Reading between the lines of visual discomfort and Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)

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Abstract

ME/CFS is a debilitating disorder affecting at least 250,000 people in the United Kingdom. This condition has a number of incapacitating symptoms including post-exertional fatigue, cognitive deficits, and flu-like symptoms. However, with an unresolved aetiology, controversial diagnosis, and no clear treatment, it is important that potential clinical features are identified and explored. Visual symptoms are often reported by patients, and, there is now a growing body of literature to experimentally support this. Nevertheless, there is a paucity of research investigating precisely how these visual symptoms impact the everyday lives for those with ME/CFS. This is especially the case for reading activities. The aim of the experiments within this thesis was to thoroughly investigate vision-related reading in ME/CFS patients. The results show that vision related reading discomfort in ME/CFS is unlikely to be a factor of impaired ocular motor function in reading, or, a poorer reading acuity. However, ME/CFS patients did demonstrate elevated levels of pattern-related visual stress. Given that text is spatially reflective of patterned stimuli that can induce visual stress distortions in those who are susceptible, this may account for some of the visual symptoms that are experienced during reading in those with ME/CFS. These findings are discussed in relation to possible therapeutic interventions and it is suggested that future, more direct, research is required in order to augment the findings.
Declaration and publications

I declare that the research reported in this thesis has been conducted by myself, and comprises of my own written work.

September 2015. Rachel L. Wilson

Studies 1-5 are in preparation for submission: Manuscript in preparation.

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Abbreviations

ME = Myalgic Encephalomyelitis
CFS = Chronic Fatigue Syndrome
CFIDS = Chronic Fatigue and Immune Dysfunction Syndrome
PVFS = Post Viral Fatigue Syndrome
WHO = World Health Organisation
CBT = Cognitive Behavioural Therapy
GET/GAE = Graded Exercise Therapy/ Graded Aerobic Exercise
NICE = National Institute for Health and Care Excellence.
QOL = Quality of life
VS = Visual Stress
RA = Reading Acuity
CPS = Critical Point Size
MRS = Maximum Reading Speed
ANOVA = Analysis of Variance
SEM = Standard Error from the Mean
N0 = No window condition
1W = 1 word window condition
3W = 3 word window condition
WRRT = Wilkins Rate of Reading Test
EEG = Electroencephalography
fMRI = Functional magnetic resonance imaging
1. General Introduction

1.1 Overview

Myalgic Encephalomyelitis (ME), also referred to as Chronic Fatigue Syndrome (CFS), is a debilitating disorder encompassing a number of symptoms including prolonged fatigue, abnormal sleeping behaviour, cognitive deficits, neurological impairments, muscle weakness, and post-exertional ‘malaise’ (Fukuda, Startus, Hickie, Sharpe, Dobbins & Komaroff, 1994; Carruthers, van de Sande, Meirleir, Kilmas, Broderick & Mitchell, 2011). The condition has an extensive impact on a number of systems, such as, the immune system (Lorusso, Mikhaylova, Capelli, Ferrari, Ngonga, & Ricevuti, 2009), the central nervous system (Chen, Liang, Moriya, Yamakawa, Sumino, Kanda & Takahashi, 2008) and the cardiovascular system (Hollingsworth, Jones, Taylor, Blamire & Newton, 2010).

Unfortunately, because of conflicting evidence, the aetiology of this complex and multifactorial disorder remains poorly understood (Kerr, Burke, Petty et al, 2008), and no definitive cause of ME/CFS has been identified. Moreover, as the illness produces a large number of heterogeneous symptoms, there is considerable debate over the development of diagnostic criteria and even the existence of the disorder itself (Holgate, Komaroff, Mangan & Wessely, 2011). As a result, there is currently no clinically recognised diagnostic test available for sufferers, who at present are diagnosed through excluding other conditions and are heavily reliant on subjective symptom reporting. As symptoms considerably overlap with those present in other illnesses, frequently depression (Griffith & Zarouf, 2008), this can lead to cases of misdiagnosis. Critically, misdiagnosing ME/CFS can be further detrimental to patients’ health and causes difficulty and delays in accessing the correct information, support services and appropriate therapies (Baker & Shaw, 2007). It has therefore recently been suggested that research should focus on investigating objective and measurable clinical symptoms (Twisk, 2014), to help understand the disorder and to move away from a subjective and controversial diagnosis.

Visual problems represent a measurable class of symptoms that are commonly reported by patients with ME/CFS. In the long term, investigating anomalous vision could potentially assist in the development of an objective clinical diagnosis, critical for delineating the
disorder from other conditions. It may also help detect possible therapeutic targets that may improve the vision-related quality of life of patients. However, despite a wealth of visual difficulties reported by patients, there has been relatively little research quantitatively examining the precise characteristics of these visual problems. Research examining the impact of the visual problems on patients’ everyday life is largely underrepresented. This is particularly the case for reading. Reading is an important ability that is essential for functioning effectively in everyday life. Many ME/CFS patients report visual and ocular problems related to their reading (Vedelago, 1997). Yet, research into the vision-related reading problems in ME/CFS sufferers has so far been ignored, despite reading also being strongly correlated to quality of life (Hazel, Latham, Armstrong, Benson & Frost, 2000), and the potential for the development of therapeutic interventions to improve reading experiences.

To this end, the primary purpose of the experiments outlined in this thesis is therefore to gain an enhanced understanding of the impact that ME/CFS has on vision, especially during reading experiences, and on vision-related quality of life.

1.2 ME/CFS

1.2.1 Definitions and diagnostic criteria

With no clear pathogenesis, a diagnosis of ME/CFS is effectively achieved by means of exclusion and is heavily based on subjective symptom reporting. As such, diagnosing and defining the condition is a difficult and controversial issue, which can result in inconclusive examinations and cases of misdiagnosis. Furthermore, there are a number of varying terms attached to the condition, each emphasising different symptoms. This has also caused further complications when trying to define and diagnose the illness.

Historically, Neurasthenia (meaning weak nerves) was a commonly used term in the 1800’s for what we now refer to as ME/CFS. This soon fell out of favour, although some clinicians still use it (Campling & Sharpe, 2000). The term CFIDS (Chronic Fatigue and Immune Dysfunction Syndrome) has also been applied which particularly highlights immune changes. However debate remains over whether immune changes cause the conditions’ symptoms. PVFS (Post Viral Fatigue Syndrome) is another term emphasising the viral
infection and is also sometimes used by doctors (Campling & Sharpe, 2000). However, ME and CFS are the two most common terms used today in research and practice. Although they are regularly used interchangeably, there is concern regarding the appropriateness of this practice.

‘CFS’ comprises of the term ‘chronic’ (defined as an illness usually lasting > 6 months) and also places emphasis on the ‘fatigue’. The diagnostic entity CFS was first introduced in 1988 to deliver a definition for individuals’ experiencing chronic fatigue of an unknown cause after the Lake Tahoe, Nevada, epidemic outbreak in the mid-1980s (Campling & Sharpe, 2000). Fukuda et al (1994) later redefined CFS placing ‘unexplained fatigue’ as the principal feature. According to Fukuda et al (1994) the ‘unexplained fatigue’ should be co-joined with four out of the following eight symptoms: sore throat, unrefreshing sleep, headaches, tender lymph nodes, muscle pain, joint pain, short-term memory loss/concentration impairment, and post-exertional malaise for 24 hours or more. Symptoms should also persist or reoccur for six consecutive months and not have preceded the fatigue. However, ‘fatigue’ and other symptoms such as ‘unrefreshing sleep’ are subjective and vague, and as such the CFS criterion selects a rather varied human population (Wilson, Hickie, Hadzi-Pavlovic et al, 2001). Indeed, Twisk (2014) claims that the heterogeneity of the CFS patient population has impeded effective research and the accurate diagnosis of patients. In response to these concerns, Carruthers et al (2011) proposed a newly defined International Consensus Criteria criterion, employing the term ‘ME’.

Carruthers et al (2011) state that applying the word ‘fatigue’ when naming the disorder is a misused and confusing criterion. Indeed, no other fatiguing disease has the term ‘chronic fatigue’ attached to its name (for example ‘chronic fatigue cancer’). Carruthers and colleagues propose that the term ME is more appropriate as it indicates underlying pathophysiology and selects a more homogenous patient group in contrast to the Fukuda et al’s (1994) CFS criteria.

The term ME is now commonly used by many patients, media, public and clinicians. It was first applied to explain the Royal Free Hospital outbreak (1955), where 292 staff members at the hospital were affected with symptoms of profound malaise, headaches,
fever, bodily pains and depression, lasting from July until October (Crowley, Nelson & Stovin, 1957; Mcevedey & Beard, 1970). In comparison to the CFS criteria, cognitive deficits, post-exertional malaise or neuro-immune exhaustion are obligatory for the diagnosis of ME. These symptoms should also be accompanied by specific neurological abnormalities such as, diminished cellular energy metabolism/transportation and immunological symptoms, gastro-intestinal symptoms, or genitourinary symptoms (Twisk, 2014). Since, these symptoms are not necessary to meet the diagnosis of CFS, and, ‘fatigue’ per se is not a mandatory requirement for the diagnosis of ME, the two may represent different things (Twisk, 2014). However, at time of writing, CFS and ME are referred to as the same illness within previous literature and also by the World Health Organisation (WHO, 2013). As such this present thesis will refer to ME and CFS as interchangeable terms.

1.2.2 Epidemiology

Changing case definitions over time coupled with a diagnosis that relies profoundly on subjective judgements, has instigated difficulties faced in epidemiological research. As such, the prevalence of ME/CFS varies widely.

Generally, prevalence estimates vary between epidemiological studies and within and between countries, with reported rates varying from 0.2-0.4% (Baker & Shaw 2007; Maquet, Demoulin & Crelaard, 2006). Age of onset is usually in young adulthood, peaking between 20 and 40 years old (Jason, Taylor, Wagner, Holden, Ferrari & Phillips, 1995). ME/CFS is more prevalent in women (for unclear reasons) with a ratio of approximately 3:2 (Lloyd, Hickie, Boughton, Spencer& Wakefield, 1990). It has also been suggested to have a higher prevalence amongst lower socioeconomic classes (Lawrie, Manders, Geddes & Pelosi, 1997).

1.2.3 Theories/Aetiology

Understanding the causal mechanisms behind ME/CFS is important for improving the diagnostic criteria, and for the development of effective treatments. However, despite a substantial body of research, a critical limitation largely present within the ME/CFS literature is the lack of clarity concerning the disorders’ aetiology. Consequently, the origin of ME/CFS is still a matter for debate, and an extensive variety of theories have been
It is beyond the scope of this thesis to critically review in detail all of the possible explanations and correlations for ME/CFS. However core aetiological arguments will be reviewed. (For a more detailed review see Maquet, Demoulin and Crielaard, 2006).

One of the best supported theories concerns viral triggers and immune deregulation. There is considerable evidence indicating that ME/CFS patients have immunological abnormalities associated with infectious disorders. Although there is some conflicting evidence, many key examples can be drawn from the numerous studies which demonstrate that ME may be linked to virus reactivation (for example herpes: Ablashi, Eastman, Owen, Roman, Freidman & Zabriskie, 2000; Di Luca Zorzenon, Mirandola, Colle, Botta & Cassai, 1995; Enbom, Linde & Evengard, 2000). Further research has also suggested that an increased production of various cytokines may also be an influencing factor. It is argued that interleukins (IL-1, IL-2, IL-6) released by cells, triggered by infectious agents, could explain fatigue (Cannon, Angel, Abod, vannier, Miletto & Fagioli, 1997). It has also been revealed that CFS patients have fewer natural killer cells, reduced lymphoytic response, and up-regulated RNase L activity (Kilmas, Salvato, Morgan & Fletche, 1990). This is an important finding as normal levels of RNase activity have been linked to better health, and high levels to a reduction of health (Suhadolnik, Peterson, Cheng et al.1999). However, at present, the extent to which immunological alterations play a role in causing ME/CFS remains fairly unclear and limited.

Other suggested causes of ME/CFS include lower basal cortisol levels in the HPA axis, although this finding is not always consistent (Himmel & Seligman, 1999). It has also been suggested that abnormal white matter may play a role, although this notion is controversial (Cope & David, 1996). De Luca, Johnson and Natelson (1993) and Graffman, Schwartz, Dale, Scheffers, Houser & Straus (1993) indicate that cognitive dysfunctions such as speed and efficiency of information processing is reported in ME/CFS. However, whether or not this is a cause or consequence remains unclear, and others have reported no cognitive dysfunctions (Schamling, DiClementi, Cullum & Jones, 1994). Sleep disturbances have also been shown to be prevalent in ME/CFS sufferers which may explain symptoms of muscular pains (Buchwald, Pascualy, Bombardier, Kith, 1994). Even psychological theories have been put forward (albeit with very little support amongst the ME/CFS community and
researchers). For example Wessely, David, Butler and Chalder (1989) propose that the connection between psychological and physiological factors demonstrate that CFS is caused by depression.

1.2.4 A Review of Treatments and NICE Guidelines

A number of therapeutic methods have been suggested to be beneficial for ME/CFS patients. However, as the cause of the disorder is unclear, therapeutic approaches are aimed at providing relief from symptoms, in order to achieve to some degree, a level of pre-illness functioning and health (Manquet, Demoulin & Crielaard 2006).

Given its link to depression and high rate of depression-like symptoms (such as poor concentration, fatigue, memory impairment), pharmacological treatments for ME/CFS mainly include anti-depressants (Kruesi, Dale & Straus, 1989). Vercoulen, Swanink and Zitman’s (1996) study of 107 CFS patients suggested that, in comparison to a placebo, Fluoxetine has been shown to be of use for significantly improving scores on the Beck Depression Inventory (Beck, Steer & Brown, 1996). However, critically, there were no differences in fatigue scores. Other antidepressant drugs such as Clomipramine and Sertraline have demonstrated non-significant results, thus raising questions over the validity of anti-depressants as an appropriate form of treatment (Behan & Hannifah, 1995; Natelson, Cheu, Pareja, Ellis, Policastro & Findley, 1996). This may be especially the case when acknowledging the large number of side effects that are linked to anti-depressant drugs, many of which are uncomfortable and serious (See Khawam, Laurencic & Malone, 2006 for overview). Other pharmacological treatments such as immunotherapy, corticosteroids, and dietary supplements have also failed to produce any significant benefits (Rowe, 1997; Rowe, Calkins, DeBusk, McKenzie, Anand & Sharma, 2001; Brouwers, van der Werf, Bleijenberg, Van Der Zee & Van Der Meer, 2002).

Non-pharmacological therapies such as Cognitive Behavioural Therapy (CBT) have been recommended. Sharpe, Hawton & Simkin, et al (1996) examined the efficacy of providing CBT (in addition to medical care) to 60 CFS patients over 16 weekly sessions. Over a 12 month period, significantly more patients who received CBT benefitted in clinical functioning, compared to the non-CBT group. Additionally, Deale, Chalder, Marks and Wessely (1997) compared patients receiving CBT or relaxation therapy. The results showed
that 70% of patients within the CBT group gained benefits in physical functioning, in contrast to 19% of those receiving relaxation therapies. Other non-pharmacological treatments such as Graded Aerobic Exercise (GAE), also commonly referred to as Graded Exercise Therapy (GET), are also suggested. Manquet, Demoulin & Crielaard (2006) states that GAE is a core part of any treatment for CFS patients. However, Twisk and Meas (2008) state that it is unethical to treat patients with programmes such as GAE and also CBT, as the evidence base is flawed and there appears to be clear serious harmful effects. In particular, GAE causes exertion, which in turn causes post-exertional malaise. As a result this can enhance musculoskeletal pain, thus worsening fatigue and amplifying feelings of weakness.

NICE guidelines

The National Institute for Health and Care Excellence (NICE) guidelines recommend a comprehensive and individualised approach to therapy (Baker & Shaw, 2007). The guidelines are based on systematic reviews of the best available evidence. Baker and Shaw (2007) summarised the guidelines for ME/CFS treatment as follows:

General referral and management recommends pharmacological treatment, sleep management and modifications to diet. However, pharmacological treatments such as antidepressants are not advised for an overall benefit. In setbacks and relapses it is recommended that patients gradually return to their previous physical activity level. A well balanced diet and dietary supplements e.g. vitamins, advice on fitness for work and education are also advised. Referral to a specialist is usually recommended when symptoms are prominent for after 6 months. Specialist care consists of adapted programmes to suit the individual, offering CBT or GAE. Overall, the guidelines suggest an integrated, multidisciplinary approach, which recognises the need for health and social assistance as well as advice for work and education. However, practically, such an extensive and tailored approach can be tough to accomplish.

1.2.5 Summary of ME/CFS literature

ME/CFS is a debilitating disorder marred with much controversy and poor understanding concerning its aetiology. This has not only led to problematic epidemiological studies but, importantly, no clear effective treatments are available. A further issue is the
lack of clarity surrounding case definitions and diagnostic criteria. Diagnosis is reliant on subjective symptoms which can lead to misdiagnosis and inconclusive examinations, causing a negative impact on the patient. This has often left patients subject to a considerable amount of controversy and stigma surrounding the condition, leaving some exposed to ridicule from medical associates and accusations of malingering or even attention seeking (Leslie, 1997).

It should however be considered that despite many of these issues, this does not alter the reality of the illness for thousands of individuals, whose quality of life is greatly affected. In order to move research forward, it is therefore important that key clinical and measurable features are identified. By doing so may help develop an understanding into the condition and improve diagnostic procedures and treatments.

1.3 Vision-Related Symptoms in Patients with ME/CFS

Visual problems represent a measurable class of symptoms that are commonly reported by patients with ME/CFS. By exploring the visual factors this may also help, in the long term, with developing a more objective diagnosis, and also to assist in the development of therapeutic interventions.

