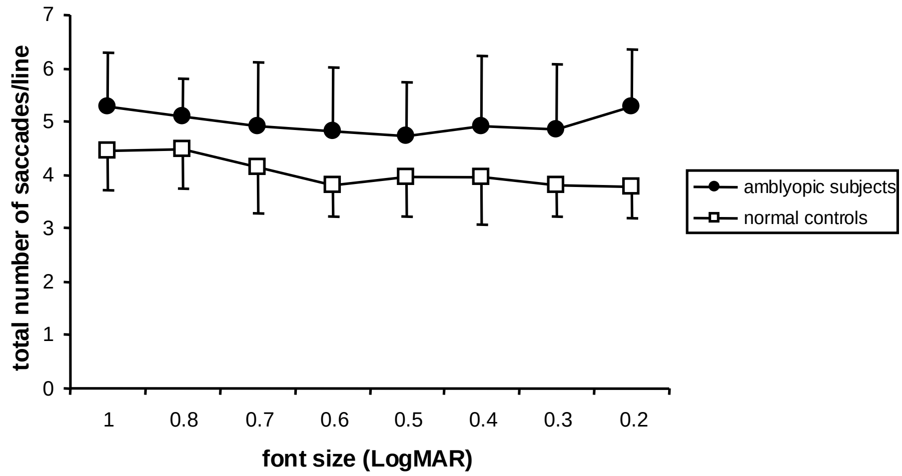
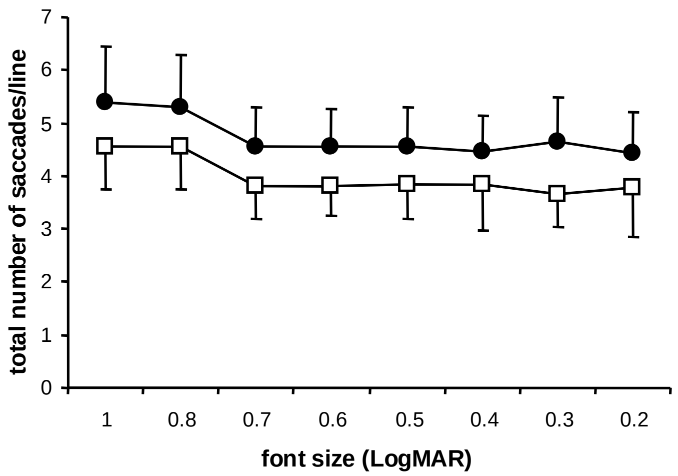


Figure 4.6. *Total number of saccades per line*

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

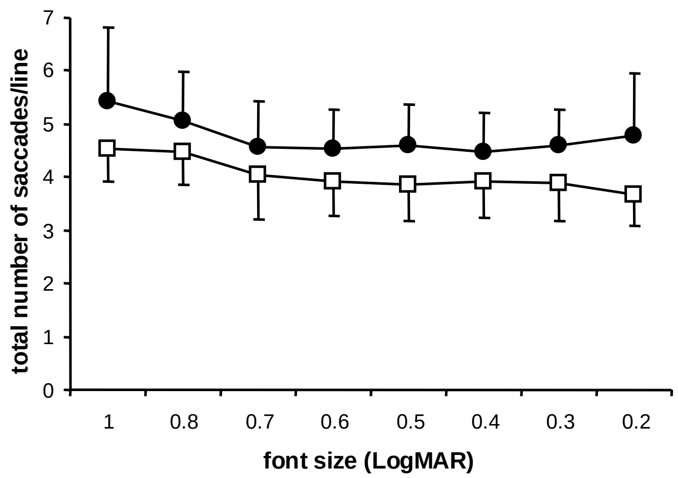
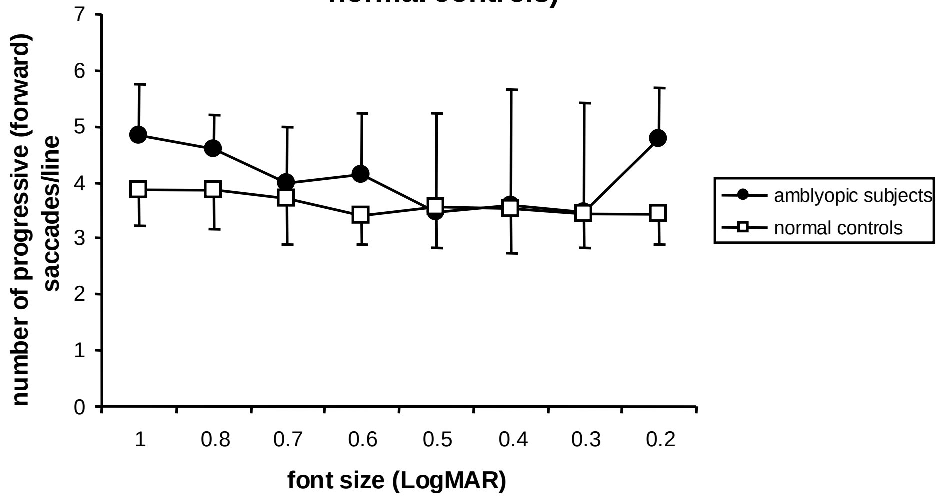
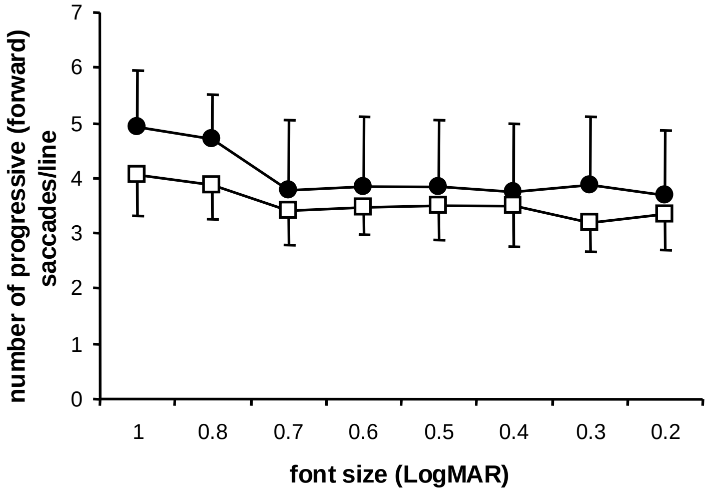


Figure 4.7. *Number of progressive/forward saccades per line*

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

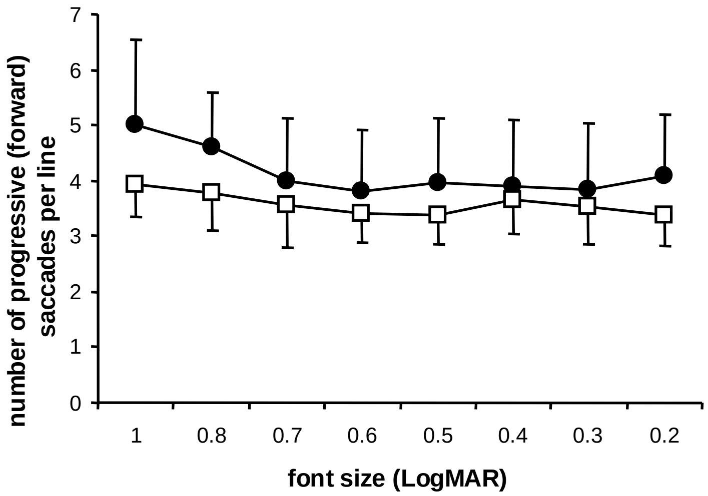
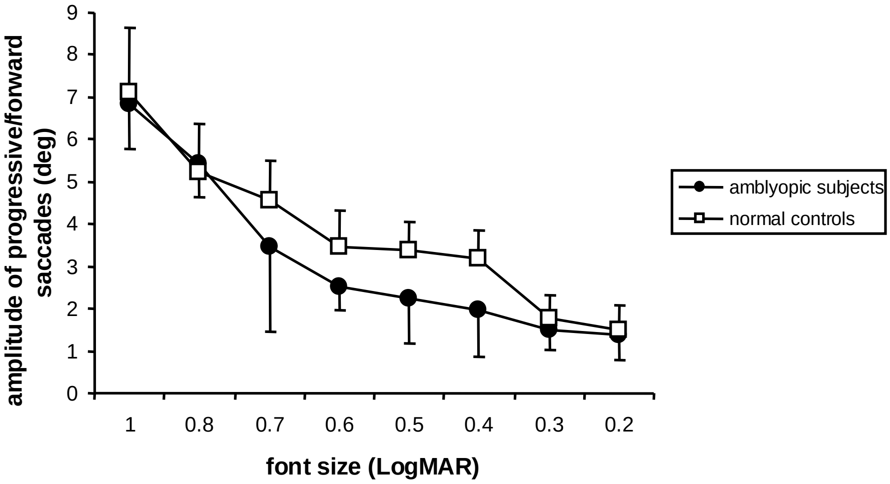
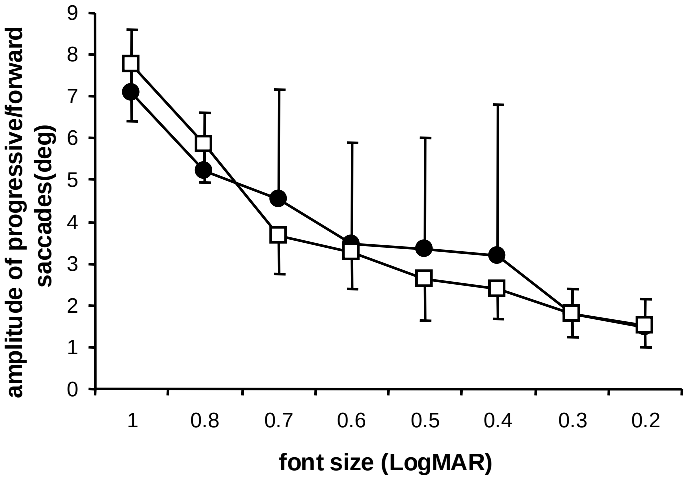


Figure 4.8. Amplitude of progressive/forward saccades (deg)