1.3.1 Self-reports

A considerable body of self-reports suggest that visual and ocular problems are prevalent in many ME/CFS patients. Caffrey (1990) first highlighted visual difficulties in patients with ME/CFS by listing the main features of visual/ocular symptoms reported as follows: blurred vision, diplopia, floaters, photophobia, dry eyes, ocular burning and non-specific eye pain. Vedelago (1997) also reported poor oculomotor control, exophoria, convergence and fixation disparity abnormalities. In line with these findings, Leslie (1997) examined three ME/CFS case studies, all of which expressed experiences of visual/ocular problems ranging from headaches, tired eyes, and accommodative dysfunctions to significant convergence insufficiency. Based on these case studies, Leslie (1997) also argued that in some ME/CFS cases general acuity and ocular problems may not always show up on routine optometric assessments. Therefore, a more thorough optometric examination is required which also takes into account patient history. Although only basing these findings
on just three cases, Leslie (1997) cautiously suggests that such an exercise could even potentially serve as an initial objective indicator for the condition. Feasibly, this practice could therefore also assist in discriminating the illness from other conditions.

Perhaps stronger self-reporting evidence can be drawn from Potaznick and Kozol’s (1992) questionnaire study, which recruited a substantially large sample of 190 ME/CFS patients and 198 matched controls. In line with previous reports, with the exception of one symptom (teary), a highly significant difference was revealed between patients’ and controls’ \( (p = .00001-.007) \) visual problems. Patients’ reported more problems than controls for the following visual symptoms: Functional (accommodative, convergence) symptoms (distance vision, near vision, foggy, distance to near, near to distance, diplopia and shadowed); Neuro-sensory symptoms (headaches – near vision, headaches – distance vision, photophobia, depth perception and moving objects); Entropic Phenomenon symptoms (black spots, white spots, coloured spots, flashing lights, others and halos) and Pathophysiological (anterior segment) symptoms (burning, gritty, dry, scratchy). Driving behaviour comparisons were also conducted, revealing that 24.7% ME/CFS patients reduced or stopped driving because of their visual symptoms, compared to only 3% of controls. However, interestingly, these findings did not corroborate general optometric assessments.

More recently, Hutchinson, Maltby, Badham and Jason (2014) also assessed patients’ visual symptoms through conducting a questionnaire study. A sample of 59 ME/CFS patients completed a newly developed standardised measure of ME/CFS symptoms: The DePaul Symptom Questionnaire (Jason, Evans, Porter et al, 2010). The questionnaire includes four visual items. It was revealed that 92% of ME/CFS sufferers experienced sensitivity to light, 88% stated difficulties with focusing visual attention, 86% suffered with eye pain, and 61% poor depth perception. These results herein offer further support to the many claims that ME/CFS patients frequently experience visual problems. It was also revealed that the severity of the visual symptoms they reported was correlated with ‘impact on everyday life’.

1.3.3 Impact on everyday life

Crucially, patients report that the visual symptoms they experience have deleterious effects on daily life (Leslie, 1997). The impact of visual problems on everyday activities can be demonstrated by Potaznick and Kozol’s (1992) finding that a markedly larger proportion
of ME/CFS patients altered their driving habits as a result of their visual symptoms, compared to a much lower percentage in the control group.

However, and of particular importance, many of those with ME/CFS claim to experience visual discomfort whilst reading. Examples of vision related reading symptoms reported often include: headaches, blurred vision, increased fatigue and difficulty tracking lines of print (Vedelago, 1997).

Reading is an extremely important behaviour which is strongly related to quality of life (Hazel et al, 2000). We use our eyes to read continuously on an everyday basis in order to take in information from our environment. We read signs, instructions, magazines, books, numbers, text messages, emails and so on. We read for many reasons, for work, pleasure, education and knowledge etc. It would thus seem that reading ability has a real significance to daily functioning and for the achievement of even the very basic every day demands of living, working and to being an effective and active member of society. If reading performance is to become impaired may consequently cause detrimental and limiting effects across a large variety of daily tasks which in effect may lead to a reduction of quality of life.

Investigating into these vision-related reading problems, could lead to the development of clinical interventions to improve reading experiences. Leslie (1997) recognises that managing visual problems in ME/CFS can be of great importance for improving the quality of life for patients suffering with the debilitating and frustrating condition. The prognosis for ME/CFS is a long recovery with variable improvement and relapses. As there is no immediate and effective treatment available, assisting to thoughtfully manage visual manifestations could help improve everyday life.

1.3.3.1 Summary of visual self-reports and effect of everyday living

It can clearly be seen from the wealth of self-reporting studies that ME/CFS patients appear to be suffering from a range of visual problems that warrant acknowledgement. This is especially the case when considering the potential deleterious effect on everyday activities that these visual problems may produce. This is largely important when reflecting
on the visual symptoms relating to patients’ reading behaviour, given that reading and quality of life are strongly correlated.

Although the above studies are based on self-reports, which limits how much one can infer, such studies are an important step in terms of clarifying symptoms and in guiding further research for which more empirical investigation can subsequently follow. However, despite a wealth of self-reported visual and ocular symptoms, a fundamental limitation within the literature for ME/CFS, is the lack of experimental and objective evidence to support such claims.

1.3.2 Experimental evidence

Although limited, a handful of studies have attempted to validate the visual symptom reports from patients with experimental studies. Caffrey, Johanson and Sameck (1994) for example reported an abnormal visual pathology in their study of 25 CFS patients, where a significant abnormality of the pre-ocular surface was revealed. Mastopasqua, Ciancaglini, Carpineto, Iezzi, Racciatti & Falconio’s (2000) also revealed, in comparison to healthy controls, CFS patients had a significantly higher distribution of exophoria, lower functional vergence (near and far), a further point of convergence, and a lower tear secretion and break up time. Furthermore, Frolo and Petrunia (2002) demonstrated in their large study of 218 ME/CFS patients, that 70.2% had vascular pathology in the eye and 52.8% had dystrophic pathology. Thus it would appear that at least some of the visual symptoms reported may be accounted for by visual/ocular abnormalities.

Furthermore, ME/CFS patients have also shown deficits in visual search and visual attention based tasks (Hutchinson & Badham, 2013). ME/CFS patients and controls completed a visual search task which assessed the ability to locate a pre-defined target in a field of simultaneously presented irrelevant visual information (distractors). Patients were significantly slower to identify whether the target was present or absent, compared to controls. Patients were also more detrimentally affected by increases in the number of search elements compared to the control group. Moreover, a Useful Field of View (UFOV) test, a widely used method to experimentally and clinically examine visual attention (Sekuler & Bennett 2000), revealed significant differences between patients and controls visual attention. The UFOV test consists of three subtests providing a measure of visual processing
speed, divided attention and selective attention. Patients and controls performed at a comparable visual processing speed during a task in identifying whether a briefly presented central target was a car or a truck. However, ME/CFS patients were impaired on the divided attention subtest. This task required participants to identify a centrally presented target, a ‘car or truck’, and indicate the radial position of a simultaneously presented peripheral target. Patients were also impaired on the selective attention subtest. This task was similar to the divided attention task, except that the peripheral surrounding the target was filled with distractors - triangles. Although, it has been suggested that to some extent these findings may also reflect abnormal eye movements (Hutchinson & Badham, 2013).

Other recent research has focused on eye movements. Vedelago’s (1997) questionnaire study has suggested that patients suffer from poor ocular control and dysfunctional saccades. This has recently been objectively supported by Badham and Hutchinson (2013), revealing that eye movement dysfunctions are prevalent in patients with ME/CFS. Patients performed worse than controls on tasks that required them to make quick, accurate pro-saccadic eye movements (towards and fixate on the presented target), and were particularly impaired on anti-saccadic eye movements (eye movement towards the hemispheric opposite of the target). This task required individuals to judge the fixation point themselves. Thus, this may also reflect that ME/CFS patients have a poorer spatial awareness, and/or an inability to swiftly recall the exact position on which to focus when directing their gaze away from the target (Badham & Hutchinson, 2013). Patients also showed deficits on a task which involved tracking a moving target (smooth pursuit) in which their performance also deteriorated over time.

1.3.2.1 Summary of experimental findings

Although limited, some of the visual symptoms that patients report have been backed by clear empirical evidence. However, despite a growing body of empirical evidence, an integral issue exists. The consequences of vision-related problems on everyday activities in those with ME/CFS remain disregarded in empirical research. This is especially the case for reading. The significance of this issue can be reflected from the strong correlation between reading and quality of life (Hazel et al, 2000).

1.4 Reading
Reading is a highly skilled and complex process. It entails efficient processing and integration of visual and perceptual features, cognitive processes (such as encoding of phonological/semantic information, and working memory participation), oculomotor factors and visual attention. However, there has been much debate over precisely how these factors work together throughout the reading process. Many now accept that cognitive processes are the driving force behind eye movements, accounting for the influence of lexical variables (White, 2008), or visual attention shifts (Morrison, 1984). However, others claim that oculomotor factors are the principle factor driving the decision as to where and when the eyes move (O’Regan, 1992).

Indeed, as previously discussed, many ME/CFS patients report visual problems relating to their reading. As of yet, there has been no direct experimental investigation into visual and ocular factors that may affect reading in those with ME/CFS.

1.4.1 Methods investigating reading

There are a number of objective methods which can be applied to investigate reading. Reading performance charts for example can be used to measure vision-related reading features that cannot be determined from basic visual acuity assessments. Such as the Radner Rate of Reading and MN READ Acuity Charts can be used to measure visual features such as, the effect of print size by assessing reading acuity (the smallest print size one can read), and critical point size (the smallest print size at which patients can read with their maximum speed.). They also give a measure of reading speed in reading rate (how many words can be read per minute). Eye tracking methods also provide an extremely useful, well-controlled and specialised measure of reading behaviour. A strength of this technique is that it is possible to examine an extensive number of variables and use special methodological paradigms to measure eye movements in order to infer: efficiency of oculomotor control, determine different reading strategies, assess a number of biomarkers of reading difficulty, evaluate visual parameters, and even to assess cognitive language processing.

1.4.1.1 Eye tracking methods in reading
Eye movement dysfunction in ME/CFS – does it translate into reading and how can this be measured?

Eye movements are motor responses that take time to plan and execute (Rayner, 2009). Badham and Hutchinson (2013) claim that reports of fatigue in tasks that involve eye movements could reflect poor muscular control. This would also be fitting with Carruthers et al (2011) claim that motor problems are a common feature in patients with ME/CFS.

It is now well documented through eye tracking measures that eye movement control during reading consists of a series of well-planned and coordinated fixations and saccades. In sum, the eyes extract visual information during very brief resting periods (approximately 150ms – 500ms), referred to as fixations. Between these fixations, the eyes move at high speed through ballistic movements called saccades (taking approximately 20-35ms). Most saccades are moving forward as we read from left to right, however about 10-15% of saccades are backwards, called regressions. (Ryaner, Pollatsek, Ashby & Clifton, 2012).

Badham and Hutchinson (2013) demonstrated that ME/CFS patients had impaired saccadic function in a task that required participants to look towards a target (pro-saccades), and away from a target (anti-saccades). Reading requires a series of high velocity and well-co-ordinated saccadic eye movements over a sustained period of time. Therefore there may be reason to suggest that impaired saccadic function could underlie some of the vision related reading difficulties they experience. However, whether or not these abnormal eye movements in ME/CFS patients translate into reading is yet to be explored.

Badham and Hutchinson (2013) also revealed that during the smooth pursuit task (tracking a moving target), patients’ performance deteriorated over time, whereas the performance of the control group did not change. The author’s claim that this is indicates that the task was able to measure patients’ increased susceptibility to the effects of fatigue over time from sustained musculature activity. Indeed, one of the key visual disturbances that patients report is increased fatigue on tasks which involve moving the eyes for extended periods of time (Vedelago, 1997). In comparison to the saccadic tasks (anti/pro saccades) which allowed for 1-2 seconds of inactivity, smooth pursuit requires sustained musculature activity for 30 seconds (whilst tracking the moving object). The authors
suggest, that during the saccadic tasks, the 1-2 seconds of inactivity may have allowed for patients to overcome the fatigue, which would not have been possible during the smooth pursuit task. Reading does not involve tracking a moving object for a length of time. But, it does involve tracking lines of print, also involving sustained musculature activity for an ongoing period of time, and problems tracking lines of print is a symptom that ME/CFS patients specifically state (Vedelago, 1997). During reading, fixations only last for approximately 250ms which may not equate to the same ‘overcoming of fatigue’ that a resting period of 1-2 second of inactivity may have done in the saccadic task. Therefore, it is also tentatively suggested that the sustained musculature activity from eye movements in reading may to some extent explain increased reports of fatigue during reading, and reading discomfort. In view of this, one might expect eye movements to deviate from their normal pattern, the longer ME/CFS patients reads for.

Eye tracking methods can be used to examine the saccadic eye movements of patients during reading for a sustained period of time by measuring a number of variables such as: saccadic amplitude, number of regressions, number of fixations, number of saccades and fixation duration.

*Other eye tracking methods*

Not only can eye tracking methods provide information about saccadic function during reading, but by employing certain techniques, the study of eye movements can also be used to assess visual, cognitive and attentional processes.

One example is to use lexical manipulation methods in order to measure eye movements to evaluate linguistic processing. The core reason for why we read is to process language, however, whether or not the visual problems that patients report affect language processing remains to be explored. It may also be worth exploring linguistic processing in ME/CFS patients given that many report cognitive deficits, such as poor working memory, information processing difficulties, and many often perceive that simple mental tasks require substantial effort (Caruthers et al, 2011).

A well-established paradigm employed to examine the influence of linguistic variables, is ‘The Word Frequency Effect’; an index of language processing. The word
frequency effect is a robust finding that in skilled readers, longer fixations are spent on infrequent words compared to frequent words, and that frequent words are more likely to be skipped. Therefore, by manipulating the frequency of words allows one to evaluate linguistic processing, and, also to assess saccadic accuracy.

It is also worth acknowledging the role of visual attention during reading. For example, spatial attention has been argued as a necessary preliminary to visual word processing (Besner, Risko, & Sklair, 2005), and indeed in many reading models (such as the EZ Reader model, Reichle, Rayner, & Pollatsek, 2003, and the pre-motor theory, Rizzolatti, 1983) it is now recognised that visual attention also impacts on eye movements. This may be especially noteworthy, given that there is evidence for visual attention impairments in ME/CFS patients (Hutchinson & Badham, 2013).

Visual factors related to attention during reading can also be explored by examining eye movements. Eye movements are necessary because of the anatomy of the retina and limitations due to acuity outside of the fovea. Although acuity is good at the fovea, it is less so in the para-foveal region, and so viewers move their eyes to place the fovea on the part of text that they wish to see more clearly. The region of effective viewing in reading is referred to as the perceptual span (Rayner, Slattery & Belanger, 2010). In skilled readers the perceptual span (in alphabetical writing) is asymmetrical and extends to 3-4 letters to the left of fixations and 14-15 letters to the right of fixation (Rayner, 1998; 2009). A reduced perceptual span has been acknowledged and used as a potential biomarker for conditions such as schizophrenia (Neale, 1971). Unskilled readers are also known to have a smaller perceptual span, as well as, those who generally read much slower (but perfectly well), the elderly, and in some visual conditions such as macular degeneration (Rayner, Castelhano & Yang, 2009; Crossland & Gary, 2006; Strauss et al, 1984; Rayner, Slattery & Belamger, 2010). However, whether or not the vision-related reading symptoms that ME/CFS patients report are related to a reduced perceptual span, is yet to be explored.

The perceptual span is also related to visual attention, and has been better thought of as an attentional span (Henderson, & Ferreira, 1990). Given patient reports of trouble focusing visual attention, and, experimental evidence indicating visual attentional deficits in
ME/CFS (Hutchinson & Badham, 2013), the question arises as to whether attentional problems may impact on para-foveal processing during reading. If a reduced perceptual span is evident in those with ME/CFS, theoretically this could mean that more eye movements are required during reading, and may result in longer reading times. It is tentatively suggested, in view of Badham and Hutchinson’s (2014) suggestion that fatigue increases during tasks which involve sustained and increased musculature activity, that a reduced perceptual span may be one potential explanation for increased fatigue during reading tasks. However, this concept has yet to be investigated experimentally.

By using specialised eye tracking methods, the perceptual span can be measured by using a gaze-contingent moving window paradigm (McConkie & Rayner, 1975). This powerful technique allows for the determination of general characteristics of the perceptual span, by controlling how much information a reader can process on each fixation, and assessing how normally an individual can read. For example, if a viewer can read well with only a very small amount of text available (such as just the fixated word), this may be indicative of a smaller perceptual span. Whereas, if reading became impaired, this may be reflective of a larger perceptual span, presumably as some of the visual information that would have usually been used to read efficiently is missing.

1.4.2 Summary of reading and eye tracking methods

Reading performance charts provide objective measures of reading which cannot be obtained during general optometric examination. Various eye tracking methods are also highly useful in assessing eye movements to evaluate ocular motor, cognitive, and visual factors that underlie the reading process, and do so in a highly controlled and empirical manner.

However, it is important to consider a range of possibilities that might contribute to the reading symptoms reported by ME/CFS patients, to allow for a comprehensive and thorough investigation. This is especially the case given the multifactorial nature of the disorder, the considerable variability in visual and ocular abnormalities, and that as vision-related reading discomfort in patients with ME/CFS is a concept that has yet to be explored.
An alternative approach could be to examine the visual symptoms reported by patients from a more perceptual angle. Indeed many of the visual symptoms that patients report such as headaches, blurriness of text, and sensitivity to light, are characteristic of the phenomenon of visual stress.

1.5 Visual Stress and Reading in Patients with CFS/ME

1.5.1 Visual stress

Visual stress, also known as Meares-Irlen syndrome (Meares, 1980; Irlen, 1983), is believed to be sensory-neural in origin, distinct from oculomotor problems, affecting approximately at least 5% of the general population (Wilkins, 2003). Perceptual distortions and uncomfortable somatic symptoms (such as headaches, colours, blurriness, flickers etc.) occur when individuals who are vulnerable to visual stress look at complex and especially repetitive geometric striped patterns. According to the theory of visual stress, nerve cells in the visual cortex of the brain fire too strongly, causing others to fire inappropriately causing the brain to be overloaded by certain images. Due to the spatial characteristics of lines of text, this can often occur during reading (Wilkins & Nimmo-Smith, 1987).

Vision-related reading symptoms that ME/CFS patients report such as headaches, blurriness of text, map well onto those characteristics of the phenomenon of visual stress. Visual stress has also been linked to photophobia. Indeed it was observations concerning photosensitive epilepsy (a neurological disorder) which led to the theory that visual stress has a neurological basis (Wilkins, 2003). It is thus perhaps interesting to note that the most common visual symptom reported in Hutchinson, Badham, Maltby and Jasons (2014) was sensitivity to light (photophobia), and that ME/CFS is also believed to have a large neurological component (Carruthers et al, 2011).

Symptoms of visual stress have been well documented in a number of other conditions such as, photosensitive epilepsy, after stroke, dyslexia, migraine, ADHD, and autism (Wilkins, Baker, Amin et al, 1999; Harle, Shepherd & Evans, 2006, Beasley & Davis, 2012, Singleton & Henderson, 2007; Robertson & Simmons, 2015). As many of the visual reports made ME/CFS patients map well onto those present in visual stress, it is somewhat
surprising that research into the overlap of symptoms between the two conditions (ME/CFS and visual stress) is lacking.

Robinson, McGregor, Roberts, Dunstan, Butt (2001) have reported exceptionally high incidences of visual stress comorbidity in their CFS subjects. Their study revealed a biological basis for the visual processing problem of Irlens Syndrome, showing significant variations in blood lipids, and, urine amino and organic acids between those with high comorbidity of CFS and visual stress than those with a much lower comorbidity. A recent questionnaire study has also emerged (Leow, Marsh and Watson, 2014) which assessed the prevalence of nine diagnostic symptoms of visual stress in 3 groups: ME/CFS patients, a visual stress group (consisting of individuals with a diagnosis of visual stress), and a control group. It was revealed that all core visual stress symptoms (slow reading, reading-related strain/fatigue, print distortions, poor depth perception, dislike of bright light/glare, reading/writing under fluorescent lighting) were reported significantly more within the CFS group than the control group. Furthermore, just two symptoms out of the nine were statistically less frequent in the CFS group compared to the visual stress group.

The current available evidence suggests that a possible connection between the two conditions may exist. However with the exception of the two studies (outlined above), research into visual stress in ME/CFS is absent. Findings from Leow et al’s (2014) study provide a good indication that visual stress may be higher in ME/CFS patients; however there is a need for a direct measure in order to quantify visual stress symptoms. More direct measures are also useful as they are strong predictors of the benefit of therapeutic intervention, particularly coloured overlays.

1.5.2 Coloured Overlays

ME/CFS patients report symptoms highly similar to those of visual stress (Leow et al. 2014). Therefore it is a reasonable assertion that therapeutic interventions used to help alleviate visual stress may also be useful in reducing reading discomfort in ME/CFS patients. The use of coloured overlays to reduce visual stress symptoms during reading are a low cost easily implementable intervention that has been employed by many.
Coloured overlays are sheets of coloured plastic designed to be placed over a page of text to colour the page without interfering with the clarity of the text. The overlays have been shown to improve reading fluency in some cases, when the colour has been selected to suit the individual. Overlays can also be placed on top of each other to create an even wider array of stronger colours. There are several types of overlays on the market however the ‘Intuitive Overlays®’ have been used in the majority of research (Wilkins, 2003). They include 9 different colours and a grey. The design was based on 2 assumptions: 1) there are certain colours that are effective, and 2) these differ from individual to another.

Reportedly, the overlays can reduce symptoms of visual stress such as blurred vision, headaches from reading, and also improve reading speed (Wilkins, 2003; Wilkins, Jeanes, Pumfrey & Laskier, 1996; Evans & Joseph, 2002). However, when claims for the benefit of coloured overlays was first introduced by Helen Irlen (1991) they were not well received, and many remained sceptical over the efficacy of their benefit. Gradually, over the years evidence has amassed and there is now a considerable volume of evidence to suggest that coloured overlays are effective in improving reading experiences (Wilkins, 2003).

Jeanes, Busby, Martin, Lewis, Stevenson, Pointon and Wilkins (1997) for example employed the intuitive overlays in primary schools. After presenting the colours, children chose the coloured overlay that improved the clarity of the text. Approximately 50% reported beneficial effects with one or more of the overlays. These children were given their best overlay to use if they wished to do so. 3 months later nearly half of the children were still using their overlay, approximately 20% of the entire sample of normal children.

Furthermore, Tyrell, Holland, Dennis and Wilkins (1995) tested reading speed in children with and without overlays (the child chose their optimal overlay from the selection which also included a clear overlay). Half the children chose a clear overlay. Reading continued for 15 minutes. Initially no differences were found in speed between the 2 conditions; however, differences began to show after ten minutes when reading began to tire. Children who had chosen a coloured overlay slowed down when reading without it and reported eye strain. Children who chose a clear overlay reported fewer symptoms and did not slow down, thus indicating no benefit from the use of the clear overlay.
Further support for the beneficial effects of coloured overlays have been demonstrated in intensive reading tasks, designed to invoke symptoms in those vulnerable to visual stress, namely The Wilkins Rate of Reading Test (Wilkins, Jeanes, Pumfrey & Laskier 1996). Wilkins and Lewis (1999) used the Rate of Reading test and a placebo control. Reading rate was measured in a number of conditions: no overlay, chosen overlay, grey overlay and grey overlay labelled ‘scientific prototype’. High levels of motivation and expectation were generated by informing children that the grey prototype was new, it combined all the colours, and they were one of the first to use it and expected to do as well as they can. Performance with the grey prototype overlay did not differ from the other grey overlay and importantly, the chosen coloured overlay was superior. These results have also been replicated by Bouldoukian, Wilkins and Evans (2001) who used a similar design, and suggest that improved reading performance is unlikely to be due to motivation or other placebo effects.

1.5.3 Summary of visual stress and coloured overlays

As many of the visual problems patients report are characteristic of visual stress, there may be reason to postulate that ME/CFS patients are more susceptible to visual stress, which may account for their vision-related discomfort during reading. Indeed Leow et al (2014) demonstrated through questionnaire methods that significantly more visual stress symptoms were prevalent in ME/CFS patients compared to controls. However more direct measures are required to support these claims. Furthermore, the use of coloured overlays as a means of reducing visual stress symptoms during reading and improving reading performance may be a useful therapeutic strategy to explore. The significance of this is high, as reading is related to quality of life. Furthermore, by providing patients with some form of control and management over their visual symptoms during reading, may give back a sense of autonomy, especially to those who are otherwise severely debilitated by their condition. The significance of this is high, as reading is related to quality of life.

1.6 General summary

People with ME/CFS frequently report a number of vision-related symptoms associated with their condition, and empirical research has now amassed to support some of the claims. An important concern is how the visual problems that ME/CFS patients
experience, impact their everyday lives. However empirical research into the effects of visual and ocular problems on daily functioning is largely ignored in this patient group. Many patients report visual discomfort when reading, a fundamental everyday behaviour that is also highly correlated with vision-related quality of life. However the characteristics underlying reading discomfort in patients with ME/CFS remain to be explored objectively. A number of methods can be employed to investigate visual and ocular reading factors in patients with ME/CFS. In particular, as research has shown evidence of impaired eye movements in ME/CFS, the question arises as to whether impaired saccadic function also exists during reading. Eye tracking methods are a useful technique to examine ocular motor processes during reading, as well as a number of linguistic and visual factors. Additionally, many of the visual symptoms reported by ME/CFS patients map well onto those that characterise visual stress. However research examining the occurrence of visual stress and ME/CFS is extremely limited and warrants a more direct approach. Coloured overlays improve reading performance and especially benefit those who experience visual stress. As such, they may prove to be a useful tool to explore to help alleviate vision-related reading discomfort in those suffering with ME/CFS.

1.7 Rationale for Study

ME/CFS is arguably a controversial illness. With very little understanding about the condition itself, and with significant problems in diagnosis and definitions, it is important that measurable clinical features are explored. Many patients report visual problems, and although experimental evidence has supported some of these claims, the effect of visual symptoms on everyday behaviours, notably reading, has been overlooked despite reading also being linked to quality of life.

To this end, the rationale of the study is therefore to develop an understanding of the impact that ME/CFS has on vision, vision-related reading experiences and general vision-related quality-of-life. Experimental research will be conducted which may offer empirical evidence to support the claims of those with ME/CFS that they find reading difficult and experience reading-related discomfort. This will be done by evaluating reading performance and through using a range of eye tracking methods to examine eye movement characteristics during reading. The present research will also more directly determine the
existence of visual stress in ME/CFS and authenticate the efficacy of coloured overlays as a means of reducing reading-related discomfort.
2. General Methodology

The following methodology was applied to all the studies that follow in this thesis. Specific methods and apparatus details are provided in the relevant experimental chapters.

2.1 Design and participants

The study used a mixed experimental design with within subjects and between subjects’ factors. There were two between subject’s comparison groups: (1) a clinical group consisting of participants with a formal diagnosis of either ME or CFS (n = 27); (2) a non-clinical control group, matched by gender, age and education where possible (n = 27). Breakdown for means ages between patients and controls is presented in Table 2.1. Participants primarily lived in the Midlands Region, although a number of patients did travel from other geographical locations in the UK (see Table 2.2).

Table 2.1
Mean (and standard deviation) age, gender, for patients and controls. ME/CFS categorisation is also shown for patients.

<table>
<thead>
<tr>
<th></th>
<th>Age range</th>
<th>Gender (f:m)</th>
<th>ME/CFS definition*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>18-68</td>
<td>24:3</td>
<td>NA</td>
</tr>
</tbody>
</table>

Note. *CFS = CFS case definition (Fukuda et al, 1994); Canadian ME/CFS = Canadian ME/CFS case definition (Carruthers et al, 2003); International ME = International consensus ME case definition (Carruthers et al, 2011).

Table 2.2
Geographical Location for patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Midlands Region*</th>
<th>Other*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>22/27</td>
<td>5/27</td>
</tr>
<tr>
<td>Controls</td>
<td>24/27</td>
<td>3/27</td>
</tr>
</tbody>
</table>

Note. *Midlands region refers to locations within the Leicestershire, Birmingham and Nottinghamshire areas. Other locations included Staffordshire, London, Stockport and Cambridgeshire.

2.2 Identifying and Approaching Potential Participants
2.2.1 Clinical Group

As the study required the recruitment of participants from a relatively small clinical population, various strategies were utilised in order to increase the response rate (Sheehan, 2001). ME/CFS support groups within the Midlands Region (e.g. ME Positive; Action for ME) were at first approached via email. This allowed the appropriate members of the support groups to circulate the study details onto ME/CFS members, who were provided with the contact details of the researcher, thereby offering participants opportunity for direct contact. Two support groups also offered to promote the study through their monthly Newsletter and social media groups, to ensure that the information about the study was disseminated further into the ME/CFS community. Potential participants were then sent an information and availability form, which included details for travel expense and reimbursement. They were also sent a pre-screening questionnaire, The DePaul Symptom Questionnaire and a MOS health survey (Medical Outcomes Survey), to determine their suitability for the study criteria. More details for pre-screening measures are outlined below in section 2.3.

2.2.2 Non-clinical Comparison Group

Matched age and gender control participants were recruited via emailing information about the study to staff and students at The University of Leicester. The study was also advertised on the staff webpage on the University of Leicester ‘Bulletin Board’, and through ‘INDEED News’ weekly emails which are sent out all staff and students every week. Liaison with the Psychology participant panel coordinator also allowed for further recruitment from the participant panel (a database of participants from the Leicester area who had already registered their interest in participating in psychological studies at the university). Other recruitment efforts were made through contact with the Quaker meeting house secretary, and the Women’s Institute, by providing study advertisements which were then distributed to members. Contact details were provided so that individuals who were interested and required further information could make direct contact with the researcher. An incentive of £7.50 an hour was provided to compensate participants for their time.

2.3. Inclusion criteria for ME/CFS patients
All ME/CFS patients had a medical diagnosis of ME/CFS. Additionally, prior to the study all potential clinical ME/CFS patients were provided with a standardised questionnaire (The DePaul Symptom Questionnaire) to confirm that they met the criteria for inclusion in the study. The DePaul Symptom Questionnaire (Jason, Evans, Porter, et al. 2010, see Appendix A, item 1) ensures that symptoms are examined in a consistent way. It provides a structured approach to collect standardised symptom information to enable researchers and clinicians to determine whether a patient meets the criteria for ME and/or CFS. Brown and Jason (2014) found the DePaul Symptom Questionnaire to have good convergent and discriminant validity, concluding that it is a valid tool for assessing ME/CFS symptoms to aid in clinical and research assessment. Jason, So, Brown, Sunnquist and Evans (2015) also demonstrated that the questionnaire has good test-retest reliability. The questionnaire is now frequently being used in more studies as a measure to ensure a level of consistency when assessing symptoms and recruiting samples for research (Jason et al, 2015; Hutchinson & Badham, 2013; Badham & Hutchinson, 2013).

The questionnaire assessed whether prospective patients met the most commonly applied case definitions: Fukuda et al’s (1994) CFS Case Definition, the ME/CFS Canadian Case Definition for ME/CFS (Carruthers et al, 2003), and the International Consensus ME Case definition (Carruthers et al, 2011). Those that met the appropriate case definitions (See Table 2.1) were then subsequently invited to attend the study.

2.4. Ethical Considerations

Ethical approval was sought and gained from The University of Leicester, School of Psychology Ethics Committee (Appendix A, Item 2). Before the study commenced, participants were provided with a Participant information Sheet that provided information about the objectives of the research (Appendix A, Item 3). All participants completed a consent form (Appendix A, Item 4). On all documents presented it was clearly stated that to participate in the study was entirely voluntary and they could withdraw their consent at any time without providing a reason. Participants were also provided with the contact details of the lead researcher and ethics committee coordinator, and were encouraged to seek clarification if necessary. Once all the information had been collected, names were removed and participants were identified by a numeric and alphabetic code on raw data. All raw data
were kept in a locked filing cabinet. Data were considered on a group basis and it was not possible to identify any individual from the results.

2.5 Data Analysis

All statistical analyses are 2 - tailed.
3. Tests of Basic Visual Functioning

Basic visual functioning of ME/CFS patients was determined using a range of methods.

3.1 Study 1. Visual Acuity

Visual acuity is a measure of central vision. Although ME/CFS patients report problems with their vision, general optometric assessments, such as acuity measures, have not revealed any significant differences between ME/CFS patients and control groups to date (Leslie, 1997; Potaznick & Kozol, 1992; Badham & Hutchinson, 2013; Hutchinson & Badham, 2013). The first aim of this chapter is therefore to rule out any visual acuity deficits in patient’s that could potentially be a factor in the visual problems they report. The assessment also served as a further screening measure for the remaining experiments. Corrected visual acuity was measured under the assumption that individuals who require corrective intervention, such as glasses or contact lenses, would use them for everyday behaviours, for instance reading. It was expected, based on the previous literature, that there will be no differences in visual acuity between patients and controls.

Methods and materials

For all tests viewing was binocular, and participants were informed that they should use corrected vision. The Institute of Optometry Near Card Test (Evans & Wilkins, 2001) was used to first examine near acuity. Participants were instructed to hold the near card at 40cm, measured from their eye line, and asked to read out loud the single words presented on the left side of the card. Once they had read the last word that they could see, they were then asked to read the corresponding phrase. The N series value was then noted and converted into a logMAR score using the conversion chart provided with the chart. Participants were then asked to stand behind a 4 meter line facing the logMAR Precision Vision Distance Acuity chart. They were then instructed to read out loud the letters from left to right starting from the top until no longer able to do so. The logMAR score was then noted. Finally, participants were asked to stand behind a line marked as 3 meters in order to carry out LogMAR Crowding Test Keeler © (McGraw & Winn, 1993). Both crowded and uncrowded acuity was measured in accordance with the instructions provided by the Keeler Crowding acuity cards. Crowded acuity was examined first. Initial letter acuity was first
determined using the screening cards. Where error was made the participant was stopped on the last successful letter response and this was used to determine the starting point for the measurement of line acuity. The appropriate card was then selected and participants were asked to identify each of the four letters presented on each card. Where the participant was able to correctly identify two or more letters on a line then the next card in the series was presented until no longer able to do so, and the logMAR score was noted. Uncrowded acuity was then examined and noted in a similar fashion using the uncrowded acuity cards (which had 2 letters per card as opposed to 4). The crowding ratio was then calculated using the following equation:

\[
\text{Crowding ratio} = \frac{\text{uncrowded acuity}}{\text{crowded acuity}}
\]

Results

Mean values are presented in Table 3.1. No significant differences were found between patients and controls for near acuity \((t(26) = 1.991 \, \text{or} \, p = .057)\), or for distance acuity \((t(26) = -0.057, \, p = .963)\). However, there was a significant difference between patients’ and controls’ crowded acuity \((t(26) = 2.247, \, p < .05)\), whereby ME/CFS patients displayed a poorer crowding acuity. However no significant differences between patients and controls were displayed for uncrowded acuity \((t(26) = .498, \, p = .623)\), nor for the crowding ratio \((t(26) = -.961, \, p = .346)\).