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

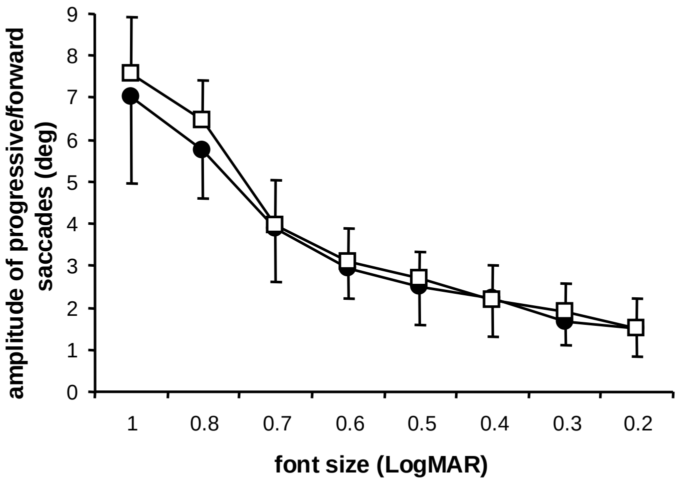
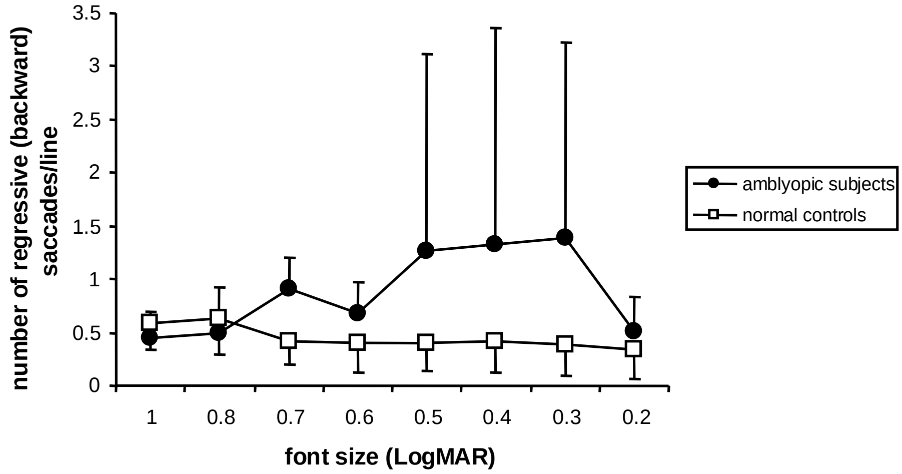
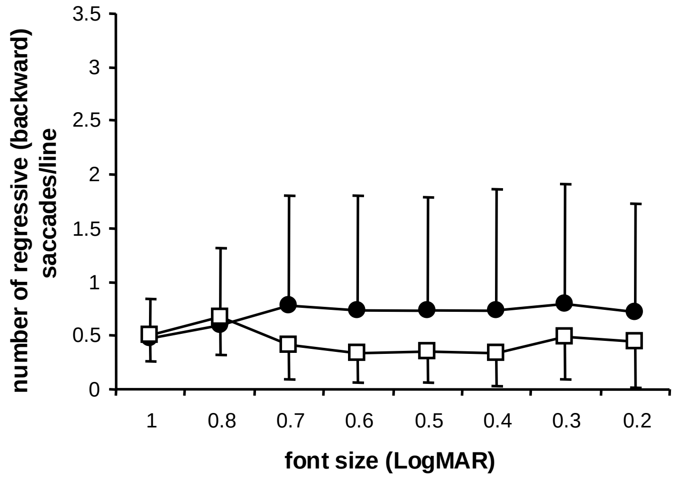


Figure 4.9. *Number of regressive/backwards saccades per line*

A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls

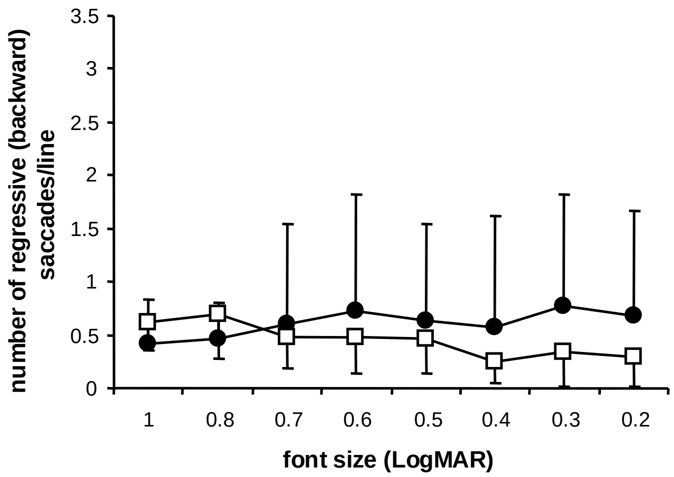
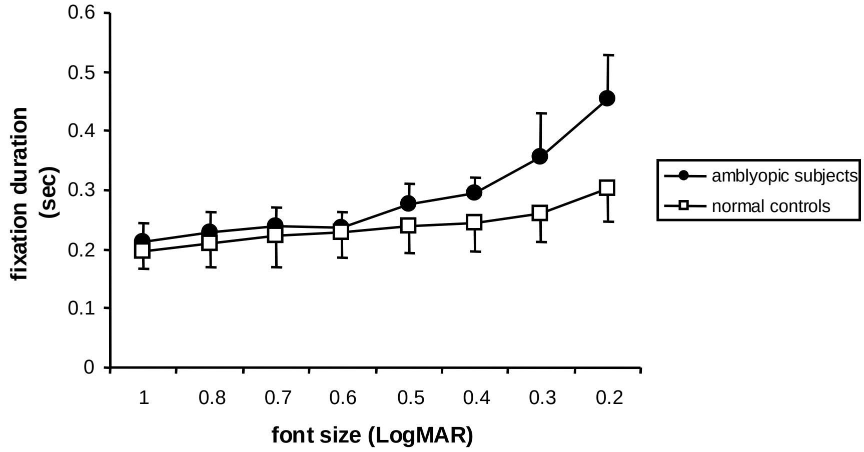
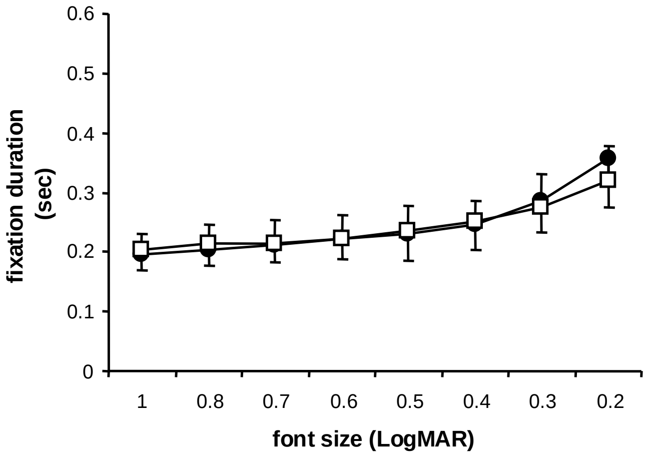


Figure 4.10. *Fixation duration (sec)*

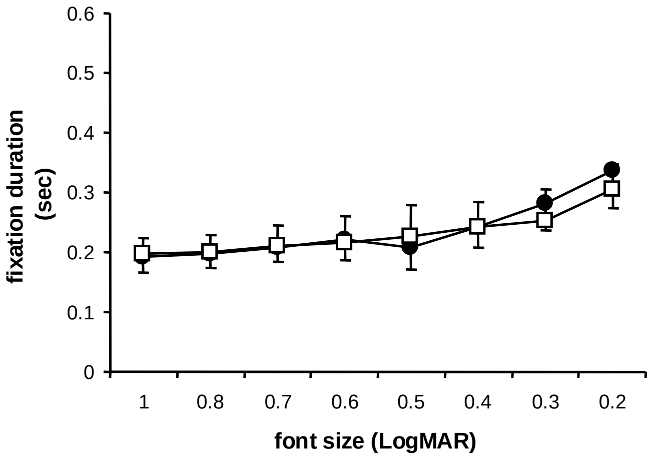
A. Amblyopic eye (amblyopic subjects) and non-dominant eye normal controls)



B. Non-amblyopic eye (amblyopic subjects) and dominant eye (normal controls)



C. Binocular reading in amblyopic subjects and normal controls



During monocular reading with the amblyopic eye of the amblyopic subjects, a variety in the reading strategies was observed, as indicated by the large standard deviations around the mean measurements. This was more profound regarding the saccadic components of the eye movement parameters, namely the number of progressive/forward saccades per line and the number of regressive/backward saccades per line.

In the following pages, three figures are displayed showing values across the different font sizes for all three conditions, where:

Figure 4.11. *Saccadic components of the eye movement parameters during monocular reading with the amblyopic eye in the amblyopic subjects (n=15).*
Figure 4.12. *Saccadic components of the eye movement parameters during monocular reading with the non-amblyopic eye in the amblyopic subjects (n=15).*
Figure 4.13. *Saccadic components of the eye movement parameters during binocular reading in the amblyopic subjects (n=15).*

Mean values are illustrated for each of the font sizes tested. The dashed lines connect the standard deviations corresponding to the mean values for each of the font sizes tested, indicating the large intersubject variability in the reading strategies.

The following legend applies to all three graphs:

(A) Total number of saccades per line,
(B) Number of progressive/forward saccades per line
(C) Number of regressive/backwards saccades per line

Figure 4.11. *Reading with the amblyopic eye of the amblyopic subjects.*

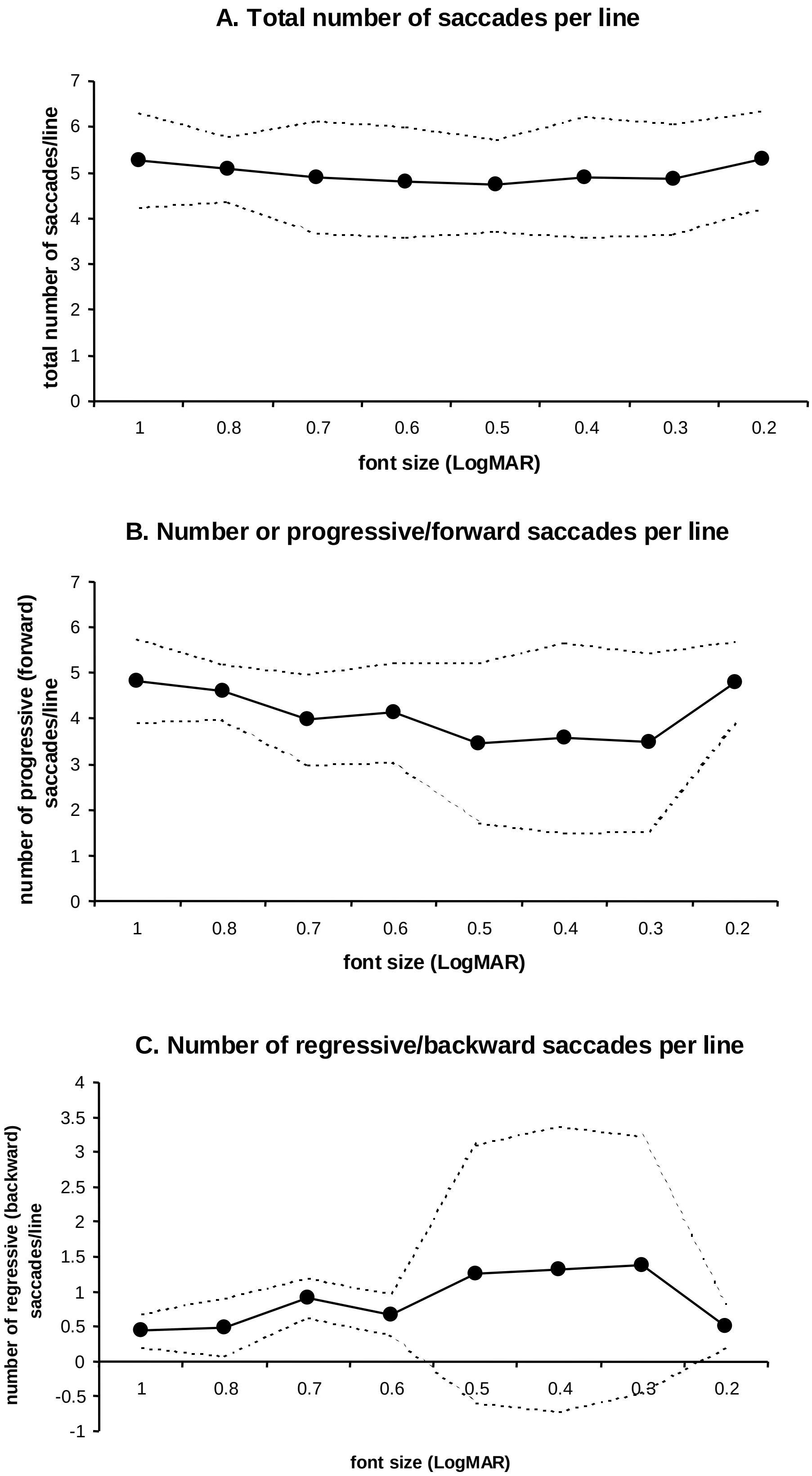
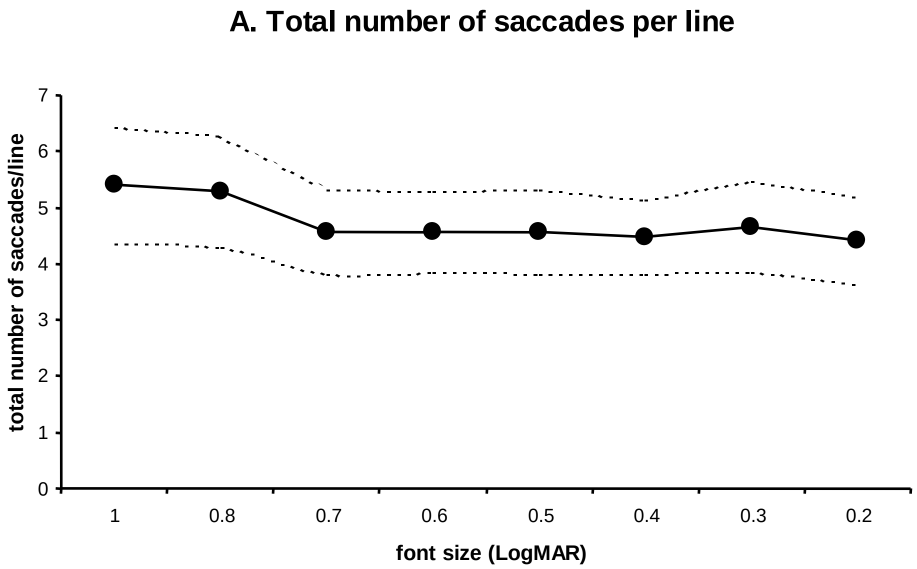
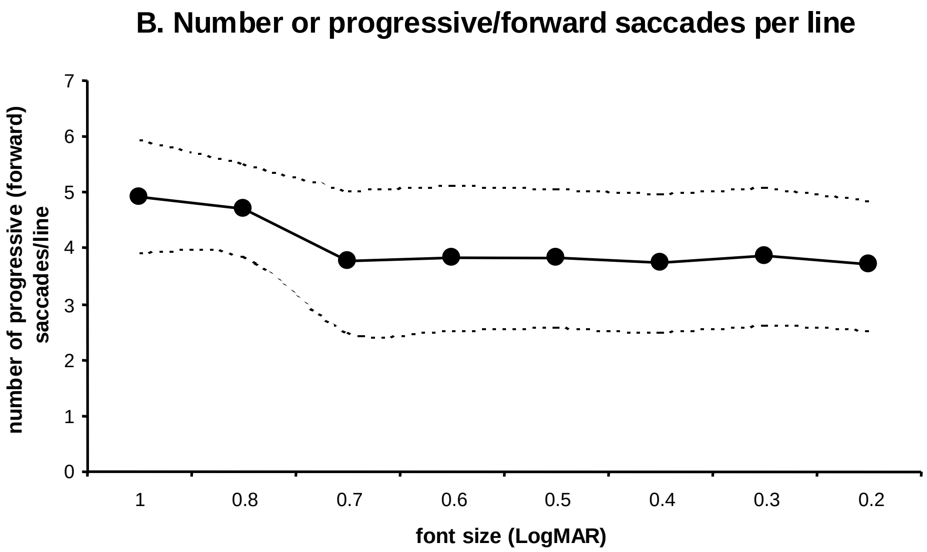


Figure 4.12. Reading with the non-amblyopic eye of the amblyopic subjects.





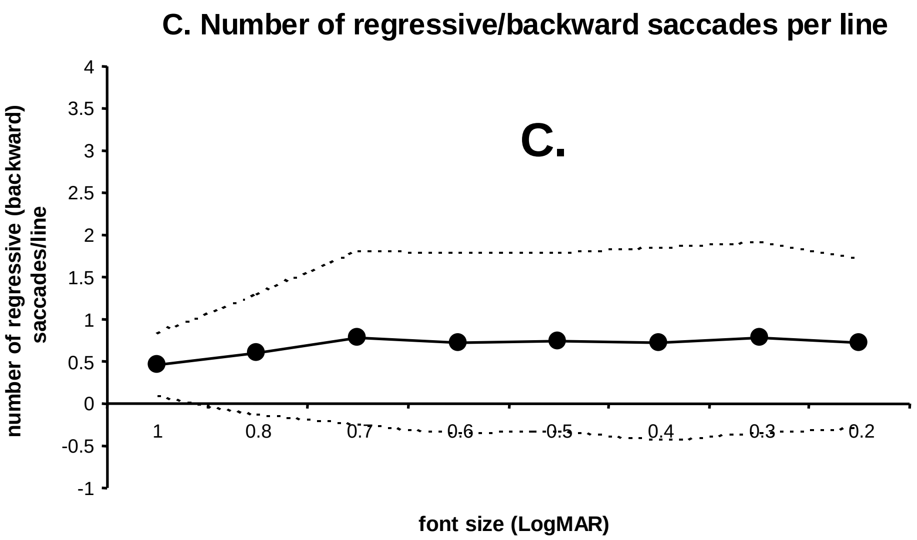
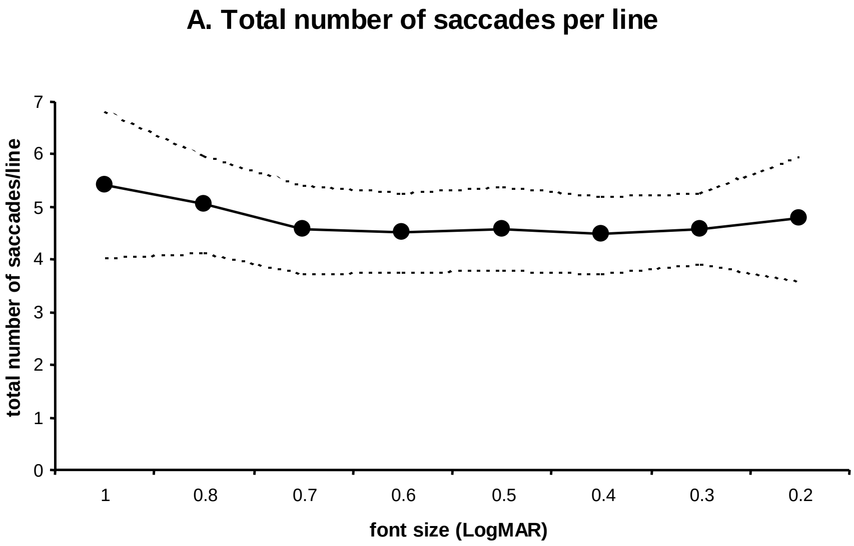
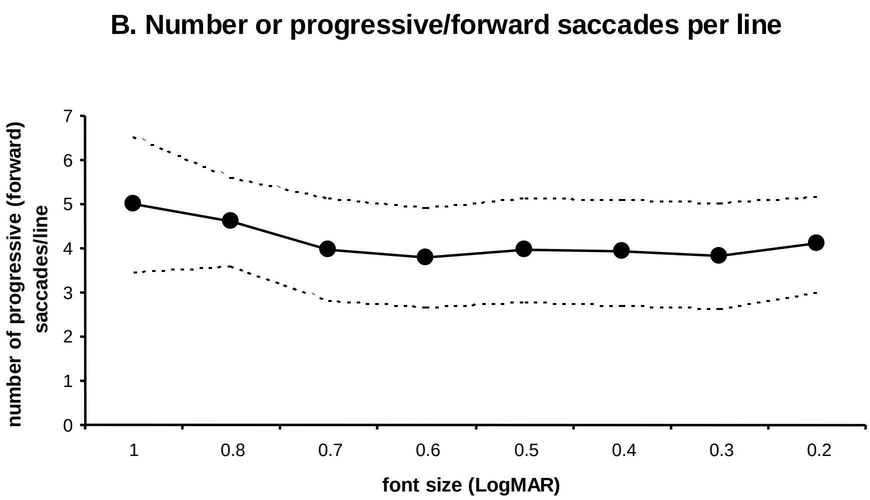
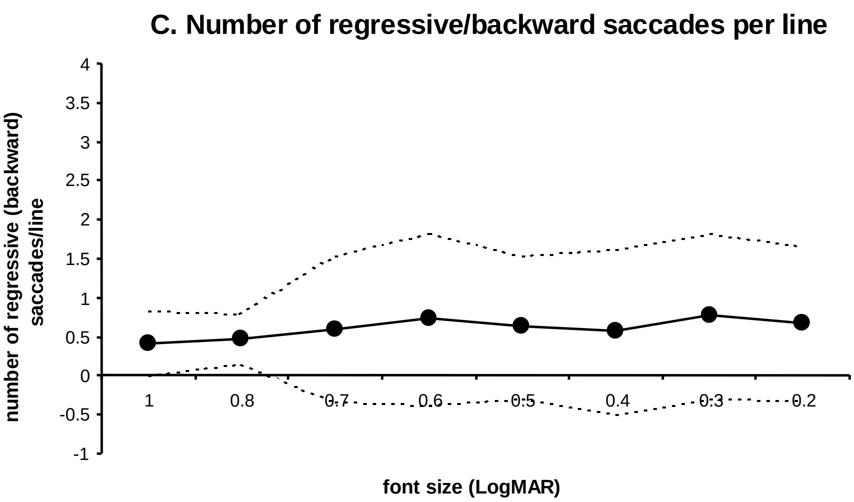


Figure 4.13. *Binocular reading of the amblyopic subjects.*







4.4.7 Results summary

In summary, reading speed was significantly slower in the amblyopic subjects during monocular reading with the amblyopic eye, the non-amblyopic eye and binocularly compared to normal controls reading with the non-dominant eye, the dominant eye and binocularly respectively. During monocular reading with the amblyopic eye, the total number of saccades per line and the fixation duration were significantly increased in the amblyopic subjects compared to normal controls reading with the non-dominant eye. During monocular with the non-amblyopic eye and binocular reading, the total number of saccades per line was also significantly increased in the amblyopic subjects compared to the normal controls reading with the dominant eye and binocularly respectively.

The changes caused by amblyopia in reading speed measurements and the related oculomotor patterns as a function of font size were similar to those recorded in the normal controls in all viewing conditions under investigation. There was a quadratic relationship between font size and reading speed with amblyopia causing the entire curve to be shifted downward. During monocular viewing with the non-amblyopic eye and binocular viewing, this was more obvious for smaller font sizes. During monocular viewing with the amblyopic eye, larger font sizes were also interestingly affected.

Reading speed measurements exhibited significant changes across the different font sizes for each of the tested groups. Regarding the oculomotor parameters, the total number of saccades and the number of regressive/backward saccades per line showed no significant alternations across the tested font sizes. However, significant changes were observed across the different font sizes with respect to the number of progressive/forward saccades per line and their amplitudes as well as the fixation duration for each of the tested groups. On the whole, after evaluating reading strategies in amblyopic subjects compared to normal controls, amblyopic subjects exhibited an increased number of saccades (comprised of an increased number of progressive/forward saccades of smaller amplitudes and an increased number of regressive/backward saccades) and kept prolonged fixation durations with diminishing print size and in all viewing conditions under investigation.

5. Discussion

5.1 Summary of findings

5.1.1 Reading deficits in amblyopes

While investigating reading performance using paragraphs of text presented at a fixed font size in an attempt to evaluate reading strategies in strabismic amblyopia, significant differences were observed between amblyopic subjects and normal controls (Figure 2.4). Mean reading speed was significantly slower in the amblyopic subjects, compared to the normal controls, during monocular reading with either eye and binocular reading. In particular, reading speed with the amblyopic eye viewing was approximately 55% of reading speed with the non-dominant eye viewing, reading speed with the non-amblyopic eye viewing was 72% of reading speed with the dominant eye viewing and binocular reading speed in the amblyopic subjects was 67% of binocular reading speed in the normal controls. In addition, mean reading speed during monocular reading with the amblyopic eye was also significantly slower compared to monocular reading with the non-amblyopic eye and binocular reading in the amblyopic group (80% and 81%, respectively).