Table 3.1. Mean scores for visual acuity in patients and controls. Values in parentheses are + 1 SEM.

<table>
<thead>
<tr>
<th></th>
<th>Near acuity</th>
<th>Distance acuity</th>
<th>Crowded acuity</th>
<th>Uncrowded acuity</th>
<th>Crowding ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>.13 (.01)</td>
<td>.92 (.05)</td>
<td>.10 (.04)</td>
<td>.03 (.03)</td>
<td>.43 (.17)</td>
</tr>
<tr>
<td>Controls</td>
<td>.11 (.01)</td>
<td>.92 (.05)</td>
<td>.01 (.02)</td>
<td>.00 (.04)</td>
<td>1.87 (1.51)</td>
</tr>
</tbody>
</table>

Note. Values for near acuity have been converted from UK N series to logMAR. Distance acuity is in decimal. All other acuity measures are in logMAR.

3.2 Study 2. Low level vision

Problems with low level vision have importance for daily functioning, and cannot always be corrected with conventional methods such as glasses, contact lenses or laser eye surgery (Legge, Rubin, Pelli & Schleske, 1985). Low level visual problems encompass other visual features such as difficulty in differentiating contrast and perceiving depth. ME/CFS patients
report problems in perceiving depth (Hutchinson, Maltby, Badham & Jason, 2014; Potaznick & Kozol, 1992) and therefore, stereo-acuity was assessed. Secondly, given its importance to performance in everyday tasks such as reading, contrast sensitivity was also examined.

3.2.2. Stereo acuity

Stereopsis is the ability to perceive depth binocularly. It is associated with visual fatigue and visual discomfort (Ukai & Howarth, 2008), declines with age (Garnham & Sloper, 2006) emphasising the need for an age-matched control group, and has also been linked to quality of life (Rahi, Cumberland & Peckham, 2008). Those with poor stereo-acuity also report higher levels of fatigue and exhaustion in completing activities which require the use of their stereo-vision (Kuang, Hsu, Chou, Tsai & Chou, 2004). A number of self-report studies have revealed that ME/CFS patients report a loss of depth perception (Potaznick & Kozol, 1992; Hutchinson et al, 2014)

Methods and materials

Stereo-acuity was determined using the Frisby Stereotest, Stereotest Ltd © J.P Frisby. Participants sat positioned straight on to a white background and were informed that they were going to see a plate containing 4 patterns. They were instructed that it was their task to discriminate one of the patterns (the target) which would either look as if it was ‘coming outwards’ or ‘going inwards’. A Perspex plate was then positioned over the white background containing the 4 circular patterns of mosaic-like of geometric shapes. One of the patterns (the target) contained a circle containing a pattern of geometric objects which was visible within the mosaic. It was the participants’ task to detect this target pattern. The test consists of three plates of varying thickness (6mm, 3mm and 1.5mm), each of which were presented at different possible distances to obtain a range of disparities. Distances were measured from the participants’ eye line to the plate using a tape measurer. The range varied from 30cm to 150cm, as shown in Table 3.2. The available disparities ranged from 600 to 5 (arc-secs). In order to avoid utilising monocular cues, it was ensured that participants had the plate placed directly in front of them and kept their head still.

---

1 Participants who failed to identify the target at 600 arc-secs were classed as stereo negative and were excluded from the analyses. This led to the removal of 4 subjects (2 matches), providing the total number of: patients n =25 and controls n =25.
Results

Figure 3.1 shows mean stereo acuity thresholds (arc sec) for patients and controls. As data was not normally distributed a Wilcoxon Signed-Ranks test was used which confirmed that patients had significantly higher (worse) stereo acuity thresholds than controls (patient median = 20, control median = 15; $Z = -2.321, p < .05$). These findings support patients’ self-reports that they experience problems related to depth perception (Potaznick & Kozol, 1992; Hutchinson, Maltby, Badham & Jason, 2014).

Table 3.2
Template for recording stereo-acuity threshold in arc-seconds

<table>
<thead>
<tr>
<th>Viewing Distance</th>
<th>Plate Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cm</td>
<td>6mm</td>
</tr>
<tr>
<td>30</td>
<td>(12)</td>
</tr>
<tr>
<td>40</td>
<td>(16)</td>
</tr>
<tr>
<td>50</td>
<td>(20)</td>
</tr>
<tr>
<td>60</td>
<td>(24)</td>
</tr>
<tr>
<td>70</td>
<td>(28)</td>
</tr>
<tr>
<td>80</td>
<td>(32)</td>
</tr>
<tr>
<td>100</td>
<td>(40)</td>
</tr>
<tr>
<td>120</td>
<td>(47)</td>
</tr>
<tr>
<td>150</td>
<td>(60)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plate Thickness</th>
<th>3mm</th>
<th>1.5mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
<td>300</td>
<td>150</td>
</tr>
<tr>
<td>340</td>
<td>170</td>
<td>85</td>
</tr>
<tr>
<td>215</td>
<td>110</td>
<td>55</td>
</tr>
<tr>
<td>150</td>
<td>75</td>
<td>40</td>
</tr>
<tr>
<td>110</td>
<td>55</td>
<td>30</td>
</tr>
<tr>
<td>85</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>55</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>40</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>25</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

*Note.* Lower numbers indicate better stereo-acuity.

Figure 3.1. Mean Stereo Acuity (arc-seconds) for ME/CFS patients and control participants. Error bars are ± 1 SEM.
3.2.2. Contrast sensitivity

Contrast sensitivity is the measure of the amount of contrast an individual requires in order to distinguish a target. More specifically, spatial contrast refers to the light-dark change perimeter in an image, which differentiates the presence of an object or pattern, and its background (Owsley, 2003). Contrast sensitivity assessments can provide valuable information, by indicating a visual impairment which is not able to be detected through acuity measures. An example of this could be night time driving or driving at dusk, which requires good contrast sensitivity (Haymes, Roberts, Creuss et al, 2003; Hawkins, Szlyk, Ardickas, Alexander & Wilensky, 2003).

There is substantial literature indicating that contrast sensitivity can strongly predict ‘real-life’ performance, allowing awareness and further understanding into an individual’s disability and also quality of life (Haymes et al 2003). For example, a significant relationship has been found between contrast sensitivity and the following abilities: performing everyday activities (Haynes, Johnston & Heyes, 2002; West, Rubin & Broman, et al 2002), mobility and walking speed (Marron & Bailey, 1982), posture and stability (Lord & Menz, 2004), face recognition (Owsley & Sloane, 1987), driving ability (Owsley et al, 1998), computer task accuracy (Scott, Feuer & Jacko 2002) and notably, reading speed (Crossland, Culham & Rubin, 2005). Indeed, as previously discussed in Chapter 1, many of those with ME/CFS have stopped driving due to their visual symptoms (Potaznick & Kozol, 1992; Vedelago, 1997), and many also report problems relating to reading (Vedelago, 1997). Whether or not these reports can be explained by a reduced level of contrast sensitivity is unknown. The aim of this experiment was therefore to assess contrast sensitivity in patients with ME/CFS.

In the present study, contrast sensitivity was measured using the Pelli-Robson contrast sensitivity chart (Pelli & Robson, 1988). This test consists of uniform letter size, with a gradual reduction of contrast from 100% to just under 5%. The decrease in contrast sensitivity between each letter is 0.15 log units. The letters are grouped in triplets and each triplet letter group has the same contrast. The chart is read from left to right, and top to bottom. The contrast of each successive letter triplet group (from left to right, top to bottom) decreases by $1/\sqrt{2}$. Contrast thresholds are calculated as the lowest contrast for
which at least two letters in a group are correctly identified. Participants were asked to stand behind a 1 metre line facing the chart and asked to read out the letters from left to right starting from the top. Scoring was conducted by marking off any incorrectly read letters.

Figure 3.2 shows the mean contrast sensitivity for ME/CFS patients and controls. A paired samples t-test showed that there were no significant differences in contrast sensitivity between the two groups ($t(26) = 1.866, p = .073$).

![Figure 3.2 Mean Contrast sensitivity threshold (log contrast sensitivity) for ME/CFS patients and control participants. Error bars are ± 1 SEM.](image)

**2.3 Discussion**

The aim of this chapter was to evaluate basic visual functioning in ME/CFS. In summary, with the exception of crowded acuity, patients did not significantly differ from a control sample in their corrected contrast sensitivity or visual acuity. The finding that patients had a worse crowded acuity score may suggest that they are more affected by the crowding effect. The crowding phenomenon suggests that identifying singular letters is easier than identifying letters that are closely surrounded in the para-fovea by other letter optotypes which may cause interference (Bouma, 1970).

The initial findings reported here also suggest that ME/CFS patients have a poorer depth perception. This finding corroborates patients’ self-reports that they have problems perceiving depth (Potaznick & Kozol, 1992; Hutchinson et al, 2014). Overall, these findings
suggest that the visual problems ME/CFS patients’ report may be more indicative of
dysfunction in the cortical visual pathways, rather than in the eye. However, there is a need
for further investigation with more controlled visual psychophysical measures.
4. Vision related quality of life and self-reported reading difficulty

The vision related symptoms that ME/CFS patients experience are likely to impact everyday functioning. For example, ~ 25 % of patients report that they have stopped driving because of their visual symptoms (Potaznick & Kozol, 1992). Many also report that they find reading difficult (Vedelago, 1997). The purpose of this chapter is to assess the impact of ME/CFS on vision-related quality of life and to also specifically examine vision-related reading difficulties.

4.1. Introduction

‘Quality of Life’ is a term used to describe an individual’s overarching sense of well-being, incorporating features such as happiness and overall life satisfaction. More specifically, The World Health Organization defines ‘quality of life’ as “the individual’s perception of their position in life in the context of the culture and value system in which they live, and in relation to their goals, standards, expectations, and concerns” (WHO QOL, 1993). Quality of life is thus an important and informative measure of how an illness can impact an individual’s life both physically and psychosocially. It has also been regarded as arguably the most significant measure for evaluating the value of treatment, particularly for patients with long-lasting and/or incurable illnesses, and is key for prevention and support. (Lindholt, Ventegodt & Hanneberg, 2002; Adigun, Oluleye, Ladipo & Olowookere, 2014). Therefore, in relation to vision, quality of life measures can assess how an illness that has a number of associated visual symptoms, can affect an individual’s quality of life, emotionally, physically, and socially.

There is no doubt that vision is vastly important for daily functioning. Incapacitation arising from visual problems embodies a large scale social, emotional, and economic encumbrance for patients, families, and society. In many cases visual problems can affect several domains of an individual’s life by causing constraints in working environments, social activities, and in general everyday life. (For instance, impacting on driving habits, computer work, shopping.) A specific example of these effects can be demonstrated by Milijanovic,
Dana, Sullivan and Schaumberg (2007), who revealed that individuals with dry eye syndrome were more likely to report problems with driving (day and night), reading, using a computer, watching the television and carrying out professional work. Additionally visual acuity impairment, and even modest visual loss, has been related to deleterious effects on physical tasks such as driving, and also to vision-related declines in mental health. Individuals with glaucoma have also reported troubles with driving, tasks that involve peripheral vision, as well as a higher dependency on others due to visual problems (Broman, Munoz & Rodriguez et al, 2002). Consequently, it is feasible, that visual symptoms can cause a broad range of problems that go beyond the root cause. Effectively this could lead to, financial struggles by preventing working lifestyle, create isolation, increase feelings of anxiety, and overall impact the quality of the life that someone leads. (Adiguyn et al, 2014).

In relation to ME/CFS, many patients report an extensive number of visual problems (See Chapter 1, Section 1.3). They also report changes in their driving habits, with many reducing or stopping driving completely as a result of their visual symptoms (Potaznick & Kozol, 1992). This could impact a number of everyday activities; getting to work, visiting friends, or even simple matters such as going to the shops. Patients’ also report vision-related reading problems, such as the headaches when reading and difficulty tracking lines of print (Vedelago, 1997). Notably, reading is an important skill for daily functioning and is also significantly linked to quality of life (Hazel et al, 2000). Despite these findings, the extent to which the visual symptoms reported by ME/CFS patient’s affects their quality of life is yet to be established.

Establishing the impact on quality of life that visuals symptoms may have for patients with ME/CFS, may help identify target areas in which patient’s require further support or management. Therefore the aim of this chapter is to measure the vision-related quality of life of ME/CFS patients’ using the standardised National Eye Institute Vision-Related Quality of Life Scale. It was hypothesised that patients would have significantly lower vision-related quality of life scores compared to controls. Furthermore, given its relation to quality of life, the chapter aims to evaluate reading difficulties in patients with ME/CFS. It was expected that patients would report more problems with reading-related activities compared to controls.
4.2. Study 3. Vision-related quality of life

Methods and materials

Vision-related quality of life was assessed using the National Eye Institute 25-item Visual Function Questionnaire (VFQ-25) 2000 Version (See Appendix B. Item 1). The VFQ-25 is a product of an item-reduction analysis of the longer version of the 51 item National Eye Institute Vision Function Questionnaire. The VFQ-25 consists of 25 vision related questions that represent 11 vision related constructs, plus an additional single item general health rating question. It also includes an appendix of additional items from the 51 item version, expanding the total number of items to 39. The VFQ-25 generates the following vision subscales: general vision, difficulty with near vision activities, difficulty with distance vision activities, limitations in social functioning due to vision, role limitations due to vision, dependency on others due to vision, mental health symptoms due to vision, driving difficulties, limitations with peripheral vision, limitations due to colour vision, and ocular pain, plus an additional general health rating question.

Patients and controls were read instructions to complete the VFQ-25 questionnaire. Instructions were also printed on the inside of the questionnaire as some patients expressed that they wished to take the questionnaires home to fill out in their own time. In this case a pre-stamped and addressed envelope was given to the patient in order to return the questionnaire’s to the researcher when complete. The questionnaire took approximately 10 minutes to complete. All questionnaires were received.

All questions had numerical responses with each number generally representing a category on a scale. Scale ratings differed depending on the item and kind of question. (For full details of the numerical values and categories for each item, and to view the questionnaire, see Appendix B. Item 1). The majority of questions asked about difficulty with activities due to vision. Responses for these questions ranged from (1) no difficulty – (5) stopped because of eye sight, and (6) stopped because of other reasons. Other questions focused on ‘how often’ activities are affected due to vision. Responses for these questions ranged from (1) all of the time – (5) none of the time. Some questions also consisted of a number of visual statements with ratings of (1) definitely true – (5) definitely false, severity
based (1) no problem – (4) severe, asked questions with responses ranging from best and worst (0) – (10).

Scoring was conducted in a 2 step process. Firstly, numerical values from the questionnaire were re-coded in accordance with the scoring rules outlined in The NEI-VFQ-25 (2000) scoring instructions. All items were re-coded so that high scores represent better functioning. All items were then converted to a 0-100 scale, where lowest possible scores were set at 0 and highest possible scores at 100. This format therefore represents the attained percentage of total possible score (i.e. 50 represents 50% of the highest possible score). Secondly, the items within each sub-scale were averaged together to create 12 subscale scores. The overall composite score was then calculated by averaging the vision-targeted sub-scale scores (excluding the general health rating question/subscale). By averaging sub scale scores as opposed to individual items this allows for equal weight to be assigned to each subscale.

Results

General vision-related quality of life was determined by comparing VFQ-25 overall composite scores between patients and controls (Figure 4.1). Wilcoxon Signed-Ranks Tests showed that patients (median = 72.45) had significantly lower composite scores than controls (median = 94.772) (Z = -4.301; p<.001). Patients also had significantly lower scores on 10 out of the 12 VFQ-25 subscales (general health, general vision, ocular pain, near activities, distance activities, mental health, role difficulties, dependency, driving, peripheral vision). Social function and colour vision were unaffected (Table 4.1).

Figure 4.1. Mean VFQ composite scores for patients and controls. Error bars = ± 1SEM
Table 4.1.
Mean and median VR-QOL scores and Wilcoxon Signed-Ranks Test values for patients and controls. Values in parentheses beside means are ±1 SEM.

<table>
<thead>
<tr>
<th>Subscales</th>
<th>Patients</th>
<th>Controls</th>
<th>Wilcoxon Signed-Rank Z Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
<td>Mean</td>
</tr>
<tr>
<td>General health</td>
<td>13.89 (4.08)</td>
<td>0</td>
<td>75.93 (2.83)</td>
</tr>
<tr>
<td>General vision</td>
<td>66.67 (3.54)</td>
<td>60</td>
<td>84.44 (2.47)</td>
</tr>
<tr>
<td>Ocular pain</td>
<td>49.07 (4.85)</td>
<td>50</td>
<td>88.43 (2.98)</td>
</tr>
<tr>
<td>Short distance vision activities</td>
<td>66.05 (3.88)</td>
<td>62.5</td>
<td>91.98 (1.86)</td>
</tr>
<tr>
<td>Long distance vision activities</td>
<td>74.54 (3.85)</td>
<td>75</td>
<td>95.68 (1.12)</td>
</tr>
<tr>
<td>Social function</td>
<td>92.13 (2.51)</td>
<td>100</td>
<td>98.61 (1.02)</td>
</tr>
<tr>
<td>Mental health</td>
<td>66.44 (4.25)</td>
<td>62.5</td>
<td>91.90 (1.59)</td>
</tr>
<tr>
<td>Role difficulties</td>
<td>53.24 (6.10)</td>
<td>62.5</td>
<td>91.20 (2.74)</td>
</tr>
<tr>
<td>Dependence</td>
<td>82.10 (3.74)</td>
<td>91.667</td>
<td>99.69 (.31)</td>
</tr>
<tr>
<td>Driving</td>
<td>63.49 (5.82)</td>
<td>75</td>
<td>92.03 (2.06)</td>
</tr>
<tr>
<td>Colour vision</td>
<td>96.30 (1.74)</td>
<td>100</td>
<td>99.07 (.93)</td>
</tr>
<tr>
<td>Peripheral vision</td>
<td>75.00 (5.37)</td>
<td>75</td>
<td>97.22 (1.54)</td>
</tr>
</tbody>
</table>

Note. Higher values represent better functioning in the range 0-100. After Bonferroni correction for multiple comparisons, the alpha level required for a statistically significant difference between group was p<.004. *denotes a statistically significant difference between patients and controls at p<.001.