In extending my investigation to reading speed changes as a function of print size, while evaluating reading performance, using paragraphs of text presented at different font sizes, significant differences were also observed between amblyopic subjects and normal controls, during monocular viewing with either eye and binocular viewing (Figure 4.5). During monocular reading with the amblyopic eye of the amblyopic subjects, reading speed was found significantly slower, across all font sizes tested, compared to monocular reading with the non-dominant eye of the normal controls. During monocular reading with the non-amblyopic eye and binocularly of the amblyopic subjects, reading speeds were reduced, compared to monocular reading with the dominant eye and binocularly of the normal controls respectively, mainly for smaller font sizes. Overall, in all three viewing conditions under investigation, the reading speed changes across the different font sizes tested followed a quadratic curve in both the amblyopic subjects and the normal controls, with amblyopia causing the curve to be shifted downwards. In both the reading experiments undertaken, the monocular visual acuity of the sound eyes, as well as the binocular visual acuity, were both comparable between the amblyopic subjects and the normal controls.

5.1.2 Oculomotor Patterns observed during reading

In addition to changes in reading speed, my results indicate the oculomotor patterns associated with the reduced reading speed that the amblyopic subjects exhibit during monocular with either eye and binocular reading, compared to the normal controls. For text presented in a fixed font size, during monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, the number of regressive/backward saccades per line and the fixation duration were found significantly increased in the amblyopic subjects. During monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls, the total number of saccades per line was found significantly increased in the amblyopic subjects. Finally, during binocular reading, the number of regressive/backward saccades per line and the fixation duration differed significantly between the two groups. In particular, the amblyopic subjects exhibited a significantly increased number of regressive/backward saccades per line and significantly prolonged fixation duration compared to the normal controls.

In addition, with respect to eye movement parameters, while evaluating reading performance using paragraphs of text presented at different font sizes, during monocular reading with the amblyopic eye of the amblyopic subjects, the total number of saccades per line and the fixation duration were found significantly increased compared to monocular reading with the non-dominant eye of the normal controls. Furthermore, during monocular reading with the non-amblyopic eye and binocularly in the amblyopic subjects, the number of saccades per line was found significantly increased compared to monocular reading with the dominant eye and binocularly in the normal controls respectively.

It was interesting to observe that, during reading performance in the amblyopic subjects, the increased number of saccades (total, progressive/forward or regressive/backward) appeared to be the variable most consistently different from the normal controls, in both the reading experiments and in the three viewing conditions under investigation. Moreover, the different proportions in the number of forward/progressive saccades to regressive/backward saccades performed during monocular with either eye and binocular reading, indicated that the amblyopic subjects followed different reading strategies. Additionally, fixation duration was significantly prolonged in monocular reading with the amblyopic eye of the amblyopic subjects compared to monocular reading with the non-dominant eye of the normal controls, while evaluating the reading strategies in both the reading experiments. In the last reading experiment, fixation duration was mostly affected at smaller font sizes.

5.1.3 Underlying Oculomotor Deficits

Using paradigms to investigate the underlying oculomotor deficits, significant differences were observed between the amblyopic subjects and the normal controls with respect to the fixation stability and the saccadic performance under monocular with either eye and binocular viewing conditions. In particular, the amblyopic eyes of the amblyopic subjects were characterized by significantly larger Bivariate Contour Ellipse Areas (BCEA), indicating poorer fixational stability, compared to the non-dominant eyes of the normal controls. No significant differences were observed while comparing the fixational stability of the non-amblyopic eyes of the amblyopic subjects to the dominant eyes of the normal controls and binocular viewing of the amblyopic subjects to binocular viewing of the normal controls.

With respect to the saccadic performance, the amblyopic eyes of the amblyopic subjects were characterized by significantly increased saccadic latencies and significantly reduced saccadic gains, while following a moving target stimulus, compared to the non-dominant eyes of the normal controls. Moreover, the non-amblyopic eyes of the amblyopic subjects were also characterized by similar oculomotor abnormalities, namely increased saccadic latencies and reduced saccadic gains, while performing the saccadic task, compared to the dominant eyes of the normal controls. Significant differerences were also observed under binocular viewing between the amblyopic subjects and the normal controls in the saccadic parameters under investigation. However, no general trends were observed in the saccadic task for all the directions (i.e. temporalward, nasalward, upward and downward) and target sizes tested (i.e. 10° and 20°). In addition, while correlating the fixational stability and the saccadic measurements to the oculomotor parameters derived from my first reading task, no significant correlations were observed in all the comparisons made.

5.2 Reading Deficits in Amblyopes

While evaluating reading performance using paragraphs of text presented on a fixed font size and with respect to the reading speed measurements, the presented findings indicate that there are impairments, not only in monocular reading with the amblyopic eye, but also with the non-amblyopic eye and binocularly. This was true, even though the monocular visual acuity of the sound eyes as well as the binocular visual acuity were both comparable between the amblyopic subjects and the normal controls.

These results are in accordance with the findings of *Stifter et al*. (177, 178), who also described the presence of a functional impairment during binocular reading performance, besides impaired monocular reading with the amblyopic eye, in children with microstrabismic amblyopia. The authors found significant differences in reading rates achieved, while comparing the reading performance of the amblyopic group and the normal control group participated in their study. In particular, monocular reading speed with the amblyopic eye of the amblyopic group (maximum reading speed=139.4±42.1 words per minute) was significantly impaired compared to monocular reading speed with either eye of the normal control group (maximum reading speed of the right eye=189.1±15.6 words per minute, maximum reading speed of the left eye=191.1±18.8 words per minute, respectively), with the amblyopic eye achieving 73% and 72% of the reading rates exhibited, respectively, by either eye of the normal control group. In my reading task, reading speed with the amblyopic eye viewing was even more reduced, equal to 55% of the reading speed of the non-dominant eye and 56% of the dominant eye viewing.

In addition, during binocular viewing conditions, *Stifter et al* (177, 178) found that maximum reading speed in children with microstrabismic amblyopia was significantly impaired (maximum reading speed=172.9±43.9 words per minute) compared to normally sighted children (maximum reading speed=200.4±11 words per minute), with the amblyopic subjects achieving a binocular reading speed equivalent to 80% of the binocular reading speed of the normal controls. These results were also in accordance with my findings, although the binocular reading speed in the amblyopic subjects in my study was even more impaired, compared to the binocular reading speed in the normal controls, representing the 67% of the binocularly recorded normal reading rate.

However, *Stifter et al* (177, 178) indicated no significant differences in monocular reading performance with the sound eyes of the amblyopic group compared to the right eyes of the normal control group, with the amblyopic subjects achieving approximately 90% of the reading speed measurements recorded on the normal controls. On the contrary, in my reading experiment, I observed that the reading speed with the non-amblyopic eye viewing was significantly impaired, equal to 72% of the reading speed achieved with the dominant eye viewing.

The observed discrepancies between the investigations may be related to the different subject groups and experimental designs used to evaluate the reading performance. In particular, *Stifter et al* (177, 178) performed their investigation in children with microstrabismic amblyopia, compared to adult amblyopic subjects with mild to moderate strabismic amblyopia, who participated in my study. They used the Radner reading chart comprised of meaningful sentences to assess reading efficiency, while the participants read aloud as quickly as possible. In comparison, my extended reading material comprised of larger paragraphs of text, while the participants read silently to obtain meaning from the passage. In addition, *Stifter et al* (177, 178) evaluated the reading rates using the maximum reading speed recorded as an index, while I used the mean reading speed measurements derived from my calculations.

In addition, while assessing reading performance in the amblyopic subjects participated in my study, reading speed was found significantly impaired in the amblyopic eye, compared to the non-amblyopic eye and binocular viewing. These results were also in accordance with the findings of *Stifter et al* (177, 178), *Rice et al* (179) and *Osarovski et al* (180), who have also indicated a marked difference in interocular reading speed measurements in patients suffering from amblyopia. In particular, *Stifter et al* (177, 178) have shown that, during monocular reading with the amblyopic eye and the sound fellow eye in children with microstrabismic amblyopia, maximum reading speed was found significantly reduced in the amblyopic eyes (maximum reading speed=139.4±42.1 words per minute) compared to the sound fellow eyes (maximum reading speed=172.4±46.7 words per minute). The same authors also noted a significant mean interocular difference of 33±19 words per minute in the maximum reading speed, recorded in a similar study, after evaluating reading rates in children with microstrabismic amblyopia. It was interesting to observe that, in eight of the children participated in the latest study, there was no significant interocular difference in the best-corrected visual acuity. Their results indicated that despite the effectiveness of the prescribed treatment in visual acuity refinement, the reading deficit was still present.

Likewise, *Rice et al* (179) compared the amblyopic with the non-amblyopic eye reading performance, using the abbreviated MNRead reading chart, in children with unilateral residual amblyopia. They concluded that the median reading speed was markedly impaired when the amblyopic eye was viewing (104.4 words per minute, [quartiles 91.9, 206.9] for the amblyopic eye compared to 143.2 words per minute, [quartiles 62.9, 149.3] for the non-amblyopic eye). In addition, *Osarovsky et al* (180) investigated the monocular reading performance with the amblyopic and the non-amblyopic eye in children with anisometropic amblyopia, using the Radner reading chart.

They found that, during monocular reading with the amblyopic eye, the mean reading speed (±SD) was 123.7±28.2 words per minute and the maximum reading speed (±SD) was 166.9± 38.3 words per minute compared to the mean reading speed (±SD) of 166.2±16.0 and the maximum reading speed (±SD) of 209.1±24.5 words per minute, during monocular reading with the non-amblyopic eye. The authors suggested that a functional deficit relevant to reading ability may be present in children with anisometropic amblyopia, similarly to previous observations in children with strabismic amblyopia.

In extending my investigation to reading speed changes as a function of print size, I assessed reading rates using paragraphs of text presented at different font sizes. I found that reading speed was significantly impaired in the amblyopic subjects compared to normal controls during monocular with either eye and binocular viewing, despite the normal visual acuity in the non-amblyopic eyes and binocularly. During monocular reading with the amblyopic eye, all the font sizes were affected while during monocular reading with the non-amblyopic eye and binocularly, only smaller font sizes were affected, even though the changes caused by amblyopia resembled those recorded in normal controls.

Legge et al (234) have shown that the classic reading rate curve of reading speed as a function of print size in normal central vision increases with increasing print size up to a critical print size, beyond which reading speed remains at a plateau level. This results in the reading rate curve exhibiting a characteristic shape, consisting of a ‘steep cliff and wide plateau’. A minimal drop in reading speed values is observed for larger font sizes. In my investigation, the reading speed changes across the different print sizes followed a quadratic curve in both the amblyopic subjects and the normal controls, with amblyopia causing the entire curve to be shifted downwards. During monocular viewing with the non-amblyopic eye and binocularly, this was more obvious for the smaller font sizes. However, during monocular viewing with the amblyopic eye, the larger font sizes were similarly affected. To my knowledge, my study was the first attempt to describe reading speed changes in strabismic amblyopia, as a function of print size, using eye movement recording techniques. Rapid Serial Visual Presentation Technique (RSVP), which eliminates the need of eye movements, has been used to investigate the rate of change in reading speed in normal central vision as a function of font size. Additionally, the reading material in my investigations consisted of paragraphs of continuous text as more representative of the usual reading context, instead of sentences lacking contextual coherence or random-word sequences used in similar investigations.

The significantly impaired reading performance in the amblyopic subjects, during monocular reading with the amblyopic eye, might possibly be associated with an abnormally functioning fovea. In strabismus, early disruption of binocular visual function leads to the presence of a suppression scotoma around the fovea of the deviating eye (86, 187-189). Extensive research has also been undertaken in reading speed changes and eye movement characteristics in normal controls with simulated central scotomas (172, 194) as well as in patients with central field loss (195-198, 200-205, 207, 208). Although the scotoma associated with these studies differs to suppression scotoma in that no visual information from the fovea reaches the visual cortex, these studies provide interesting comparisons to my own data in terms of the recorded reading rates and the oculomotor patterns associated with interruption of foveal vision.

Rayner et al (166, 167, 172), in their seminal experiments, using the moving mask techniques to investigate the effects of artificial scotomas on reading performance in normal individuals, observed that even a 1-letter size foveal mask caused a reduction in reading speed to one-half its normal value. As amblyopic central vision is suppressed, the reduced reading rates recorded in the amblyopic subjects, during monocular reading with the amblyopic eye, were similar to the reduced reading rates observed in normal subjects with simulated central scotomas or in patients with central field defects. In addition, in strabismic amblyopia, the presence of the central suppression scotoma is likely to be associated with the reduced reading rates observed during binocular viewing compared to binocular reading performance of normally sighted controls.

My observations provide further support to the notion that amblyopic foveal vision has similar characteristics to the normal peripheral vision in relation to changes in reading with font size (133, 134, 151, 169, 184-186). In an attempt to illustrate the reading rate curve as a function of font size in normal peripheral vision, *Chung et al* (169, 235) investigated the effect of print size at different eccentricities using the Rapid Serial Visual Presentation Technique. The authors concluded that, even though the rate of change in reading speed as a function of print size remained invariant in both central and peripheral vision, maximum reading speeds were still lower in peripheral vision compared to central vision. Interestingly, in my investigation, mean reading speeds during monocular reading with the amblyopic eye of the amblyopic subjects were significantly lower compared to mean reading speeds during monocular reading with the non-dominant eye of the normal controls. This was consistent in all the font sizes tested, even though the derived reading rate curves were comparable in shape in both the amblyopic subjects viewing with their amblyopic eye and the normal controls viewing with their non-dominant eye. My findings once again highlighted the unique characteristics of the normal fovea in accomplishing satisfactory rates, while performing a visually demanding task.

The crowding effect may significantly contribute to the reduced reading rates observed in the amblyopic subjects during monocular reading with the amblyopic eye and binocularly, compared to the normal controls reading with their non-dominant eye and binocularly, respectively. Crowding has been suggested to affect reading in normal peripheral vision resulting in reduced reading speeds compared to normal central vision (169). Recently, *Levi et al* (174, 183) suggested that reading rates in amblyopic vision were not restricted by the print size, but they were dependent on letter spacing. The authors investigated the rate of change in reading speed in amblyopia as a function of letter spacing, after they had speculated that reading rates in amblyopia could have been adequately predicted by the uncrowded span theory. According to the uncrowded span theory that is related to reading performance in general, reading rates are proportional to the uncrowded span. The uncrowded span is defined as the number of characters preceding each fixation which are not crowded, separated from one another beyond the smallest distance between letters that inhibits crowding. The authors observed that maximum reading rates with the amblyopic foveal vision equalled maximum reading rates with the normal foveal vision, after accounting for the increased critical spacing required. Furthermore, maximum reading rates with the amblyopic peripheral vision remained invariant compared to maximum reading rates with the normal peripheral vision.

One key difference between the study undertaken by *Levi et al* (183) and my investigation is that, they used the Rapid Serial Visual Presentation Paradigm in their experimental set-up, eliminating the need to make eye movements to read. In contrast, in my study I used infrared eye movement recording equipment in order to evaluate the contribution of each of the eye movement parameters to the recorded reading speed changes. In addition, *Levi et al* recruited a limited number of amblyopic subjects and normal controls for their study (seven amblyopic subjects and two normal controls) compared to my investigation (fifteen amblyopic subjects and eighteen normal controls).

Chung et al (169, 237, 238) argued that increasing letter spacing had beneficial effect on reading rates in both central and peripheral vision in normally sighted individuals. The authors (237) studied whether reading speed could be improved in normal central and peripheral vision by increasing letter spacing, in both small and large print, using the Rapid Serial Visual Presentation technique. They concluded that even when character size was not a restricting factor and oculomotor demands were minimized with the Rapid Serial Visual Presentation technique, increased horizontal letter spacing beyond the standard size did not lead to an increase in reading rates in normal central or peripheral vision. The same authors (238), on the contrary, observed that increased vertical word spacing seemed to be advantageous in reading performance, resulting in higher reading rates. This benefit proved to be greater in the peripheral than the central normal vision. One of the most interesting future research questions could be to investigate reading speed changes as a function of letter or word spacing using the eye movement paradigm to evaluate the contribution of the letter or word spacing to the oculomotor patterns observed during reading.

During binocular reading performance, significant differences were similarly observed between the amblyopic subjects and the normal controls with respect to the reading speed. The sensory adaptations that occur in binocular vision after the onset of strabismus, especially the abnormal functioning of the fovea and the presence of the suppression scotoma around the fixation point of the deviating eye (77, 86, 187-189), may contribute to impaired binocular reading rates observed in the amblyopic subjects. Additionally, the increased crowding effect in the amblyopic eye (86, 102, 210) may be partially associated with the reduced reading rates that the amblyopic subjects exhibited, during binocular reading compared to normal controls.

Surprisingly, my results indicated that monocular reading with the non-amblyopic eye of the amblyopic subjects was significantly impaired compared to monocular reading with the dominant eye of the normal controls, even though the distance visual acuity was comparable between the two groups. In strabismic amblyopia, sensory and oculomotor defects, similar to those that characterize the amblyopic eye, have been found to occur in the fellow, non-deviated eye. These include unsteady and eccentric fixation (102, 143, 145, 233), smooth pursuit and optokinetic nystagmus asymmetry (102, 123, 145, 146, 232) and small deficits in contrast sensitivity and Vernier acuity (102, 147-153). Recently, *Levi et al* (183) also suggested an increased crowding effect to exist in the non-amblyopic eye as well as the amblyopic eye. Moreover, the impaired reading performance of the non-amblyopic eye might possibly be related to the applied occlusion therapy as the majority of the participants in my investigation underwent occlusion therapy for the treatment of amblyopia in the past. It has been shown that in amblyopia treatment, occlusion therapy may have as a consequence occlusion amblyopia affecting the occluded eye (86, 103, 113).

On the whole, my results indicate that, in strabismic amblyopia, reading is impaired not only under monocular viewing with the amblyopic eye, but also with the non-amblyopic eye with normal visual acuity and with both eyes. Therefore, it might be suggested that reading speed measurements should be included in the evaluation of the visual function and the effectiveness of treatment in patients suffering from strabismic amblyopia.

5.3 Oculomotor Patterns observed during reading

My findings highlight for the first time the oculomotor patterns that might be associated with the reduced reading speed that amblyopic subjects exhibit compared to normal controls under monocular with either eye and binocular viewing, namely the increased number of saccades and the prolonged fixation duration.

The increased number of saccades appeared to be the most consistent variable related to the reduced reading rates in both the reading experiments and in all the viewing conditions under investigation. Furthermore, a decreased progressive/forward saccades to regressive/backward saccades ratio consistently characterized the saccadic patterns in the amblyopic subjects compared to the normal controls. To some degree, the reading parameters in the amblyopic subjects resemble the eye movement patterns observed during reading in normal subjects with simulated central scotomas and in patients with central field loss.

In simulations of central scotomas using the eye-contingent display change technique to create foveal masks, *Rayner et al* (166, 167, 172) found that increasing the mask size resulted in an increase in the number of progressive/forward saccades, the number of regressive/backward saccades and the fixation duration in normally sighted observers. Similarly, while investigating the eye movement patterns during reading in normal subjects with simulated central scotomas, *Fine et al* (206) also concluded that the reduced reading speed recorded was primarily associated with an increase in the number of saccades and extended fixation durations. In addition, *Mc Mahon et al* (207) explored the strength of the relationship between saccadic frequencies and reading rates in patients with age related macular degeneration and concluded that higher saccadic frequencies were significantly associated with reduced reading rates. All the authors suggested that the reduced visual span, deriving from the simulated central scotomas in normal subjects or the actual scotomas in patients with central field loss, resulted in poor saccadic accuracy and a subsequent increase in the number of saccades in order to reach the visually presented stimulus.

Reading performance is determined by the size of the visual or the perceptual span. The significance of the foveal processing in reading performance was explored by *Legge et al* (171), who defined the visual span as the number of characters in a line of text that can be read without moving one's eye. The authors suggested that reading performance was limited by the number of letters acquired in each fixation. Furthermore, *Rayner et al* (172, 173) highlighted the importance of the parafoveal processing in reading rates, after evaluating the region from which useful information can be encoded during reading, using their moving window paradigm. The authors determined that the effective visual span (described as the "perceptual span") was the range of characters relative to the current fixation that significantly affect the eye movements in reading. When the centre of the visual field is obscured, reading speed declines and eye movement pattern changes (172, 194, 195-198, 200-205, 207, 208). The oculomotor patterns observed during monocular reading with amblyopic eye, in both the reading experiments in my investigation, indicated that in strabismic amblyopia the reading strategies, necessary for correctly directing saccades to new words and locating new lines, were similar to the reading strategies exhibited by normal individuals with simulated central scotomas or patients with central field loss.

In my attempt to investigate the rate of change of the oculomotor patterns during reading performance as a function of font size, it was interesting to observe the variety in reading strategies followed by the amblyopic subjects during monocular viewing with the amblyopic eye, as indicated by the large standard deviations around the mean measurements. This was more profound regarding the saccadic components of the eye movement parameters, namely the number of progressive/forward saccades per line and the number of regressive/backward saccades per line. The large standard deviations usually indicate large intersubject variability; therefore, it might be assumed that the amblyopic subjects tended to use different strategies to accomplish the reading task under investigation. One of the future interesting research questions might be to describe the variety in reading strategies observed in further detail and to investigate whether there are any specific patterns associated with them. In my experiment, no significant correlations were observed while correlating the derived reading speed measurements with the visual acuity of the amblyopic eye (r=-379, p=0.099), the visual acuity of the non-amblyopic eye (r=-0.328, p=0.158) and the binocular visual acuity (r=-0.232, p=0.325) in the amblyopic group. Furthermore, the amblyopic subjects, who exhibited eccentric fixation in direct ophthalmoscopy, did not demonstrate differences in their reading strategies compared to the other amblyopic participants during monocular reading with their amblyopic eye. *Siepman et al* (217) have shown that, in strabismic amblyopes with eccentric fixation, the locus of fixation is shifted to the fovea by extended recognitional effort while performing visually demanding tasks. In my reading investigation, a similar adaptation might possibly be related to the similarities in the oculomotor patterns recorded in amblyopic subjects with central and with eccentric fixation.

During monocular reading with the amblyopic eye of the amblyopic subjects, the eye movement parameters were characterized by significantly increased fixation duration and a significantly increased number of regressive/backward saccades per line, compared to the oculomotor patterns observed during monocular reading with the non-dominant eye of the normal controls. The visual information required for reading, in normal reading conditions, can be perceived within the first 50msec and this information is available during a fixation (166, 167, 172). Taking into account that a fixation in reading lasts on average for 200-250msec, it seems that the remaining duration of a fixation is used to program the next eye movement and for the processes concerned with the integration of the characteristics of the text at higher levels (166, 167). A frequent failure, therefore, to acquire the desired information from a fixation or difficulties in integrating information across saccades may lead to increases in the duration of fixations. Furthermore, the associated difficulties in determining where to direct the subsequent saccade to, considering that the exact localization of the next target might probably be affected by the amblyopic deficit (102, 145, 190-193, 211-225, 233), may result in a high regressive/backward saccades ratio.

This assumption is consistent with the oculomotor adaptations observed in patients with central field loss (206-208). *Bullimore et al* (208), after investigating reading strategies in patients with age related maculopathy, concluded that the reduced reading rates recorded were significantly associated with an increased number of saccades and prolonged fixation duration. The authors suggested that their findings might be related either with the subject's inability to obtain the desired information from a fixation or a lack of efficacy to integrate the perceived information across saccades, when the central part of the visual field was blocked from view. Regressive/backward saccades are highly associated with problems with linguistic processing as well as oculomotor errors (166, 167). In my investigation, any potential difficulty with linguistic processing was minimized, as the reading material comprised of paragraphs of text well below the reading ability of the participants. Furthermore, the matched NART scores between the amblyopic subjects and the normal controls indicated a balance in the intellectual level of the subjects. Therefore, in amblyopia, the oculomotor abnormalities observed might be interpreted in terms of a deficit in processing the visual information at the cortical level, leading to a frequent delay or failure to acquire the desired information from the fixation. Alternatively, they might be the result of difficulties in integrating information across saccades.