4.3. Study 4. Reading difficulty

Reading has been significantly linked to quality of life (West, Rubin, Broman, Munoz, Bandeen-Roch, & Turano, 2002; Friedman, Munoz, Rubin, West, Bandeen-Roche, & Fried, 1999; Hazel et al, 2000) and difficulties related to reading are commonly reported by ME/CFS patients (Potaznick & Kozol, 1992; Veledgo, 1997, Wearden & Appleby, 1997).

Method and materials

There is a paucity of standardised self-report measures of vision-related reading problems. To examine this issue in more detail, reading problems were assessed using a
reading scale questionnaire, previously developed by Hazel et al. (2000) to assess reading difficulty in macular disease.

The reading scale questionnaire comprises 15 items. All items asked the same question of ‘How much has your eyesight interfered with the ability to read with the following...’ (Dials, labels, coins, cheques, handwriting, forms, general reading, ordinary print, large print, small print, reading mail, medicine label, wristwatch, telephone, telephone directory). Each item had six possible answers, each of which were assigned a value on a Likert scale of (0) through to (5), where (0) indicated not at all; (1) hardly at all; (2) a little; (3) a fair amount; (4) a lot; (5) cannot do because of eyesight. Hazel et al (2000) revealed Cronbach α coefficient of .98, which was comparable to .97 demonstrated in the present research.

Results

A composite reading scale score was calculated by summing the scores for individual scale items (Figure 4.2). Wilcoxon Signed-Ranks Tests showed that patients (median = 18) had significantly higher composite reading scale scores than controls (median = 2) ($Z = -3.615; p < .001$). Patients also exhibited significantly higher scores for 7 of the 15 questions: reading coins, general reading, ordinary print, small print, reading mail, reading a wristwatch, and the telephone directory (Table 4.2).

*Figure 4.2. Mean RS composite scores for patients and controls. Error bars = ± 1 SEM*
Table 4.2.
Median reading scale scores and Wilcoxon Signed-Rank values for patients and controls.
*Note* ‘Question content’ on Table 2 refers to the question ‘How much has your eyesight interfered with reading the following item...’

<table>
<thead>
<tr>
<th>Scale items</th>
<th>Patients</th>
<th>Controls</th>
<th>Wilcoxon Signed-Rank Z Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dials</td>
<td>1</td>
<td>0</td>
<td>-2.826</td>
</tr>
<tr>
<td>Labels</td>
<td>2</td>
<td>0</td>
<td>-2.849</td>
</tr>
<tr>
<td>Coins</td>
<td>1</td>
<td>0</td>
<td>-3.011*</td>
</tr>
<tr>
<td>Cheques</td>
<td>0</td>
<td>0</td>
<td>-2.692</td>
</tr>
<tr>
<td>Handwriting</td>
<td>0</td>
<td>0</td>
<td>-2.676</td>
</tr>
<tr>
<td>Forms</td>
<td>1</td>
<td>0</td>
<td>-2.835</td>
</tr>
<tr>
<td>General reading</td>
<td>3</td>
<td>0</td>
<td>-3.508**</td>
</tr>
<tr>
<td>Ordinary Print</td>
<td>2</td>
<td>0</td>
<td>-3.519**</td>
</tr>
<tr>
<td>Large print</td>
<td>0</td>
<td>0</td>
<td>-2.699</td>
</tr>
<tr>
<td>Small print</td>
<td>3</td>
<td>1</td>
<td>-3.525**</td>
</tr>
<tr>
<td>Reading mail</td>
<td>1</td>
<td>0</td>
<td>-3.322**</td>
</tr>
<tr>
<td>Medicine label</td>
<td>2</td>
<td>0</td>
<td>-2.386</td>
</tr>
<tr>
<td>Wristwatch</td>
<td>1</td>
<td>0</td>
<td>-3.277**</td>
</tr>
<tr>
<td>Telephone</td>
<td>0</td>
<td>0</td>
<td>-2.627</td>
</tr>
<tr>
<td>Telephone directory</td>
<td>2</td>
<td>0</td>
<td>-3.109*</td>
</tr>
</tbody>
</table>

Note: Higher values represent more difficulty (in the range ‘0’ not at all to ‘5’ cannot do because of eyesight). After Bonferroni correction for multiple comparisons, the alpha level required for a statistically significant difference between groups was p<.003. * denotes a statistically significant difference between patients and controls at p<.003. ** denotes a statistically significant difference at p<.001.

4.3.1 Determining the relationship between reading scale and VFQ scores

Given that ME/CFS patients reported more visual problems related to reading than controls, and that reading is significantly related to quality of life (Hazel et al, 2000), the relationship between these two factors was explored. A Pearson Correlation was employed to test the relationship between overall vision-related quality of life (VFQ composite scores) and overall reading difficulty (reading scale composite scores) in the ME/CFS patient group. As expected, there was a strong negative correlation between the two factors \( r = -0.803, p < .001 \). For completeness, this analysis was also performed on control data. Once more, overall reading difficulty and vision-related quality of life were negatively correlated \( r = -0.660, p = <.001 \).

4.4 Discussion

The aim of this chapter was to establish the profile of vision-related quality of life in ME/CFS patients, and additionally, to examine self-reported reading difficulties in this
patient group. As expected, patients reported significantly lower overall vision-related quality of life scores compared to controls. Inspection of subscales revealed that patients also scored significantly lower for vision-related domains in general health, general vision, ocular pain, near activity, distance activity, mental health problems due to vision, role difficulties due to vision, dependency on others due to vision, driving, and peripheral vision. Patients’ and controls’ scores were comparable for social function and colour vision. These findings suggest that ME/CFS has a marked impact vision-related quality of life.

The particular discovery that patients scored significantly lower visual quality of life in relation to ‘driving’ supports Potaznick and Kozol’s (1992) finding that many patients’ report reducing or stopping driving due to their vision. However, the present research also builds on the literature in two ways. Firstly, it extends findings such as Potaznick and Kozol’s (1992) results, by suggesting that driving behaviors are not the only areas of life that are affected by patients’ visual symptoms. Instead the effects of their visual symptoms are much broader. Secondly, given that there is very little research into ME/CFS and vision problems, by establishing that visual symptoms impact the quality of life for ME/CFS sufferers, provides justification for research to consider studying further into this field, and highlights areas for further study. Furthermore, this also provides valuable information of where to target further support. ME/CFS is an incapacitating disorder, and in severe cases patients are bed bound, therefore any adjustments to improve quality of life are crucial.

Of particular importance, and relevance for the research presented in this thesis, one of the visual domains where patients reported significantly poorer quality of life was that of ‘near activities’. Although reading can take other forms, it is generally classified as a near activity. Moreover, in comparison to controls, patients reported a significantly higher overall reading difficulty score. Out of the fifteen sub scales (see Table 4.2), patients’ expressed significantly more difficulty compared to controls for reading coins, general reading, ordinary print, small print, reading mail, wristwatches, and the telephone directory. This suggests that ME/CFS has an impact on a number of forms of reading, and thus supports Vedelago (1997) that they find reading difficult. The findings also show that reading difficulty was significantly linked to visual quality of life for both patient and control groups, thus supporting Hazel et al, 2000).
However, caution should be conducted when interpreting the results from the reading scale questionnaire. One of the main limitations of the study is that the items on the reading scale questionnaire are not especially clear. For example, the item concerning ‘small print’ could correspond to other items such as ‘medicine labels’ or ‘mail’, and therefore, perhaps causing difficulty or confusion in completing the questionnaire. However, there appears to be a lack of standardized reading scales available within this research field. The reading scale used in the present study was used primarily as a starting point and serves as an initial indicator. It is therefore suggested that there is a need for a robust standardized reading scale to be developed, and utilized in future studies.

In summary, the study does reveal some notable findings. ME/CFS patients reported a poorer visual quality of life than the control group. Therefore, these results extend on the previous literature (that they experience visual symptoms) by demonstrating the broader detrimental effects of their visual problems, thus indicating the importance of further researching this field. Future research could consider the findings when developing methods to improve vision for patients with ME/CFS, in order to ensure that target problem areas are addressed. The present research also reveals that patients’ experience significantly more reading difficulties compared to controls, and supports Hazel et al’s (2000) finding that reading is related to visual quality of life. Further research is warranted with more direct objective measures to assess reading difficulty in patients with ME/CFS in order to provide robust evidence to back up these reports, and to help understand the precise nature of their reading problems.
5. Reading performance

Many of the vision-related complaints reported by ME/CFS patients involve difficulties relating to reading. Reports include headaches during reading, blurred vision, increased fatigue, and problems concentrating. Patients also report difficulty tracking lines of print, stating that they become confused and distracted by lines above and below the one being read (Potaznick & Kozol, 1992; Vedelago, 1997, Wearden & Appleby, 1997).

5.1. Introduction

The ability to read is a key feature of visual function. In our present ‘information-based’ culture, the ability to read is an essential skill in daily living, playing a central part in work and everyday activities. Therefore, as previously discussed in Chapter 4, difficulties with reading may have a significant effect on quality of life (West et al, 2002; Freidman, Muniz, Rubin et al, 1999; Hazel et al, 2000). However, despite a number of vision related symptoms reported during reading, information regarding reading performance for ME/CFS patients is non-existent.

Reading is a complicated process entailing highly specialised eye movements and cortical visual functioning. General visual acuity assessments are not adequate for predicting reading ability (Maaijwee, Mulder, Radner & Meurs, 2008). Therefore it may not be so surprising, that, despite reporting problems with their reading, ME/CFS patients have shown no significant general visual acuity impairment (Potaznick & Kozol, 1992; Hutchinson & Badham, 2012; Badham & Hutchinson, 2013). Reading performance assessments, however, are instead required for a clinical examination of reading function, and offer a more thorough evaluation and informative measure of visual problems relating to reading (Burggraaff, Nispen, Hoek, Knol & van Rens, 2010).

Reading performance charts such as The Minnesota Reading Acuity Chart (MNREAD) (Mansfield & Legge, 2007) and Radner Rate of Reading charts (Radner, 2008), provide a direct and reliable measurement of reading ability in normal and in visually impaired individuals (Maaijwee, Mulder, Radner & Meurs, 2008). Both charts consist of short sentences, but hold different principles of test item standardisation. For example, the MN READ acuity chart contains sentences similar in number of lines and characters, but does not
control for word length or position. However, since sentence complexity can affect reading speed, Radner Rate of Reading Charts were developed on the importance of standardisation and the concept of sentence ‘optotypes’ to ensure standardised examination. These sentences have been developed in order to keep geometric proportions as constant as possible and are thus comparable in terms of word length, number of syllables, position of words, syntactical complexity, and lexical difficulty (Radner, 2008; Rader & Diendorfer, 2014). This utilization of high standardisation may be an advantage over the MN READ charts.

MN Read acuity charts are however, regularly used in clinical practice and have been used to reliably evaluate reading ability in a number of vision-related conditions such as glaucoma (Ishii, Seki, Harigai, Abe & Fukuchi, 2013) retinitis pigmentose (Virgili, Pierrottet, Parmeggiani, & Pennino, 2004), and age related macular degeneration (Patel, Chen, Cruz, Rubin & Tufail, 2011). Similarly, Radner Rate of Reading Charts have also been used in the in clinical assessment of reading performance of low vision patients (Burggraaff, Nispen, Hoek, Knol & van Rens, 2010).

Many ME/CFS patients complain of difficulties related to reading. Examples include, increased fatigue, headaches during reading, and difficulty tracking lines of print (Potaznick & Kozol, 1992; Veledgo, 1997). However no study to date has examined the reading performance of ME/CFS patients. Therefore, the aim of the experiments outlined this chapter was to directly explore, and objectively evaluate, reading performance in patients with ME/CFS.

5.2 Study 5. Reading performance charts

Methods and Materials

Both the MN Read acuity and Radner Rate of Reading charts measure a number of factors relating to reading performance. Reading performance is expressed in terms of reading acuity, critical point size and reading rate. Reading rate that is not restricted by print

2 Note. 1 patient (and the paired control) was excluded from the following experiments due to feelings of exhaustion.
size and is stable throughout a large range of print sizes is termed the maximum reading speed (MRS). When print size decreases, the point at which reading speed starts to slow down, often as a sharp demarcation, is known as the critical print size (CPS), which is essentially the smallest print size at which patients can read with their optimal speed. This is important as it indicates the minimum magnification required for effortless reading. Finally the smallest print size, where some words can still just be read, is termed reading acuity (RA). MN Read acuity charts allow for the measurement of all of the above objective reading parameters simultaneously. Similarly, Radner Rate of Reading charts also provide values for all of the above measures, plus an extra measure of average of reading speed.

Inclusion based on Vocabulary

As an initial control to ensure that reading performance was not influenced by any limitations of vocabulary, the WAIS (Weschler Adult Intelligence Scale) IV vocabulary test (WAIS IV, Wescher © 2008 NCS Pearson Inc) was administered prior to all reading tasks. This provides a standard measure of vocabulary. As expected, there was also no significant difference between patients’ ($M = 48$) and controls’ ($M = 48.89$) vocabulary scores ($t(52) = .462, p = .646$).

5.2.1. MN Read acuity chart

The MN Read acuity chart (MN READ © 2012 The Research Foundation of SUNY, University of Minnesota) was used to assess reading performance. Participants were read out loud instructions to read each sentence on the chart aloud as quickly and as accurately as possible. The MN Read acuity chart was then positioned at 40cm from the participants’ eye line. A stopwatch was used to measure the time it took to read each sentence which was noted down, along with any mistakes. Participants were encouraged to read until they could not see any of the words. Participants read the chart binocularly and care was taken to ensure that the chart was evenly illuminated so that no glare would interfere with reading.

The chart consists of sentences of nineteen differing print sizes. The recommended viewing distance is 40cm, giving the print sizes a range from $1.3$ to $-0.5$ logMAR. Every sentence (from the top to the bottom of the chart) decreases in size by 0.1 logMAR units. The design
of the sentences provide reading material that is able to mandate the necessary visual processing capabilities and eye movement control required for normal text reading. Every sentence consists of 60 characters, including spaces between words, and is printed on 3 lines which are evenly margined. The vocabulary chosen was words frequently used in second and third grade reading material (US), which is comparable to Key stage 1 Years 3 and 4 (ages 7 – 9) in the UK (The Good School Guide. International, UK* - US Education Comparison Chart). The font is proportionately spaced and is comparable to print in newspapers and books (approximately 8 % contrast) An example can be seen in Figure 5.1.

![Figure 5.1](image)

**Figure 5.1.** Sentence examples for MN Read Acuity chart.

The MN read Chart yields 3 measures of reading performance: reading acuity, critical print size, and maximum reading speed. These were calculated in accordance with the MN READ acuity chart © 1994 instructions.

Reading acuity (in logMAR) was calculated as the smallest print size at which the participant could read without significant errors, using the equation as follows:

\[
Acuity = 1.4 - \text{sentences} \times 0.1 + \text{(number of errors} \times 0.01).
\]
Reading speed was expressed as words per minute (wpm) which was calculated for each print size. As each sentence had 10 standard length words, reading speed was calculated as follows:

\[
\text{Reading speed} = (10 - \text{no. errors}) \times 60 / \text{time in seconds}.
\]

Maximum reading speed can then be identified as the reading speed when performance is not limited by print size. The critical print size (CPS) can then be identified as the smallest print size at which patients can read with their optimal speed.

The MN Read acuity chart provides a plotting paper with a graph enabling these measures to be calculated quickly. MN read acuity chart instructions state that it is not necessary to calculate reading speed for sentences if this plotting paper is used. For this experiment, in accordance with the manufacture instructions, the plotting paper was used (See Figure 3.2 below for example). The scale on the horizontal axis refers to reading time and corresponds to reading speed, also present on the graph. The vertical scale is the logMAR print size. This also makes it easy to identify the CPS, as when reading speed is plotted on the graph, the print size where reading speed suddenly declines in a steep slope can clearly be seen.

![Figure 5.2 Example of plotting paper taken from MN Read Acuity Chart instructions (1994).](image)

5.2.2. Radner Rate of Reading Chart
The Radner Rate of Reading Charts © Radner (2009) consists of three charts allowing for monocular and binocular testing in a randomised order with minimal order effects. Stifter et al (2004) demonstrates that all three charts have high inter-chart reliability, indicating equality, and state that clinical results attained with different Radner reading charts are comparable and unaffected by the choice of chart. Each chart contains 14 sentences, each containing 14 words, with print sizes ranging from 1.1 to -0.2 logRAD (reading equivalent of logMAR), when viewed from the recommended distance of 40cm. An example of the sentences is shown in Figure 3.