5.4 Underlying Oculomotor deficits

In my investigation, stability of fixation, assessed with the bivariate contour ellipse area (BCEA), was found significantly impaired in the amblyopic eye of the amblyopic subjects compared to the non-amblyopic eye of the amblyopic subjects and either eye of the normal controls (in amblyopic subjects, log BCEA values for amblyopic eye=2.194±0.435 minarc^2 compared to log BCEA values for non-amblyopic eye=1.933±0.531 minarc^2 [t=2.030, p=0.037] and in normal controls, log BCEA values for non-dominant eye=1.690±0.244 minarc^2 [t=4.505, p<0.0001] and dominant eye=1.796±0.138 minarc^2 [t=3.886, p=0.001]). This observation was in agreement with the findings of *Srebro et al* (211)), who observed that the amblyopic eyes drifted more than the non-amblyopic eyes of amblyopic subjects or the normal eyes of normally sighted controls. *Westall et al* (216) also described an increased variance in eye position in the amblyopic eyes compared to the non-amblyopic eyes. Furthermore, *Schor et al* (212) suggested that, in amblyopia, the fixational instability composed mainly by nasalward slow drifts and occasionally by abnormally large saccades. *Ciuffreda et al* (213-215) extended these observations, suggesting that the increased fixational drifts were associated with the presence of amblyopia, while the saccadic intrusions were related to the presence of strabismus.

Both sensory and oculomotor adaptations have been implicated as a possible cause of the unsteady fixation of the amblyopic eyes. In a review of the experiments investigating the features of the fixational eye movements in amblyopia, *Flom et al* (218) noticed that amblyopic eyes frequently attempt to fixate with an eccentric retinal locus having higher acuity than the fovea. Furthermore, *Siepmann et al* (217) after assessing the fixation behaviour in strabismic amblyopia, noticed that an underlying defective motor control, associated with an impaired fixation reflex, resulted in an unsteady fixation and therefore, a decreased visual acuity in the strabismic amblyopic eyes.

However, in my study, the fixational nasalward drift, described in the existing literature, was observed only in few amblyopic subjects. This was probably associated with the deficit being less severe in the patient group participated in my investigation or, possibly, because amblyopic subjects were all treated at a young age.

The large bivariate contour ellipse areas, recorded in the amblyopic eye of the amblyopic subjects in my study, are consistent with the extended bivariate contour ellipse areas found, after evaluating the fixational features in patients with central scotomas in their visual field (250-254). Patients with central visual field defects, due to macular disease, may exhibit sizable bivariate contour ellipse areas, as they presumably use more than one preferred retinal loci to serve fixation (250-254). In amblyopia, abnormal fixational eye movements could be attributed to both sensory and oculomotor mechanisms (217, 218), resulting from a deficit in the processing of the visual information at the cortical level or a defective motor control of fixation.

The fixation stability and the characteristics of the fixational eye movements of the non-amblyopic eyes have also been investigated. *Srebro et al* (211), *Schor et al* (212), *Ciuffreda et al* (213) and *Westall et al* (216) noticed no marked differences to exist between the non-amblyopic eye of the amblyopic subjects and either eye of the normally sighted individuals. These findings were in agreement with my observations, in which no significant differences were observed regarding the stability of fixation in the non-amblyopic eye of the amblyopic subjects, compared with either eye of the normal controls (in amblyopic subjects, log BCEA values for non-amblyopic eye=1.933±0.512 minarc^2 and in normal controls, log BCEA values for dominant eye=1.796±0.138 minarc^2 [t=1.152, p=0.262] and non-dominant eye=1.690±0.244 minarc^2 [t=1.192, p=0.067]). However, in amblyopia, fixational abnormalities have been described by some authors to affect the non-amblyopic eye. In particular, *Kandel et al* (233) observed that the non-amblyopic eyes of amblyopic subjects exhibited an eccentricity of monocular fixation with an obvious nasal component. Furthermore, *Bedell et al* (145) similarly found that the non-amblyopic eyes were characterized by unsteady fixation with minute fixational eccentricity and increased velocity of nasalward drifts.

With respect to the characteristics of the saccadic eye movements, differences were observed between the amblyopic subjects and the normal controls regarding the saccadic latency and the gain of the initial/primary saccade performed to reach the target stimulus, in both target sizes (10° and 20°) and in all viewing conditions under investigation. *Ciuffreda et al* (221, 222) have suggested processing delays in the amblyopic eyes resulted in increased saccadic latencies in patients with constant strabismic amblyopia. More specifically, the authors noticed a significant difference to exist in saccadic initiation between the amblyopic eye and the non-amblyopic eye, while following a target stimulus (280±99msec and 223±49msec, respectively). In my study, for the 20° amplitude target stimulus, the saccadic latency of the amblyopic eye of the amblyopic subjects (223±38msec) was found significantly increased compared to the non-dominant eye of the normal controls (199±26msec). Similar results derived for the 10° amplitude target stimulus, after comparing the saccadic latency of the amblyopic eye of the amblyopic subjects (222±26 msec) to the non-dominant eye of the normal controls (192±24msec).

Interestingly, in my investigation, a processing delay in saccadic initiation was found to occur in the non-amblyopic eye of the amblyopic subjects compared to the dominant eye of the normal controls. For the 20° amplitude target stimulus, the saccadic latency of the non-amblyopic eye of the amblyopic subjects (218±32msec) was significantly increased compared to the dominant eye of the normal controls (194±27msec). Similarly, for the 10° amplitude target stimulus, the saccadic latency of the non-amblyopic eye (201±28msec) was significantly prolonged compared to the dominant eye of the normal controls (189±20msec). These discrepancies between the investigations may probably be associated with the different methods used to record the eye position and estimate the saccadic latencies. In particular, in the investigation of *Ciuffreda et al* (221, 222) a photoelectric method was used to record the horizontal eye position, while the saccadic latencies were measured directly from the eye-position traces on a strip-chart paper, possibly resulting in a less accurate estimation of the parameters under study. The use of automated methods in my study allows me to look at averages of a larger number of trials.

Significant differences were also observed in my study regarding the amplitude of the initial/primary saccade (expressed by the gain measurement) between the amblyopic subjects and the normal controls in both target stimuli tested. In particular, for the 20° as well as the 10° amplitude target stimuli, the amplitude of the initial/primary saccade performed by the amblyopic eye of the amblyopic subjects was significantly reduced (or hypometric) compared to the amplitude of the initial/primary saccade of the non-dominant eye of the normal controls. *Schor at el* (225) have highlighted an interocular difference in strabismic amblyopia, while performing a saccadic task, with reduced saccadic amplitudes when viewing with the amblyopic eye compared to the non-amblyopic eye. Interestingly, in my study, no significant interocular differences were observed in the amblyopic subjects, as the non-amblyopic eye of the amblyopic subjects was similarly found to execute initial/primary saccades of significantly reduced amplitudes compared to the dominant eyes of the normal controls. The differences in the accuracy of the equipment used to record the eye movement changes may account for the observed differences. In the investigation of *Schor et al* (225), the saccadic tracking movements were recorded using a pair of infrared sensitive diodes, while the horizontal components of the eye movements were recorded using a dual channel DC strip chart recorder. Also, the limited number of amblyopic subjects included might possibly be associated with the discrepancies observed, while comparing my investigation to both the investigations related to the saccadic latency and the gain of the initial/primary saccade in strabismic amblyopia. *Ciuffreda et al* (221, 222) have recruited six amblyopic subjects with constant strabismic amblyopia, while *Schor et al* (225) based their observations on data derived from five strabismic amblyopes.

I have shown from my reading investigations that, in strabismic amblyopia, reading was impaired not only under monocular viewing with the amblyopic eye but also with the non-amblyopic eye and with both eyes. Moreover, significant differences were observed between the amblyopic subjects and the normal controls with respect to the fixational stability and the saccadic performance. *Crossland et al* (200) proposed that reading deficits in patients with a recently developed macular disease could be correlated to impairments in fixation stability, since 54% of the variation in the movement patterns of the reading eye was associated with changes observed in fixation stability. Similarly, the underlying oculomotor deficits, observed in the strabismic amblyopes participating in my study, might be related to the impaired reading performance that the amblyopic subjects exhibit during monocular with either eye and binocular viewing. Therefore, I correlated the bivariate contour ellipse areas values with the reading speed and fixation duration measurements derived from the reading task under monocular, with either eye and binocular viewing conditions. Fixation duration was selected from the eye movement parameters during reading as being the mostly functionally related oculomotor parameter to fixational stability. However, in all the comparisons made, no significant correlations were observed.

The evaluation of the fixational patterns in patients with central field loss results in large bivariate contour ellipse areas frequently associated with two or more preferred retinal loci (250-254). The necessity of using more than one preferred retinal loci, although resulting in an excess of saccadic eye movements compared to normally sighted controls, appears to be beneficial in individuals with central field loss and eccentric viewing (196, 201, 202). In particular, while investigating reading strategies in patients with age-related macular degeneration, Deruaz *et al* (196, 201) observed that different PRLs were used in order to obtain a global view of the text and to distinguish one or two adjacent letters in further detail. The authors suggested that the fixation instability recorded during eccentric viewing could be a strategy to reduce perceptual fading or Troxler's phenomenon. Therefore, they concluded that purposeful changes in fixational eye movements, while attempting to decode letters or words, could improve the perception of reading text. *Safran et al* (202) also argued that the changes in fixation position and the oculomotor patterns during eccentric viewing, comprising of backward saccades and unexpected line losses, although significantly associated with reduced reading rates, could similarly facilitate reading.

The fixational unsteadiness recorded in the amblyopic eye of the amblyopic subjects might similarly be related to voluntary changes in oculomotor strategies aiming to improve text perception and facilitate reading performance, although this requires more investigation. The fact that the bivariate contour ellipse area values were not significantly correlated with neither the reading speed nor the fixation duration measurements derived from my reading investigation, it may be related to noise introduced by the higher cognitive processes involved during reading. In my reading task, prolonged fixation duration was significantly associated with reduced reading speeds. In reading, fixation duration represents the acquisition of the desirable information from the reading text or the integration of the perceived information across saccades (166, 167). Possibly, the evaluation of the fixation stability may not be a reliable index for the length of the fixation duration during reading.

In addition, while correlating the horizontal components of the saccadic performance (latency, gain and number of saccades to reach the target) to the related oculomotor parameters during reading (fixation duration, amplitude of the progressive/forward saccades and total number of saccades), no significant correlations were observed for any of the viewing conditions under investigation. These negative results could be related to the fact that reading is a more complex task compared to the reflexively driven saccadic task, not only requiring accurate eye movements but also sufficient visual acuity, ability to integrate foveal and parafoveal information and adequate comprehension and cognitive involvement.

5.5 Potential sources of bias and noise in the studies

Potential sources of bias in the studies are:

Measurement bias: This is related to the noise associated with the eye movement recording equipment. The noise associated with the eye movement recordings is very small because of the technical characteristics of the eye movement recording equipment. In particular, the EyeLink eye tracker has a resolution of 0.005° and a spatial noise level of less than 0.01°/RMS, allowing a velocity noise level of less than 2°/RMS to be achieved. The 250 sampling rate gives high temporal resolution of 4 msec resulting in high accuracy of the recordings for the gaze data.

Selection bias: To control for selection bias to account for the possibility of differences between amblyopic subjects and normal controls, a matched control group to the amblyopic subjects was used for the comparisons made. In particular, a number of measures were introduced to account for the possibility of differences in reading ability not related to amblyopia. These included: (i) all participants were native English speakers, (ii) the NART score was used to estimate the educational/intelligence level of the participants and there was no statically significant difference in the NART scores between the two groups (p=0.312 for the 1st reading test and p=0.971 for the 2nd reading test), (iii) all participants were high school graduates and had a full scale NART score of 90 or above while no one scored more than 2SDs below average, (iv) the text used as reading material for the reading tests was below the reading ability of the subjects, and (v) attention and comprehension was checked after all reading trials. In addition to these measures, statistical significance was also tested after including age, gender, NART score and visual acuity into the general linear model used for the descriptive and inferential data analysis. A significant difference in reading speed measurements under each viewing condition between the two groups was present after including these factors.

Time-dependant bias: This could result from familiarity with the equipment or experiment or the time in the day the experiment took place. These factors could influence level of attention. However, none of the tested participant performed the reading tests twice and the reading tests were undertaken in both the amblyopic subjects and the normal controls during different hours in a day (for example, all the amblyopic subjects were not tested in the afternoon while the normal controls were tested in the morning). In addition the order in which the tests were performed (i.e. left eye viewing, right eye viewing, binocular viewing) was randomized in each trial.

5.6 Significance of the results

Reading is a key visual task related to daily living. Amblyopia is a visual impairment affecting substantially both children and adults at various age distributions. However, the impact of amblyopia upon reading has been poorly investigated.

I have observed in my study that reading speed in strabismic amblyopes is significantly impaired compared to normal controls during monocular reading with the amblyopic eye and binocularly, despite normal binocular visual acuity. This is true for a range of print sizes, when comparing monocular reading with the amblyopic eye of the amblyopic subjects to monocular reading with the non-dominant eye of the normal controls and binocular reading in both the amblyopic subjects and the normal controls. Furthermore, in the amblyopic subjects, reading with the amblyopic eye viewing is also significantly worse compared to the non-amblyopic eye viewing. These findings are consistent with the limited literature existing with respect to reading rates and reading ability in amblyopia (176-181, 183).

Interestingly, it has been observed for the first time that reading speed during monocular reading with the non-amblyopic eye in the amblyopic subjects is also significantly impaired, compared to monocular reading of the normal controls fulfilling the same task with the dominant eye viewing. In amblyopia, changes have been shown to occur in the non-amblyopic eye (102, 143-157) as well as the amblyopic eye (102, 115-142). The non-amblyopic eye of strabismic amblyopes, even though referred to as normal, exhibit sensory and oculomotor abnormalities described in the literature, such as abnormal contour integration, inaccurate eye movements, reduced contrast perception and position uncertainty (102, 143-157). The deficient reading performance recorded in my study adds an interesting and quite novel observation to the existing knowledge regarding the abnormalities observed in the non-amblyopic eye in strabismic amblyopia. This reading deficit may be attributed to a genuine disorder existing as a part of spectrum associated with amblyopic visual loss or as a consequence of the applied occlusion therapy similar to occlusion amblyopia (86, 103, 113).

Eye movement recording techniques have contributed greatly to the understanding of the process underlying reading (166-167). Furthermore, they have been widely used to investigate reading strategies, following a variety of pathology affecting the visual system such as age-related macular degeneration (195, 200, 204-205, 207-208), as well as with aging (239). This is the first time that eye movement recording techniques have been used to assess reading ability and investigate reading strategies in strabismic amblyopia. The eye movement recording equipment and the relevant software contributed greatly to my aim to ascertain the impaired reading rates in the group under investigation compared to normal individuals in an objective and reliable way. Moreover, it was the first time that the oculomotor patterns associated with the deficient reading performance in strabismic amblyopia, namely the increased number of saccades and the prolonged fixation duration, have been recorded. These data provide a valuable insight into the specific reading strategies followed during monocular with either eye and binocular reading in strabismic amblyopes. My intention is that this study will lay the groundwork for determining the sensory and oculomotor deficits in reading ability, resulting from strabismic amblyopia and that it should contribute to a greater understanding of the functional visual deficit caused by this visual impairment.

5.7 Clinical Implications of the study

With respect to amblyopia monitoring in clinical practice, assessment of the visual disorder and improvements in visual function are usually charted using methods, such as high-contrast visual acuity charts, which only access foveal vision (116). During treatment regimes, amblyopic patients may exhibit significant improvement in a number of visual function parameters such as contour integration, stability of fixation, low contrast perception and motion detection, despite the fact that minor or absent improvement could be established while evaluating visual acuity with the use of the traditional visual acuity charts (116). As monocular reading speed with either eye and binocularly is impaired in strabismic amblyopia, it appears reasonable to assume that reading speed measurements using standardized reading charts should be included in the assessment of visual function and the effectiveness of treatment in patients suffering from strabismic amblyopia.

5.8 Future research

Further research is needed in order to determine whether similar changes in reading rates and the associated oculomotor patterns are also present in patients suffering from anisometropic amblyopia, as well as in children with amblyopia. It would be interesting to measure improvement in reading ability in amblyopic children during treatment regimen and correlate changes in reading speed to common clinical measures of visual function, such as visual acuity and other visual function parameters (i.e. contrast sensitivity or vernier acuity). It is now also possible to compare improvements in reading ability to compliance to occlusion therapy (i.e. number of hours patched) using occlusion dose monitors (108-112). Furthermore, it might be interesting to investigate whether residual reading deficits remain in children considered as successfully treated according to the normal clinical evaluation.

Random observations in adult anisometropic or strabismic amblyopes after loss of vision in their non-amblyopic eye or deliberate treatment interventions beyond the well-defined period early in life during which amblyopia is considered reversible (89) have revealed that an improvement of visual acuity can develop in the amblyopic eye (90-101). This improvement in visual function provides evidence for a remaining plasticity in the adult nervous system. In addition, the use of perceptual learning in order to improve a specific visual function parameter has been found to be beneficial in other parameters of visual function as well (100, 101, 255-267). A marked improvement in contrast sensitivity or vernier acuity, following extensive and repetitive practice in adult strabismic amblyopes, is usually associated with an improvement in visual acuity, therefore confirming the remaining neural plasticity in adults suffering from amblyopia. Thus, it might also be challenging to evaluate reading performance in individuals suffering from amblyopia, who lose vision in the non-amblyopic eye due to ocular trauma or as part of the aging process, and are left to cope with reading using the amblyopic eye. Any recordable change in reading ability might (or might not) provide further support to the notion that residual plasticity in the visual pathway still exists, even beyond the critical period of visual development. This would indicate that the age for initiation or continuity of amblyopia treatment is much higher than is commonly practiced today.

6. Appendix

6.1 Differences in reading speed measurements between the amblyopic subjects and the normal controls while controlling for age, NART score and visual acuity (experiment 1).

It has to be noted that with respect to the reading speed measurements and for all viewing conditions under investigation, significant differences were still observed between the amblyopic subjects and the normal controls after controlling for age, NART score and visual acuity. More specifically, while comparing monocular reading with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, the difference in reading speed measurements was still significant after controlling for age ($F=37.511$, $p<0.0001$), NART score ($F=36.224$, $p<0.0001$) and visual acuity ($F=4.955$, $p=0.032$). Similarly, while comparing monocular reading with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls, the reading speed measurements also differed significantly between the two groups after controlling for age ($F=16.535$, $p<0.0001$), NART score ($F=15.530$, $p<0.0001$) and visual acuity ($F=15.866$, $p<0.0001$). Finally, while comparing binocular reading between the two groups, a significant difference in reading speed measurements was still observed between the amblyopic subjects and the normal controls after controlling for age ($F=23.076$, $p<0.0001$), NART score ($F=23.997$, $p<0.0001$) and visual acuity ($F=21.403$, $p<0.0001$).

6.2 Saccadic performance of the amblyopic subjects and the normal controls for each direction (temporalward, nasalward, upward, downward) of the 20° and 10° amplitude target shifts (experiment 2).

While evaluating the saccadic performance of the amblyopic subjects and the normal controls in the second experiment, the averages of the derived measurements for each direction (temporalward, nasalward, upward, downward) separately for the 20° and 10° amplitude target shifts were used to evaluate the differences between the two groups in order to facilitate the statistical analysis of the collected data. The mean saccadic latencies (sec), the saccadic gains and the number of saccades derived for each moving direction (temporalward, nasalward, upward, downward) separately for the 20° and the 10° amplitude target shifts are included in the tables 6.1 to 6.6. Differences between the amblyopic subjects and the normal controls were assessed by the non-parametric Mann-Whitney U test, as data did not meet the assumption of normality for parametric techniques (independent-samples t-test).

6.2.1 Monocular saccadic performance with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls

Table 6.1: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Standard deviations are included in the brackets. Z-statistic (non-parametric data) and the associated p-values are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	Amblyopic subjects	Normal controls	z-statistic p-value
LATENCY	Temporalward	0.230 (0.049)	0.217 (0.050)	z=-1.131 p=0.258
	Nasalward	0.209 (0.035)	0.182 (0.022)	z=-2.416 p=0.016*
	Upward	0.233 (0.062)	0.192 (0.027)	z=-2.404 p=0.016*
	Downward	0.224 (0.039)	0.204 (0.035)	z=-1.701 p=0.089
GAIN	Temporalward	0.714 (0.220)	0.784 (0.187)	z=-1.572 p=0.116
	Nasalward	0.731 (0.246)	0.819 (0.128)	z=-1.003 p=0.316
	Upward	0.651 (0.235)	0.727 (0.209)	z=-1.097 p=0.273
	Downward	0.685 (0.247)	0.796 (0.163)	z=-1.695 p=0.090
NUMBER OF SACCADES	Temporalward	1.483 (0.301)	1.613 (0.275)	z=-1.632 p=0.103
	Nasalward	1.432 (0.289)	1.644 (0.314)	z=-2.096 p=0.036*
	Upward	1.461 (0.443)	1.642 (0.412)	z=-1.642 p=0.101
	Downward	1.787 (0.618)	1.666 (0.460)	z=-0.420 p=0.675

Table 6.2: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls. Standard deviations are included in the brackets. Z-statistic (non-parametric data) and the associated p-value are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	Amblyopic subjects	Normal controls	z statistic p-value
LATENCY	Temporalward	0.243 (0.051)	0.204 (0.038)	z=-2.432 p=0.015*
	Nasalward	0.205 (0.020)	0.197 (0.034)	z=-0.997 p=0.319
	Upward	0.223 (0.028)	0.176 (0.019)	z=-4.296 p<0.0001*
	Downward	0.218 (0.054)	0.192 (0.031)	z=-1.782 p=0.075
GAIN	Temporalward	0.641 (0.224)	0.818 (0.215)	z=-3.204 p=0.001*
	Nasalward	0.666 (0.234)	0.896 (0.128)	z=-3.561 p<0.0001*
	Upward	0.850 (0.194)	0.848 (0.202)	z=-0.825 p=0.410
	Downward	0.816 (0.257)	0.825 (0.257)	z=-1.733 p=0.083
NUMBER OF SACCADES	Temporalward	1.314 (0.309)	1.495 (0.253)	z=-1.922 p=0.055
	Nasalward	1.299 (0.294)	1.520 (0.257)	z=-2.417 p=0.016*
	Upward	1.562 (0.519)	1.592 (0.360)	z=-0.855 p=0.393
	Downward	1.589 (0.541)	1.514 (0.468)	z=-0.312 p=0.755