![Example of Radner Rate of Reading Chart sentences](image)

**Figure 5.3** Example of Radner Rate of Reading Chart sentences

Similar to the MN Read acuity chart, the Radner Rate of Reading charts were presented at 40cm, which was verified with a tape measure throughout for consistency, and only viewed binocularly. Participants were verbally instructed to uncover each sentence one at a time and read the sentence out loud as quickly and as accurately as possible. Participants were also informed to read sentences in full before correcting any errors. A stopwatch was used to measure the time it took to read each sentence, which was noted down along with any reading errors. Participants were encouraged to read until they could not see any of the words.
Measurements for reading acuity, mean and maximum reading speed, and critical print size were calculated in accordance with the instructions printed on the Rader Rate of Reading Chart © Radner (2009).

Reading acuity was measured in logRAD, the reading equivalent for logMAR. Reading errors were marked on the form and errors were counted, even if corrected, and were included when calculating the logRAD score as follows:

\[ \text{LogRAD Score} = \text{LogMAR of last sentence read} + (0.005 \times \text{no. of syllables of the incorrectly read words}) \]

Similar to the MN Read Acuity Charts, reading time was measured with a stop watch. The reading speed was calculated in terms of words per minute (wpm) as using the following equation:

\[ (14 - \text{Number of any incorrect/missed words}) \times 60 = \text{time in seconds.} \]

The maximum reading speed (MRS) was then defined as the greatest number of words per minute calculated for a sentence. The critical print size (CPS) could then be identified as the smallest print size the patients read with their optimal reading speed.

The average reading speed was the mean reading speed (wpm) of all sentences that had been read, calculated as follows:

\[ \frac{\text{Sum of all reading rates of each sentence read}}{\text{number of sentences read}} \]

**Results**

All descriptive data are presented in Table 5.1 (next page).
Table 5.1
Reading performance scores for ME/CFS patients and controls. Mean scores for reading acuity (RA), critical point size (CPS) and maximum reading speed (Max RS) as determined by MN READ Acuity chart and Radner Rate of Reading Chart. Mean reading speed (Mean RS) is also given for the Radner Rate of Reading Chart. Values in parentheses are ± 1 SEM.

<table>
<thead>
<tr>
<th></th>
<th>MN READ Acuity Chart</th>
<th>Radner Rate of Reading Chart</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>CPS</td>
<td>Max RS</td>
</tr>
<tr>
<td>Patients</td>
<td>-.04 (.03)</td>
<td>.04 (.03)</td>
</tr>
<tr>
<td>Controls</td>
<td>-.07 (.02)</td>
<td>.05 (.02)</td>
</tr>
</tbody>
</table>

Note. RA and CPS are expressed in logMAR (MNRead)/logRAD (Radner). Reading speed measures are in words per minute (wpm).

For reading acuity, there were no significant differences in reading acuity between patients and controls. This was the case for the MN READ acuity chart (t(26) = -.950, p = .351) and Radner Rate of Reading Chart (t(26) = -1.60, p = .122). Critical point size was also found to be similar in patients and controls (MN Read acuity chart: t(26) = -.238, p = .814; Radner Rate of Reading Test: t(26) = .296, p = .769). However, there was a significant difference between patients’ and controls’ maximum reading speed with the MN Read acuity chart, where patients were significantly slower compared to controls (t(26) = -2.570, p < .05). No significant differences between patients and controls was found for maximum reading speed using the Radner Rate of Reading Test, (t(26) = -1.178, p = .249). There was however, was a significant difference between patients and controls mean reading speed during the Radner rate of reading test (t(26) = -.2.125, p < .05), where again, patients exhibited a slower reading speed (see Figure 5.4).

![Figure 5.4](image-url) Reading speed across Radner Rate of Reading Charts and MN Read acuity Chart. Error bars = ± SEM.
5.3. Discussion

The findings from the studies outlined in Chapter 5 revealed that, although ME/CFS does not appear to affect reading acuity or critical point size, it may deleteriously affect reading speed. Patients exhibited a significantly slower maximum reading speeds compared to controls during reading the MN Read Acuity Chart. Additionally, during the Radner Rate of Reading Test, although their maximum reading speed was comparable to controls, patients’ mean reading speed was also significantly slower. These initial results perhaps indicate that patients read more slowly than controls. Differences in reading speed, as opposed to reading acuity, may suggest that patients could be using a different reading strategy. Indeed, it is well established that other population groups who are known to read much more slowly (such as the elderly) are thought to adopt a riskier reading strategy than their younger counterparts (Rayner, Reichle, Stroud et al, 2006). However, based on findings from Chapter 2, it is also acknowledged that slower reading may also be a factor of poorer crowded acuity.

Although patients did read more slowly for all three reading speed measures, this was only significant for two out of the three measures. These initial results perhaps indicate the need for further testing with a more controlled, objective, and specialised methodology to provide a greater insight. Differences in the tests themselves could have also had an impact. For example, the Radner Rate of Reading test employs highly standardised sentence optotypes, whereas sentences in the MN Read acuity chart are less well controlled. Indeed, Maajawee et al (2008) compared results obtained with the Rander Rate of Reading Charts, and, results acquired from MN Read acuity charts. Significant differences across all reading measures between the two tests were found. Maajawee et al (2008) concluded that such differences are most likely to be related to the use of sentence optotypes in the Radner test, or maybe even the use of different fonts (i.e. the Radner Charts use Ariel, a sans-serif font, whereas the MN Read acuity charts use Times New Roman, a serif font). However, reading differences between fonts are small, and are usually only found in low vision individuals (Mansfield, Legge & Bane, 1996).

Overall, the present findings suggest that vision-related reading difficulty reported by ME/CFS patients is not understood in terms of a poorer reading acuity or critical point
size. Instead differences in reading speed perhaps indicate that patients may be using a
different reading strategy. However, in consideration of the differences between both the
MN Read Acuity and Radner Rate of Reading Charts (e.g. standardisation), and as the
findings were not replicated across all measures, a better controlled and objective
investigation is warranted to explore further.
6. Eye tracking experiments

Experiments in Chapter 3 and 5 suggest that the reading difficulty reported by ME/CFS patients is unlikely to be attributable to a poorer visual acuity, contrast sensitivity, or reading acuity. Rather, patients’ may be using a different reading strategy based on findings of a slower reading rate compared to controls. This chapter uses eye-tracking techniques to explore this further by examining eye-movements during reading.

6.1 Introduction

Reading is a complicated process involving visual, cognitive, and ocular motor processes, as well as attentional influences. Essentially, visual information is obtained during fixations and is influenced by visual parameters such as print size, blur and the size of the perceptual span (the region of effective vision). Once brought into view, words can be identified, decoded, and semantically constructed within working memory. Careful ocular motor programming and eye movements (saccades which bring the material into foveal view) then select the next place of fixation on the text. Eye movements, however, are also modulated by linguistic characteristics of words, which can influence ocular motor programming and thus affect where the eyes land and how long for (Rayner, 1978; 1998).

Abnormalities in ocular motor control have already been demonstrated in patients with ME/CFS during non-reading tasks (Badham & Hutchinson, 2013). However, whether or not eye movement dysfunction is also experienced during reading remains to be explored in this patient group. Therefore, the first aim of this chapter was to determine whether a range of eye movement variables of skilled reading differ between ME/CFS patients and controls. Further to this, this chapter will also evaluate saccade targeting by manipulating word frequency which is also an index of linguistic processing. This will be done by using the Word Frequency Effect (the contention that we skip frequently used words and fixate longer on unusual words). Finally, this chapter will determine the size of the perceptual span in ME/CFS patients.³

³ Four patients were excluded from the experiments outlined below due to calibration difficulties, high levels of fatigue and visual distortion. One outlier was also identified within the control sample; as such this subject (and matched patient) was excluded from the analyses of all experiments presented in this chapter. This left a
6.2 Study 6. Ocular motor control, linguistic processing and saccade accuracy

Experiment 1 is split into 2 separate analyses (Section 6.2.1 and 6.2.2). As will be discussed below, the experiment presented normal sentences with some words manipulated as either frequent words or infrequent words. This allowed for the examination of eye movements for both global sentence-level analyses, and local analyses of target words.

6.2.1. Ocular motor control in sentence level analyses

Eye movements in reading involve the programming of a series of well-planned high velocity eye movements. As previously discussed, Badham and Hutchinson (2013) have revealed impaired saccadic function in ME/CFS patients during non-reading tasks. Therefore to examine whether saccadic function was also impaired during reading, a range of eye movement variables were compared between patients and controls. It is well documented that eye movements during reading are conducted through a series of fixations and saccades (consisting of forward progressions and regressions). Therefore, the aim here was to determine whether there are differences in saccade amplitude, number of saccades, fixation duration, number of fixations and reading time, during reading between ME CFS patients and matched controls.

Method and Materials

Text materials consisted of 168 syntactically simple sentences. See Figure 6.1 for sentence examples.

The police closed off the dangerous catacomb yesterday.
Paul asked whether the autopsy would take a long time.
Beth wanted to study zoology at a college in Canada.
John was able to repair the broken trellis very quickly.
We tried to get the celebrity’s attention but we could not.
I told Betty about the long argument that I had last week.
Clive hates studying science because he finds it very hard.
Sara rushed her husband to the doctor after he hurt himself.

Figure 6.1 Sentence examples from experiment 1.

total of forty four (22 ME/CFS patients and 22 matched control subjects participating in the experiments. All participants were native English speakers.
**Apparatus**

Eye movements were recorded with an EyeLink 1000 desktop mounted system with a sampling rate of 1kHz, spatial resolution of 0.01°, and a mean accuracy of 0.25°. (SR-Research, Mississauga, Ontario, Canada). Although viewing was binocular, eye movements were recorded from the right eye only. Eye movements were calibrated at the start of the experiment using a 3 point horizontal line, covering to the length of the longest sentence, to ensure that the degree of error was less than 0.3 degrees. A drift correction point/calibration check was also presented before the onset of each sentence trial covering the same sentence area to ensure tracking accuracy. Head movements were minimised by padded chin and head rests. Sentences were presented on a 19 inch monitor with a screen resolution of (1078 x 786 screen pixels). Viewing distance was 80 cm and all sentences were displayed on a single line in a black Courier font, on a white background.

**Procedure**

Participants were instructed to read normally, silently to themselves, and for comprehension. The onset of each trail was initiated by fixating on a small gaze contingent cross located at the start of the first word of each sentence. The experiment was split into 2 halves, each with 84 sentence trials. To become familiarised with the task, participants first read 4 practice sentences at the beginning of each half of the experiment. They then read a further 80 sentences within each part, totalling to 8 practice trials and 160 study trials. Participants pressed a button on a controller pad after reading each sentence. To ensure that participants maintained attention while reading, evenly distributed simple yes/no comprehension questions appeared after ~ 30% of the experimental trials, to which the participant responded with a button press. An example of the comprehension questions that were asked are presented in Figure 6.2. In total the experiment took around 30-40 minutes.

**Figure 6.2.** Example of comprehension question.
Data Analyses

Fixations shorter than 80ms and longer than 1200ms were eliminated from the analyses, and practice trials (sentences 1 – 4) were also removed.

Results and discussion

Descriptive data is presented below in Table 6.1.

Table 6.1.
Means for reading measures in sentence level analyses. Values in parentheses are ± SEM.

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading time</td>
<td>2413.72 (145.36)</td>
<td>2387.11 (160.65)</td>
</tr>
<tr>
<td>Average fixation duration</td>
<td>222.07 (4.05)</td>
<td>222.47 (5.58)</td>
</tr>
<tr>
<td>Fixation count</td>
<td>11.78 (0.47)</td>
<td>11.55 (0.44)</td>
</tr>
<tr>
<td>Progressions count</td>
<td>7.33 (0.32)</td>
<td>7.27 (0.28)</td>
</tr>
<tr>
<td>Regressions count</td>
<td>3.51 (0.22)</td>
<td>3.40 (0.22)</td>
</tr>
<tr>
<td>Saccade amp</td>
<td>2.85 (.09)</td>
<td>2.85 (.09)</td>
</tr>
<tr>
<td>Regression amp</td>
<td>4.01 (.13)</td>
<td>3.94 (.13)</td>
</tr>
<tr>
<td>Progression amp</td>
<td>2.53 (.10)</td>
<td>2.55 (.09)</td>
</tr>
</tbody>
</table>

Note. Reading time and average fixation duration (milliseconds); saccade amp, regression amp and progression amp are in degrees.

Comprehension accuracy was above 90% for both patients and controls. Paired t-test analyses showed no significant differences between patients and controls in their reading time \((t(21) = .123, p = .903)\), number of fixations \((t(21) = .353, p = .728)\), average fixation duration \((t(21) = .055, p = .956)\), saccade amplitude \((t(21) = .013, p = .990)\), number of regressions \((t(21) = .560, p = .581)\) or progressions \((t(21) = .130, p = .898)\), regression amplitude \((t(21) = .353, p = .727)\) or progression amplitude \((t(21) = .119, p = .907)\).

The above results suggest that patients and controls executed similar basic eye movement control during reading. This therefore demonstrated clear, objective, evidence that eye movement control during reading is not impaired in ME/CFS, and therefore, the reading discomfort that they report is unlikely to be due to factors relating to anomalous ocular motor control. This indicates that eye movements during reading are of a different sort compared to those required tasks conducted in Badham and Hutchinson (2013), which
may not be reflective of the saccadic function necessary in reading. For example, the discrepancy of results between Badham and Hutchinson’s (2013) study and the present findings, could be as eye movements during reading are extremely specialised which are also subject to influences that are present during reading, (but not in Badham & Hutchinson, 2013), such as linguistic variables of the text. Eye movements in reading are also much smaller than those measured in Badham and Hutchinson (2013) which required patients to produce eye movements from the middle to the outside of a computer screen, predominantly demonstrating impaired anti-saccades than prosaccades.

However one particular surprising finding is that patients did not show a difference in reading time, indicating that they read at a comparable speed to the control group. This result is therefore not in agreement with results found in Chapter 5, which indicated that ME/CFS patients read at a slower rate. There are a number of possibilities for this discrepancy of results. It is important to consider the differences between the tests themselves. For example, the reading performance charts present a passage-like text over 3 lines. However text material used during the eye tracking experiments was presented on a single line. This may be particularly noteworthy given the results in Chapter 3 Study 1 that crowded acuity was significantly worse for patients compared to controls. Other differences include the distance of which the sentences were presented. The reading performance charts were presented at 40cm, whereas sentences on the computer screen during the eye tracking experiments was viewed at 80cm. This may be significant in relation to vergence influences when considering previous experimental findings of vergence anomalies in CFS (Mastopasqua et al, 2000). Another possibility could be related to the experimental conditions. During the eye tracking experiments, participants were positioned in a chin and head rest, in a dimly lit room, with the computer for the main source of light, and asked to remain still. This may have been particularly challenging for patients due to muscular symptoms associated with their condition. Moreover, since photophobia is a frequently reported symptom of ME/CFS, the bright light projecting from the computer screen may have caused sensitivity and discomfort. Taken together, these conditions may have resulted in patients perhaps wanting to complete the experiment quicker, and thus may have read at a slightly quicker pace than those experienced during the reading performance charts.

Experiments using reading performance charts were completed in an evenly lit room and
although participants were positioned 40cm away from the chart they were much less restricted in movement.

It should also perhaps be noted that reading time only consisted of the time when patients were engaged in the experiment, and did not account for, number of, and length of breaks. During the eye tracking experiments patients did receive considerably more and longer breaks, although precise data for this was not recorded. It should also be considered that reading itself was conducted in a different way between the two investigative methods (reading performance charts and eye tracking experiments). For example, the reading performance charts required participants to read every word in a sentence, out loud, as quickly and as accurately as possible. However, during the eye tracking experiments, reading was conducted silently, and so patients and controls may have skipped words. A future recommendation could be to repeat the eye tracking experiment, but ask patients to read out loud. This would enable one to determine if participants correctly recognised the word (although there may be some difficulty in terms of calibration with more head movements).

Overall, the findings here suggest that ocular motor control is unlikely to be factor affecting vision-related reading discomfort in patients with ME/CFS. Patients also read at a comparable speed to the control sample. It is therefore important to consider other factors within the reading process.

6.2.2 Linguistic processing and saccade accuracy

Reading is a skill that requires mental effort and concentration, and at the very core of why we read is the ability to process language. It is now well accounted for in many reading models (e.g. The EZ Reader Model) that cognitive processes can influence when and where the eyes move. For example, as activation of meaning is essential to the reading process, the judgment to conduct an eye movement is influenced by lexical access (a process of orthographic and phonological word identification in order to retrieve semantic information) (Rayner, 1998). Evidence for the influence of linguistic variables on eye movements can be demonstrated through the word frequency effect: a robust finding that in skilled readers, longer fixations are spent on infrequent words compared to frequent words, and that frequent words are more likely to be skipped. Therefore this also allows for a measure of accuracy of saccade targeting during reading.
Whether or not language processing is affected as a result of the visual problems patients report is not known. Although patients do not explicitly report problems in language processing, they do report increased mental effort and lose place in the text, and have to reread text (Wearden & Appleby, 1997; Vedelago, 1997). Examining linguistic processing in reading may be of further interest considering that cognitive deficits are a common feature of ME/CFS, and many report substantially increased mental effort and concentration in completing simple tasks, notably reading (Wearden & Appleby, 1997). The word frequency effect was therefore examined in patients and controls by conducting local analyses on infrequent and frequent words.

**Method and materials**

All apparatus, procedures, data analyses, and materials utilised was the same as section 6.2.1. The critical words were a) infrequent and b) frequent. Figure 6.3 presents examples of the critical words (frequent and infrequent) used within the sentences. Out of the 80 study sentence trials, 40 contained a frequent critical word, and 40 contained an infrequent critical word. These 2 conditions (frequent and infrequent) were manipulated within the 2 groups of participants, (ME/CFS patients and controls), in order to examine any differences in the word frequency effect across both groups.