6.2.2 Monocular saccadic performance with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls

Table 6.3: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Standard deviations are included in the brackets. Z-statistic for non-parametric data and the associated p-value are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	Amblyopic subjects	Normal controls	z statistic p-value
LATENCY	Temporalward	0.218 (0.040)	0.192 (0.033)	z=-2.445 p=0.014*
	Nasalward	0.209 (0.052)	0.181 (0.025)	z=-2.181 p=0.029*
	Upward	0.216 (0.035)	0.195 (0.034)	z=-2.030 p=0.042*
	Downward	0.239 (0.061)	0.208 (0.042)	z=-1.643 p=0.100
GAIN	Temporalward	0.643 (0.274)	0.787 (0.205)	z=-1.681 p=0.093
	Nasalward	0.704 (0.241)	0.840 (0.217)	z=-2.533 p=0.011*
	Upward	0.667 (0.235)	0.760 (0.271)	z=-1.722 p=0.085
	Downward	0.709 (0.244)	0.779 (0.168)	z=-0.897 p=0.370
NUMBER OF SACCADES	Temporalward	1.562 (0.337)	1.617 (0.288)	z=-0.651 p=0.515
	Nasalward	1.637 (0.354)	1.696 (0.258)	z=-0.774 p=0.439
	Upward	1.547 (0.342)	1.658 (0.377)	z=-1.220 p=0.222
	Downward	1.466 (0.350)	1.642 (0.442)	z=-1.248 p=0.212

Table 6.4: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls. Standard deviations are included in the brackets. Z-statistic (non-parametric data) and the associated p-value are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	**Amblyopic subjects**	**Normal controls**	**z-statistic p-value**
LATENCY	Temporalward	0.201 (0.036)	0.196 (0.028)	z=-0.286 p=0.775
	Nasalward	0.206 (0.039)	0.186 (0.032)	z=-1.874 p=0.061
	Upward	0.200 (0.033)	0.182 (0.021)	z=-1.761 p=0.078
	Downward	0.203 (0.040)	0.191 (0.034)	z=-0.748 p=0.454
GAIN	Temporalward	0.691 (0.208)	0.895 (0.073)	z=-3.830 p<0.0001*
	Nasalward	0.835 (0.226)	0.825 (0.158)	z=-1.634 p=0.102
	Upward	0.625 (0.187)	0.827 (0.207)	z=-3.243 p=0.001*
	Downward	0.781 (0.142)	0.807 (0.235)	z=-1.893 p=0.058
NUMBER OF SACCADES	Temporalward	1.469 (0.338)	1.496 (0.458)	z=-0.217 p=0.828
	Nasalward	1.452 (0.306)	1.456 (0.255)	z=-0.285 p=0.776
	Upward	1.671 (0.348)	1.411 (0.218)	z=-2.632 p=0.008*
	Downward	1.637 (0.231)	1.529 (0.294)	z=-1.332 p=0.183

6.2.3 Binocular saccadic performance in the amblyopic subjects and the normal controls

Table 6.5: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***20° amplitude target shifts*** *with both eyes of the amblyopic subjects and the normal controls. Standard deviations are included in the brackets. Z-statistic (non-parametric data) and the associated p-value are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	Amblyopic subjects	Normal controls	z statistic p-value
LATENCY	Temporalward	0.215 (0.072)	0.187 (0.025)	z=-1.106 p=0.269
	Nasalward	0.212 (0.068)	0.191 (0.028)	z=-1.012 p=0.311
	Upward	0.212 (0.046)	0.198 (0.027)	z=-0.532 p=0.595
	Downward	0.233 (0.070)	0.207 (0.038)	z=-0.882 p=0.378
GAIN	Temporalward	0.806 (0.190)	0.886 (0.083)	z=-0.570 p=0.568
	Nasalward	0.801 (0.168)	0.849 (0.224)	z=-2.008 p=0.045*
	Upward	0.704 (0.231)	0.772 (0.131)	z=-0.868 p=0.385
	Downward	0.699 (0.228)	0.805 (0.145)	z=-1.818 p=0.069
NUMBER OF SACCADES	Temporalward	1.567 (0.353)	1.600 (0.290)	z=-0.217 p=0.828
	Nasalward	1.560 (0.335)	1.544 (0.297)	z=-0.355 p=0.722
	Upward	1.574 (0.528)	1.614 (0.258)	z=-0.367 p=0.714
	Downward	1.393 (0.409)	1.549 (0.352)	z=-1.737 p=0.082

Table 6.6: *Mean saccadic latency (sec), saccadic gain and number of saccades per target shift while following* ***10° amplitude target shifts*** *with both eyes of the amblyopic subjects and the normal controls. Standard deviations are included in the brackets. Z-statistic (non-parametric data) and the associated p-value are illustrated. A two-sided p-value was considered to indicate statistical significance highlighted by an asterisk.*

	Variable	Amblyopic subjects	Normal controls	z-statistic p-value
LATENCY	Temporalward	0.201 (0.052)	0.201 (0.034)	z=-0.721 p=0.471
	Nasalward	0.218 (0.079)	0.183 (0.022)	z=-2.192 p=0.028*
	Upward	0.200 (0.038)	0.179 (0.015)	z=-1.397 p=0.163
	Downward	0.212 (0.048)	0.194 (0.024)	z=-1.074 p=0.283
GAIN	Temporalward	0.830 (0.210)	0.898 (0.141)	z=-0.561 p=0.575
	Nasalward	0.809 (0.300)	0.868 (0.205)	z=-0.551 p=0.582
	Upward	0.740 (0.185)	0.867 (0.131)	z=-2.542 p=0.011*
	Downward	0.774 (0.196)	0.821 (0.065)	z=-0.082 p=0.935
NUMBER OF SACCADES	Temporalward	1.344 (0.310)	1.390 (0.269)	z=-1.050 p=0.293
	Nasalward	1.333 (0.291)	1.433 (0.206)	z=-1.604 p=0.109
	Upward	1.482 (0.317)	1.467 (0.203)	z=-0.341 p=0.733
	Downward	1.328 (0.234)	1.502 (0.175)	z=-2.201 p=0.028*

6.3 Differences in the derived reading speed measurements between the two reading tests

With respect to the reading speed measurements, in the second reading experiment (with text presented in different print sizes) the differences between the amblyopic subjects and the normal controls under monocular with either eye and binocular viewing, although obvious, seemed to be more subtle compared to the first reading experiment (with text presented in a fixed print size). In particular, amblyopic subjects read significantly slower compared to normal controls, when the reading material was presented in a fixed font size as in the first reading experiment. Possible reasons for the differences observed in the results of the two experiments may include the following: (i) Type of subjects and controls, (ii) Different experimental conditions, (iii) Different variables in the models (in terms of statistical analysis) and, (iv) Random error.

(i) Regarding the type of subjects and controls, by conducting a General Linear Model analysis comparing the amblyopic subjects and the normal controls participating in the two experiments, while controlling for age, NART score and visual acuity, no significant differences were found between the two sets of amblyopic subjects and normal controls. In particular, for the amblyopic subjects, the variable under examination, the F-statistic and the derived p-value after running the model were as follows: age (F=0.0008, p=0.930), NART score (F=0.648, p=0.426), visual acuity of the amblyopic eye (F=0.193, p=0.663), visual acuity of the non-amblyopic eye (F=1.069, p=0.309) and binocular visual acuity (F=1.714, p=0.200). For the normal controls, the variable under investigation, the F-statistic and the derived p-value after running the model were as follows: age (F=0.055, p=0.816), NART score (F=0.001, p=0.970), visual acuity of the non-dominant eye (F=0.119, p=0.732), visual acuity of the dominant eye (*F*=0.015, *p*=0.903) and binocular visual acuity (*F*=0.079, *p*=0.780). Additionally, in the first experiment, there were twenty amblyopic subjects (eight male and twelve female) and in the second experiment there were fifteen (six male and nine female). In the first experiment there were twenty normal controls (nine male and eleven female) while in the second experiment there were eighteen (seven male and eleven female). Therefore, all study participants were well matched in terms of the demographic and clinical variables required for inclusion in the investigation.

(ii) With respect to the experimental conditions, in the first reading experiment the reading material was composed by longer text comprising a continuous story presented in a fixed print size, while in the second reading experiment the reading material consisted of small paragraphs of text, each with different content, presented in different font sizes. In my first experiment as more data were available for the analysis, I aimed to explore whether any difference in reading performance existed between the two groups under monocular and binocular viewing. Moreover, I aimed to distinguish in which eye movement parameters this difference (if any) laid, as the experimental conditions were more representative to natural reading. After I established the fact that there were differences between the amblyopic subjects and the normal controls, I decided to explore the changes in reading strategies as a function of print size, in which the second reading experiment contributed greatly.

Apart from the differences in the contextual characteristics of the reading material used in the two reading assessments, there was also a difference between the two tests in the contrast (luminance) with which the black letters were presented in the white background. In the first reading experiment, the reading stimuli were presented as black letters (luminance 0.88 cd/m^2) on a white background (luminance 14.3 cd/m^2) resulting in a letter contrast of 93.84%, while in the second experiment the reading stimuli were presented as black letters (luminance 0.45 cd/m^2) on a white background (luminance 12.0 cd/m^2) resulting in a letter contrast of 96.25%. Additionally, longer effort in the first experiment (meaning more time to read continuous text and more effort to acquire coherent comprehension) may probably cause more severe sensory and oculomotor disorders in the amblyopic subjects, which could subsequently result in the decreased reading rates in the first experiment compared to the second one.

(iii) Regarding the data analysis, the analysis of the eye movement recordings was consistent between the two experiments, as the same software was used and the same investigator undertook it. In terms of statistical analysis of the derived measurements, the models used for both the experiments were consistent, as the same variables were included in the models and the descriptive and inferential statistics used were appropriate for the analysis. Furthermore, in both the experiments, the results were similar (lower reading rates in amblyopic subjects compared to normal controls in all viewing conditions under investigation) and the association of the derived measurements and the tested group was strong as the partial eta-squared value reveals. In view of the fact that this subtle difference existed in the two experiments, it might be interesting to assess the importance of the findings by calculating the 'effect size' (or 'strength of association'). This set of statistics, the most common of which is eta squared, describes the amount of variance in the dependent variable that is predicted from the independent variable. In further detail, the importance of the impact of group on reading speed measurements can be evaluated using the effect size statistic provided by SPSS: Partial Eta Squared. Partial eta squared represents the proportion of the variance in the dependent variable (reading speed) that can be explained by the independent variable (group). In other words, while the p-value indicates that the results are statistically significant, the partial eta squared points out how large the association is between the variables or how important this association is. While comparing the monocular reading performance with the amblyopic eye of the amblyopic subjects and the non-dominant eye of the normal controls, the value of the partial eta squared is 0.337, which is considered quite a large effect. Moreover, while comparing the monocular reading performance with the non-amblyopic eye of the amblyopic subjects and the dominant eye of the normal controls, the value of the partial eta squared is 0.127. Finally, while comparing the binocular reading performance of the amblyopic subjects and the normal controls, the value of the partial eta squared is 0.136 (both considered as quite large effects).

(iv) Regarding the random error, while comparing the reading speed measurements of the amblyopic subjects in the first reading test to the reading speed measurements of the amblyopic subjects reading the same font size (0.7 LogMAR equivalent) in the second reading investigation, a quite constant difference was observed for each viewing condition. In particular, while comparing monocular reading of the amblyopic subjects reading with the amblyopic eye in the two reading assessments, the mean difference in reading speed measurements was 5.17 characters with spaces/sec; while comparing monocular reading with the non-amblyopic eye, the mean difference was 4.58 characters with spaces/sec and while comparing binocular reading performance, the mean difference in reading speed measurements was 5.45 characters with spaces/sec. This observation almost excludes the possibility of a random error, especially since only subtle differences were observed in the reading speed measurements while comparing the relevant viewing conditions in the normal controls. In further detail, while comparing monocular reading with the non-dominant eye of the normal controls between the two reading tasks, the mean difference in reading speed values was 0.63, while comparing monocular reading with the dominant eye the mean difference was 0.61 and while comparing binocular reading, the mean difference was equal to 1.33 characters with spaces per sec.

Summarizing, the differences observed in reading speed measurements in the amblyopic subjects between the two reading tests compared to the normal controls may be related to a wider and more severe crowding effect that causes the patients to find more dense text to be read more difficulty.

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