1. The police closed off the dangerous *catacomb* yesterday.
2. Paul asked whether the *autopsy* would take a long time.
3. Beth wanted to study *zoology* at a college in Canada.
4. John was able to repair the broken *trellis* very quickly.
5. We tried to get the *celebrity’s* attention but we could not.
6. I told Betty about the long *argument* that I had last week.
7. Clive hates studying *science* because he finds it very hard.
8. Sara rushed her husband to the *doctor* after he hurt himself.

**Figure 6.3.** Examples of high and low frequency words. Critical words are in italics and underlined. Sentences 1-4 represent infrequent words and 5-8 frequent words.

**Results and discussion**

The influence of word frequency on saccadic programming for ME/CFS patients and controls was assessed by examining: fixation durations on the critical word, skipping rate of
the critical word, and regressions into, and out of, the critical word. A mixed between-within measures analysis of variance (ANOVA) was conducted across both conditions (frequent and infrequent word) for both groups (ME/CFS and control). Figure 6.4 shows mean reading time measures for the critical word.

![Figure 6.4](image)

**Figure 6.4.** Mean reading times on the critical word for each condition (frequent and infrequent word) across groups (ME/CFS patients and controls). Error bars = ± SEM. Note. All values represent milliseconds. Standard errors are shown in parentheses. **First fixation duration** refers to the duration of the first fixation on the target word; **single fixation duration** refers to cases where only a single fixation is made on the target word; and **gaze duration** refers to the sum of all fixations on a word prior to moving to another word. **Total time** refers to total fixation duration.
There was a significant main effect of word frequency condition \( (F(1, 42) = 20.547, p < .001, \text{partial } \eta^2 = .339) \) on first fixation duration of critical word, but no main effect of group \( (F(1, 42) = 1.189, p = .282, \text{partial } \eta^2 = .028) \). There was however, a marginally significant interaction between group and the word frequency condition, \( (F(1, 42) = 3.801, p = .058, \text{partial } \eta^2 = .083) \). There was also significant main effect of word frequency condition \( (F(1, 42) = 16.453, p < .001, \text{partial } \eta^2 = .281) \) on single fixation duration of the critical word, but again no main effect of group \( (F(1, 42) = 1.080, p = .305, \text{partial } \eta^2 = .025) \). However, similarly, there was a significant interaction between group and the word frequency condition \( (F(1, 42) = 5.558, p < .05, \text{partial } \eta^2 = .117) \). Specifically, although for both patients and controls’ the duration of first and single fixations increased for infrequent words, this increase was more pronounced for controls, suggesting controls were more influenced by the word frequency condition on cases for first and single fixations on the critical word than patients, who appeared to be less affected.

There was a significant main effect of word frequency condition \( (F(1, 42) = 53.502, p < .001, \text{partial } \eta^2 = .560) \) on gaze duration of the critical word. However there was no main effect of group \( (F(1, 42) = 2.177, p = .148, \text{partial } \eta^2 = .049) \), nor was there an interaction effect \( (F(1, 42) = .756, p = .390, \text{partial } \eta^2 = .018) \). Again, there was a significant main effect of word frequency condition \( (F(1, 42) = 42.705, p < .001, \text{partial } \eta^2 = .504) \) on total reading time. However there was no main effect of group \( (F(1, 42) = 2.177, p = .148, \text{partial } \eta^2 = .049) \), nor was there an interaction effect \( (F(1, 42) = .018, p = .895, \text{partial } \eta^2 = .000) \).

Table 6.2 shows skipping rate for the critical word for each condition across groups.

<table>
<thead>
<tr>
<th>Reading measure</th>
<th>Frequent Patients</th>
<th>Frequent Controls</th>
<th>Infrequent Patients</th>
<th>Infrequent Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skip</td>
<td>.32 (.02)</td>
<td>.29 (.03)</td>
<td>.32 (.02)</td>
<td>.29 (.03)</td>
</tr>
</tbody>
</table>

Note. Values represent probabilities.

There was no significant main effect for word frequency condition \( (F(1, 42) = .153, p < .698, \text{partial } \eta^2 = .004) \), with all participants showing a similar probability of skipping high
and low frequency words. There was also no main effect of group, thus skipping probabilities did not differ between patients and controls ($F(1, 42) = .961, p = .333$, partial $\eta^2 = .022$). There was also no interaction between group and word frequency condition ($F(1, 42) = .213, p = .727$, partial $\eta^2 = .003$), suggesting that patients and controls displayed the same skipping rate across both high and low frequency word conditions.

Regression rates out of and into the critical word are presented in Table 6.3.

**Table 6.3**
Regression rate ‘into’ and ‘from’ of the critical word. Values in parentheses are $\pm$ SEM

<table>
<thead>
<tr>
<th>Reading measure</th>
<th>Frequent Patients</th>
<th>Frequent Controls</th>
<th>Infrequent Patients</th>
<th>Infrequent Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression ‘into’</td>
<td>.19 (.02)</td>
<td>.17 (.02)</td>
<td>.17 (.02)</td>
<td>.15 (.02)</td>
</tr>
<tr>
<td>Regression ‘from’</td>
<td>.41 (.02)</td>
<td>.38 (.02)</td>
<td>.41 (.02)</td>
<td>.36 (.02)</td>
</tr>
</tbody>
</table>

*Note.* Values represent probabilities.

There was no main effect of condition for regressions *into* the critical word ($F(1, 42) = 3.373, p = .073$, partial $\eta^2 = .086$). There was also no significant main effect of group ($F(1, 42) = .537, p = .468$, partial $\eta^2 = .013$) nor was there an interaction between group and word frequency condition ($F(1, 42) = .032, p = .858$, partial $\eta^2 = .001$), indicating that both groups showed similar regressions into the target word across both conditions. There was also no significant main effect of condition for regressions *out of* the critical word ($F(1, 42) = 1.226, p = .267$, partial $\eta^2 = .029$), suggesting that the condition had no effect on the number of regressions out of the target word. However there was a marginally significant main effect when comparing the two groups; ME/CFS and control group ($F(1, 42) = 3.875, p = .056$, partial $\eta^2 = .084$). There was no significant interaction effect between group and word frequency condition ($F(1, 42) = .144, p = .706$, partial $\eta^2 = .003$).

The word frequency effect is a robust finding that for skilled readers fixation duration is longer on infrequent words, and that the probability of skipping infrequent words is lower. There was no difference between patients’ and controls’ probability of skipping the critical word across both word frequency conditions, implying that there really is no indication of a difference in their saccadic accuracy.
For reading time measures, both patients and controls produced a similar pattern of increasing the duration of their fixations on infrequent words. However, during cases when only a single fixation was made on the critical word this effect was much larger for controls, whose increase in duration for infrequent words was much more pronounced than was for ME/CFS patients. This may suggest that for cases of single fixations on the critical word, the control group were more influenced by the word frequency condition than patients, who appear to be less affected. In a similar fashion, this also was the case (although very marginally) for initial fixations on the target word.

These findings could reflect a number of possibilities. It has been suggested that less frequency effects occur during less careful reading where comprehension is less engaged, or during mindless reading (Reichle, Reineberg & Schooler, 2010; Schad, Nuthmann, & Engbert, 2012). Whereas larger frequency effects have been demonstrated in more careful reading strategies (Radach, Huestegge & Reilly 2008; Whitford & Titone, 2014). However comprehension accuracy was high for patients, and also comparable to controls, thus this is an unlikely explanation. Less frequency effects have also been proposed to occur during skimmed reading (Just & Carpenter, 1987). However sentence level analyses show that although not significant, patients in fact read more slowly than the controls group.

It is perhaps unlikely that such effects are a result of the visual or ocular problems reported by patients. An alternative theoretical explanation, stemming from a more cognitive perspective, could be that during patients’ first fixation and instances when only a single fixation is executed on an infrequent word, there may be, to some degree, a lack of access to, or a deficit in cognitive resources required for linguistic processing of unfamiliar words. Cognitive deficits are a key feature of ME/CFS, and patients have previously reported problems with their concentration during reading, and an increase in fatigue during tasks that require mental effort. In comparison to controls, as patients displayed a smaller increase of their fixation duration on infrequent words (for first and single fixations), this could reflect that less linguistic information, in comparison to controls, is extracted and decoded in that time. This limited processing may not be enough to disrupt comprehension, but could perhaps increase the work of other stages of the reading process, such as working memory in order to retain the information that was able to be extracted during that fixation, or within the information processing system in decoding the word. This may
consequently increase the mental effort required during reading and feasibly increase fatigue. This argument is well fitting with patient reports of concentration difficulty and memory during reading, and claims that in some cases they may have to re-read text that they have failed to take in (Wearden & Appleby, 1997). However it is strongly emphasised that this argument is only theoretically based, and is not directly supported by the objective evidence.

It could also be that patients generally require longer fixation durations to encode words irrespective of whether they’re frequent or infrequent, and thus it may not be necessary to increase their fixation duration to as larger degree as controls. Essentially, there may be little difference between lexical encoding for frequent and infrequent words because patients may require more mental effort for reading tasks in general. However, it is important to remember that this was only the case for first and single fixations on the critical word. Analyses for both first fixations and single fixations only take into account one fixation. However, variables of gaze duration and total fixation time consider multiple fixations. For these latter two variables patients and controls exhibited similar reading behaviours across both frequent and infrequent conditions. This may be as further fixations allow for the retrieval of further lexical information.

Lastly, it was found that patients executed more (although only marginally) regressions out of the target word than controls; however this was irrespective of whether the word was infrequent or frequent. In comparison, patients and controls showed similar regressions into the critical word. This perhaps suggests in some cases, re-reading of information prior to the critical word was required for patients, but this was independent of whether it was frequent or infrequent.

Overall, it appears that ME/CFS patients do display some different reading behaviours in comparison to controls when manipulating linguistic characteristics. However, differences were only small, and necessitate clarification.

6.3 Study 7. The perceptual span
The perceptual span is ‘the region of effective vision during eye fixations in reading’, referring to the amount of para-foveal material that is able to be obtained during a single fixation (Rayner, Slattery & Belanger, 2010). Examples of the type of information extracted in this region is outlined in (Rayner, 1988), such as information for word identification, word length, and letter shapes. Although acuity does not limit the perceptual span (Miellet, O’Donnell & Sereno, 2009), the perceptual span is restricted. In skilled readers, the perceptual span is asymmetric, (in alphabetical writing) extending to 3-4 letters to the left of fixation and 14-15 letters to the right of fixation (Rayner, 1998; 2009). However a reduced perceptual span to the right of fixation has been demonstrated in unskilled readers, believed to be as they may assign more recourses to foveal as opposed to parafoveal processing (Henderson & Ferreira, 1990). As discussed in Chapter 1, section 1.4.1, a reduced perceptual span has been found in other groups and with normal reading comprehension, e.g., older adults, people with macular degeneration and even some psychological conditions such as schizophrenia and affective disorders (Rayner, Castelhano & Yang, 2009; Crossland, Michael, Rubin & Gary , 2006; Neale, 1971; Strauss, Bohannon, Stephens, & Pauker 1984). And also in individuals who generally just read more slowly than average (Rayner, Slattery & Belamger, 2010).

A well established and powerful technique used to determine characteristics of the perceptual span is the Gaze-Contingent Moving Window Paradigm (McConkie & Rayner, 1975). The paradigm works by controlling the amount of information that can be read at each fixation. For example, in a condition that only allows for 1 word (the fixated word) to be viewed normally, all other letters are masked with X’s or other random letters. When the eyes move to fixate onto the next word, the new fixated word is presented normally and all other characters are obscured by X’s or random characters. Therefore, the impact of larger reductions in window size, would less affect the reading of those with a smaller perceptual span. Rayner et al (1982) used the moving window paradigm to investigate the perceptual span in skilled college readers. They found that during a three-word window (fixated word and two to the right) reading rate was normal. Normal reading reduced slightly during a two-word window (fixated word and the word to the right) where reading rate was approximately 90% normal, and during a one-word window (fixated word), reading was the most affecting as reading rate was approximately 60% normal.
Whether or not the visual problems of ME/CFS patients complain of affect parafoveal vision during reading remains to be explored. This experiment uses the moving window paradigm to examine whether the perceptual span is smaller for ME/CFS patients compared to controls. If a reduced perceptual span is found in ME/CFS patients, this could be used as a potential biomarker for the condition. Chapter 1, section 4.111 suggested that if a reduced perceptual span is evident in ME/CFS, this may result in more eye movements. Therefore, based on conclusions from Badham and Hutchinson’s (2013) smooth pursuit task (see page 24), an increase in musculature activity, could exacerbate fatigue and offer an explanation for reading discomfort. However, findings from Experiment 1 found no differences in number of saccades between patients and controls. Nevertheless, exploring the perceptual span in ME/CFS patients may be of particular importance due a number of reasons. For example, a reduced perceptual span may be a factor of elevated crowding, which can make reading rate worse (Crossland & Rubin, 2005; Falkenberg, Rubin & Bex, 2006), and ME/CFS patients exhibited a worse crowding acuity compared to controls (see Chapter 3 Study 1). Chapter 6 also demonstrated that patients’ may read more slowly than controls, and prior research has shown that individuals who read more slowly (Rayner, Slattery & Belamger, 2010; Rayner, Castelhano & Yand, 2009) have smaller perceptual spans. Furthermore the perceptual span is regarded to some degree to be attentionally-constrained, and previous research has revealed attentional deficits in patients with ME/CFS (Hutchinson & Badham, 2013).

The aim of Experiment 2 was therefore to assess the size of ME/CFS patients’ perceptual span.

**Method and materials**

The classic gaze-contingent moving window paradigm (McConkie & Rayner, 1975; Rayner & Berertera, 1979) was used to determine the size of the perceptual span for ME/CFS patients and controls. This paradigm allowed examination of global aspects of reading performance such as total reading time, forward fixation duration and number of fixations during reading.
Text materials consisted of 120 syntactically simple sentences across three moving window conditions. The experimental sentences were divided into the three moving window conditions (120 sentences in total; 40 sentences per condition), that manipulated the amount of para-foveal information available at each fixation in a gaze-contingent fashion. Condition 1 represented normal sentences, a no window (NW) condition consisting of full text. Condition 2 consisted of a 3 Word (3W) window condition (the fixated word and 2 words to the right of fixation). Finally, Condition 3, the narrowest window condition consisted of a 1 word (1W) window condition (the fixated word). During fixation, text was presented normally within the window, however beyond the window of normal text, characters were replaced with orthographically similar other characters. Sample sentences in each condition are presented in Figure 6.6.

It was expected that controls reading would be slowed down considerably in the 1W condition and no disruption would occur in the 3W or NW condition. The question we addressed was whether patients would show a data pattern similar to that of the control participants or whether they would reach asymptote in reading performance with the 1W window, thus reflecting a smaller perceptual span.

(Apparatus)

All apparatus was the same as that used in Experiment 1 (see section 6.2 for details).
Procedure

Participants were instructed that sentences may be partially masked by other letters, and that they should read silently and at their normal pace for comprehension despite the other letters. The onset of each trail was initiated by fixating on a small gaze contingent cross located at the start of the first word of each sentence. The experiment was split into 2 halves, each with 60 sentences. To become familiarised with the task, participants first read 5 practice sentences with each condition. They then read the 55 sentences in each part. In total 10 practice and 110 experimental trials. Participants pressed a button on a controller pad after reading each sentence, and to ensure that participants maintained attention while reading. Again simple yes/no comprehension questions appeared after ~ 30% of the experimental trials which were evenly distributed.

Data Analyses

Fixations shorter than 80ms and longer than 1200ms were eliminated from the analyses. Practice trials (sentences 1 – 5) were also removed.

Results and discussion

Comprehension accuracy for control subjects was 94.62% and for ME/CFS patients was 94.16 %. Reading time is believed to be the most informative measure to determine characteristics of the size of the perceptual span in ‘moving window’ experiments (Rayner, Slattery & Belanger, 2010). Average fixation duration and fixation count were also inspected.

Mean values for global variables: sentence reading time, average fixation duration and fixation count are presented in Figure 6.6 (next page).
For total sentence reading time, there was a significant main effect for condition of window (NW, 3W, 1W), \(F(2, 41) = 82.784, p < .001, \text{ partial } \eta^2 = .802\) on sentence reading time, with both groups reading times in the (1W) 1 word window condition. Reading was markedly quicker in the (3W) 3 word window condition and in the (NW) no window condition (all text/normal sentence), which was the condition for the fastest reading time for both groups (see Figure 6.7 for means). However, there was no effect of group \(F(1, 42) = .277, p = .602, \text{ partial } \eta^2 = .007\), and no interaction between group and window condition \(F(2, 41) = 1.563, p = .227, \text{ partial } \eta^2 = .070\).
There was a significant main effect for window condition (NW, 3W, 1W), \((F(2, 41) = 94.058, p < .001, \text{partial eta squared } = .841)\) on average fixation duration, with both groups displaying longer average fixation durations in the (1W) 1 word window condition. Fixation duration time was much less in the (3W) 3 word window condition, and in the (NW) no window condition (all text/normal sentence), which had the lowest average fixation duration for both groups (see Figure 6.7 for means). There was no effect of group \((F(1, 42) = .048, p = .827, \text{partial } \eta^2 = .001)\) nor was there an interaction effect between group and window condition, \((F(2, 41) = .106, p = .900, \text{partial } \eta^2 = .005)\).

There was a significant main effect for window condition (all text, 1 word window and 3 word window) on number of fixations \((F(2, 41) = 101.549, p < .001, \text{partial } \eta^2 = .832)\), with both groups displaying more fixation counts in the (1W) 1 word window condition. Fixation count was much lower in the (3W) 3 word window condition, and in the (NW) no window condition (all text/normal sentence), which had the least number of fixation counts for both groups (see Figure 6.7). There was no effect of group \((F(1, 42) = .182, p = .672, \text{partial } \eta^2 = .004)\) and no between group and window condition \((F(2, 41) = 1.867, p = .168, \text{partial } \eta^2 = .083)\).

The aim of experiment 2 was to determine whether ME/CFS patients have a smaller perceptual span. If a smaller perceptual span was present, ME/CFS patients would be far less affected by the 1W condition. However, ME/CFS patients displayed similar sentence reading behaviours to control subjects. Both patients and controls demonstrated that reading was significantly disrupted by the 1W condition as indicated by significantly longer reading times, longer average fixation durations and number of fixations. Therefore these results show that a ME/CFS patient’s perceptual span in reading is of normal size, and therefore reveal no para-foveal processing anomalies during reading. In sum, a reduced perceptual span is unlikely to account for the vision-related reading difficulties that they report.

6.4 Discussion
The aim of the 2 experiments outlined in Chapter 6 was to use a range of specialised eye tracking techniques to establish a great understanding of vision and ocular discomfort during reading for ME/CFS patients.

Taken together the results presented in Study 6 and Study 7 suggest remarkably clear evidence that eye movement control during reading is not disrupted for ME, and, that those with ME/CFS do not have a reduced perceptual span. However, it is tentatively suggested that subtle differences between patients and controls from the word frequency effect may, to some degree, reflect some slight cognitive differences during language processing. Although the objective evidence does not directly support this and thus it is essential that more extensive and rigorous investigations are conducted before this can be confirmed. Moreover, a cognitive approach would not effectively solve patients’ reports of vision related problems during reading such as blurriness of text or difficulty tracking lines of print.

*Preliminary to Chapters 7 and 8*

Thus far it has been shown that the vision-related symptoms reported by ME/CFS patients, are unlikely to be a result of poorer reading acuity, reduced perceptual span size or eye movement dysfunctions during reading. However, it is important to recognise that ME/CFS impacts on a number of systems. As well as impairing motor function, ME/CFS also consists of a large neurological component (Carruthers et al, 2011). In consideration of this, and the previous findings, perhaps a more perceptual approach is required to understand vision related reading discomfort in those with ME/CFS. This may be especially case, given that one of the most frequent visual symptoms that patients report is photophobia, a core symptom of the neurological condition visual stress.
7. Visual stress

Findings from Chapters 3 and 5 suggest that visual acuity is unlikely to be the cause of reading-related discomfort in ME/CFS. Furthermore Chapter 6 indicated that para-foveal visual constraints, or impaired saccadic function are also unlikely to explain their reading problems. Taken together, these findings suggest that the visual problems experienced by ME/CFS patients during reading cannot be accounted for based on the effects of the condition on the eye itself. As vision-related reading discomfort in patients with ME/CFS is a concept that has yet to be explored it is important thoroughly and comprehensively investigate a range of possibilities that might contribute to their reading symptoms. The results thus far may suggest that visual problems during reading may be more likely to be accounted for by changes in the neural visual pathways (i.e. within the visual cortex).

Many ME/CFS patients report visual symptoms that are characteristic of the condition visual stress (VS). For example, they report severe headaches, glare from the page, photophobia, sensitivity to visual patterns and difficulty tracking lines of print (Vedelago, 1997; Leslie, 1997; Potasnick & Kozol, 1992; Hutchinson et al, 2014). Visual stress is a visual dysfunction that can interfere with the ability to read (Tyrrell et al, 1995), and is not typically measured in optometric assessments (Wilkins, Huang and Cao, 2004). To date, no direct measurement of susceptibility to visual stress in patients with ME/CFS has been carried out. The aim of this chapter is therefore to determine the existence of visual stress in patients with ME/CFS.

7.1 Introduction

Those who experience visual stress are unable to see comfortably and experience a range of perceptually and visually distorting symptoms such as blurring, flickering, fading and shimmering. Other unpleasant somatic symptoms such as eye strain and headaches are also common. These effects, which are exacerbated as a result of encountering visual stimuli, have been proposed as being sensory in origin unlike ocular motor abnormalities (Wilkins, 2003).

The characteristics of visual stimuli that are suggested to most likely to induce visual stress have been described by Wilkins (1995) and consist of very specific spatial features. In
essence, presentation of a visual display that is high in contrast and comprises a striped pattern can provoke illusions and distortions. The bright and dark stripes should have approximately equal width (a duty cycle of 50%), and the spatial frequency of the pattern should be approximately 3 cycles per degree. Presentations of these stimuli to individuals who are highly susceptible to visual stress, such as those with epilepsy (Wilkins, Baker, Amin, Smith, et al. (1999), migraine (Harle, Shepard & Evans, 2006), and stroke (Beasley & Davis, 2012), provokes perceptual distortions and uncomfortable symptoms.

The effects of visual stress can also occur in everyday life. Individuals who are vulnerable to visual stress can experience a similar discomfort when encountering visual stimuli in a similar pattern configuration, such as escalators and striped clothing. More notably, reading lines of text has large potential to evoke visual stress, given its spatial characteristics (Wilkins & Nimmo-Smith, 1987). Visual stress during reading was first noted by Meares (1980) and Irlen (1983), and has been widely acknowledged in the field. Many now refer to the condition as Meares-Irlen Syndrome.

Essentially, lines of text in a passage reflect a striped pattern with the spatial characteristics that provoke distortions. A vast range of distortions can occur when viewing text, such as colour illusions, shapes (diamond lattice,) and motion. As a result, these effects can cause a slower reading performance (Wilkins & Nimmo-Smith, 1984). Evidence to suggest that it is the pattern from the lines of text that causes the discomfort can be illustrated from recorded EEG abnormalities in patients prone to visual stress, such as photo-sensitive epilepsy. For example, abnormalities were reduced when using a reading mask (where lines of text were covered above and below the line being read), suggesting that the perceptual distortions and discomfort was likely to be because the text resembled a striped pattern (Wilkins, 1995). Indeed ME/CFS patients claim they experience difficulty tracking the lines of print, where it is often reported they become confused by the lines above and below the one being read (Vedelago, 1997).

The neurological theory behind visual stress is that the symptoms occur when nerve cells in the visual cortex of the brain fire too strongly, causing others to fire inappropriately which causes the brain to be overloaded by certain images. Indeed, computer based pattern glare studies have revealed higher levels of cortical hyper excitability neurotransmission
The effects of this during reading can be alleviated in many ways such as alterations to design, layout of text, and notably, the use of colour (Wilkins, 1995). (The use of colour to reduce visual stress during reading will be discussed in further detail in Chapter 8.)

The condition of visual stress has been well documented in a number of conditions such as migraines, photosensitive epilepsy, dyslexia, autism, stroke patients and anxiety (Ludlow, Wilkins, & Heaton, 2006; Wilkins et al, 1984; Harle et al, 2006; Beasley & Davis, 2012; Singleton & Henderson, 2007; Robertson & Simmons, 2015; Nulty, Wilkins, & Williams, 1987). However, as discussed in Chapter 1, section 1.5, despite many of the characteristics of visual stress map well onto the visual symptoms reported by ME/CFS patients (Veledgo, 1997; Leslie, 1997; Potasnick & Kozol, 1992; Hutchinson et al, 2014) very little research has examined the existence of visual stress in this disorder.

In particular, visual stress has been linked to photophobia. Hutchinson, Badham, Maltby and Jason (2014) revealed that 92% of ME/CFS patients reported sensitivity to light, and aversion to light has been highlighted in other ME/CFS studies (Potasnick & Kozol, 1992; Veledo, 1997; Leslie, 1997). Indeed photophobia is also existent in other neurological disorders which are known to have a high vulnerability to stress. For example, brain injury (Jackowski, Sturr, Taub, & Turk, 1995), migraine (Drummond, 1986) and stroke (Shuaib, 1991), and has been attributed to hyper excitability in the occipital cortex.

As noted in Chapter 1, recent evidence has indicated a high occurrence of visual stress in ME/CFS. Leow, Marsh and Watson’s (2014) questionnaire study showed that ME/CFS patients reported significantly more core symptoms associated with visual stress compared to controls. Although employing questionnaires methods are a good indication to suggest further investigation, a more direct measure is required to objectively quantify the occurrence of distortions. The aim of this chapter is therefore to use a more direct behavioural paradigm to quantify symptoms of visual stress in ME/CFS; The Pattern Glare Test. It was expected that visual stress would be higher in patients compared to controls.

7.2 Study 8. The pattern glare test
Method and materials

The Pattern Glare Test © (Wilkins & Evans, 2001, 2012) was used to assess levels of visual stress in ME/CFS patients.

The Pattern Glare Test contains three presentation cards each containing a high contrast striped grating pattern within a circular aperture. The orientation of the pattern gratings is horizontal, in order to mimic text. At the recommended viewing distance of 40cm, the duty cycle of each pattern was 50%, and each grating pattern subjected an angle of 13.63 degrees. Pattern 1 has low spatial frequency (0.3 cycles per degree, c/deg) and is used as a control, thus this pattern should elicit very few to no distortions. Evans and Wilkins (2008) state the main purpose of this pattern is to identify participants who may be suggestible and to ensure participants provide accurate responses. Pattern 2 is of mid-spatial frequency (2.3 c/deg) and should maximally stimulate pattern glare. Therefore individuals who experience the symptoms of visual stress in daily life should report a high number of distortions for this pattern. Pattern 3 represents another form of control. It is of high spatial frequency (9.4 c/deg), and distortions produced from this pattern are believed to be of an alternative kind to those from Pattern 2, reflecting more optical rather than neurological factors (Conlon et al, 2001). The test has been used effectively in a number of studies (Beasly & Davis, 2012; Evans & Stevens, 2008; Harles, Shepard & Evans, 2006), and, Evans and Stevenson (2008) claim that the test is now regarded as being a recognised and effective way to detect individuals with visual stress.

Prior to the experiment, participants were asked whether they had experienced any form of epilepsy, as this was the exclusion criteria. No patients or control participants expressed any prior experience of epilepsy. The pattern glare test was administered in accordance with Evans and Wilkins (2012) instructions. Participants were informed that they would be presented with 3 black and white striped patterns and asked to look at the centred dot where they may or may not see distortions. In order to familiarise participants with the distortions that may or may not appear, participants were read the list of distortions provided with the test. Participants were then instructed to view pattern 1 (low-SF). After 5 seconds, each distortion was read out loud and participants were asked to report any of the following effects: (1) colours, (2) bending of lines, (3) blurring of lines, (4)
shimmering or flickering, (5) fading, (6) shadowy shapes, and any other effects (to be specified). Participants were also asked to state whether these distortions were present predominantly on the left side of the pattern, the right or on both. This process was repeated for pattern 2 (mid-SF) and then for pattern 3 (high-SF).

Scoring was conducted by marking down each distortion a participant reported which was then added together to create a total number of distortions for each pattern. Additionally, a mid-high SF difference was calculated by subtracting the total number of distortions for pattern number 3, from pattern number 2. According to Evans and Stevenson (2008) having a high score of distortions in response to Pattern 2, or a score on Pattern 2 that is higher than the score for Pattern 3 is indicative pattern glare. It is not clear which is the better indicator; as such both were considered.

Results

Descriptive data are presented in Figure 7.1 (next page). Paired sample t-tests revealed that scores (number of distortions) were significantly higher in ME/CFS patients compared to controls for the Mid-SF pattern (pattern 2) ($t(25) = 4.200, p < .001$), indicating increased susceptibility to visual stress (Figure 7.1). A larger mid-high SF difference in patients than controls ($t(24) = 5.473, p < .001$) was also revealed further supporting, greater pattern-related visual stress in ME/CFS (Figure 7.2). As expected there was no significant difference between patients’ and controls’ scores for the Low-SF pattern (pattern 1) ($t(25) = .122, p = .904$). Neither was there a significant difference between patients’ and controls’ scores for the High-SF pattern (pattern 3) ($t(24) = .1088, p = .287$).
The aim of this chapter was to more directly determine the existence of pattern-related visual stress in ME/CFS. In support of, and building upon Leow et al’s (2014) questionnaire findings, the results revealed that pattern-related visual stress was significantly higher in ME/CFS patients than controls. This may account for some ME/CFS vision-related symptoms such as reading-related strain, fatigue and headaches during reading. It may also be worth noting that the present findings are also fitting with other recent literature into visual stress and previous ME/CFS research. For example, visual search performance has been shown to be impaired in individuals high pattern-related visual stress (Allen, Gilchirst & Hollis, 2008), and it has previously been found that, relative to controls, ME/CFS patients were impaired on visual search tasks (Hutchinson & Badham, 2013).

The findings may also provide some insight into possible neurological substrates of ME/CFS in the visual cortex. Indicating that ME/CFS increases susceptibility to pattern-related visual stress, suggests that altered visual perception in ME/CFS may reflect ME/CFS-related changes in the sensory neural pathways. As pattern-related visual stress has been attributed to hyper-excitatory neurotransmission, this supports the notion that ME/CFS is a neurological disorder, and, that many of the characteristics of ME/CFS might be understood,
in part, within the general context of abnormal neurotransmitter activity (Carruthers et al, 2011).

It is important to consider that the study does have some notable limitations. The question arises of what can be learned from the test itself. The experiment uses the pattern glare test in a very standard way. Although the test is suggested to infer cortical hyper-excitability, the test does not directly measure this. What it does measure is number of categories of visual illusions/disturbances experienced. Although the measure is direct, it is also reliant on subjective report of symptoms. However a strength of the materials used is that it has in-built controls to help ensure that any significant results are not due to response biases.

In summary the present findings indicate that ME/CFS increases vulnerability to visual stress. This may account for some of their vision related symptoms during reading. Further research could therefore explore the efficacy of coloured overlays as a means of therapeutic intervention. Although the study investigated the occurrence of visual stress in a standard way, it is the first quantitative measure of visual stress in ME/CFS.
8. Coloured overlays as a therapeutic intervention for reading-related visual discomfort in ME/CFS

Chapter 7 suggested that ME/CFS patients have an increased vulnerability to pattern-related visual stress. This may explain many of their visual-related reading symptoms such as increased headaches and difficulty tracking text. The benefit of coloured overlays to reduce symptoms of visual stress during reading has been acknowledged, and has been suggested as a potential approach to improve reading performance. The aim of this chapter is to verify the efficacy of coloured overlays as a means for improving reading performance in patients with ME/CFS.

8.1. Introduction

A central focus in visual stress research has been to explore the potential beneficial effects of coloured filters in reducing perceptual distortions and discomfort during visual tasks. In particular, a wealth of literature has demonstrated that coloured overlays and lenses can make significant improvements in reading. Perceptual distortions experienced during reading, such as blurred vision and uncomfortable headaches, can often be reduced by covering text with a coloured overlay (Wilkins, 2003). Notably, several studies have shown that using coloured overlays can also improve reading speed. For example, when reading with one’s own choice of coloured overlay, reading speed in impaired readers has shown to increase by 25% or more. (Tyrell et al, 1995; Wilkins, Jeane, Pumfrey & Laskier, 1996; Evans & Joseph, 2002). However, reading speed is not the only improvement coloured overlays have shown to have. Other improvements include sentence comprehension and reading accuracy (Robinson & Foreman, 1999; Robinson & Conway, 1994).

The strength of the benefit of coloured overlays can be gleaned from placebo studies and studies controlling for motivation (Wilkins & Lewis, 1999; Bouldoukian, Wilkins & Evans, 2001 as discussed in Chapter 1). Such robust evidence has even lead to the practice of using coloured overlays as a diagnostic tool for pattern-related visual stress or Meares-Irlen syndrome (Kriss & Evans, 2001. Also confirmed in Allen, Gilchrist & Hollis, 2008).
There is however, some conflicting evidence for the efficiency of coloured overlays, and many still remain sceptical about their benefit. For example, Blaskey, Scheiman, Parisi, Ciner, Gallaway and Selznick (1990) revealed no significant improvements in reading rate with coloured overlays. Menacker, Breton, Breton, Radcliffe & Gole (1993) and Iovino, Fletcher, Breitmeyer & Foorman (1998) also failed to find any beneficial effects on reading performance with coloured overlays and lenses in children with dyslexia and ADHD. However these latter two studies only compared a small number of coloured overlays which may have restricted the choice of overlay for the individual. Indeed it has been suggested that there is considerable variability in preferred choice of overlay, and an important step required to achieve reading speed effects is that individuals must select an overlay to suit themselves with careful precision (Wilkins, 2003; Wilkins, Evans, Brown et al, 1994).

However, this concept of ‘choice’ itself raises questions. Wilkins et al (1994) emphasises that the effect of a particular colour on reading performance is idiosyncratic, with individuals supposedly necessitating a different colours. Therefore for optimal beneficial effects to occur, then the colour of the overlay or lens must be carefully and individually chosen. However, for unknown reasons, children do occasionally change their preferred coloured overlay (Wilkins, 2003). In addition, the matter still exists, that in the majority of studies examining the effects of overlays, individuals are choosing their own personal coloured overlay. Thus this notion of making an individual choice or decision may, to some degree, contain a psychological element which could impact performance (i.e. they may want to do well with that colour, because they chose that colour).

Indeed, the mechanism underlying coloured overlays’ benefitting properties during reading is poorly understood. Although one possible suggestion is that overlays redistribute the activity within the visual cortex in such a way as to reduce the amount of excitation in locally hyper excitable regions (Wilkins, Huang & Cao, 2004). However, a lack of understanding about the precise mechanisms should not distract from the fact that, for many, overlays do show significant improvements in reading performance.

Regarding ME/CFS, the previous chapter revealed that patients may have an increased vulnerability to visual stress, and improvements in reading speed with coloured overlays have been displayed in adults with visual stress (Hollis and Allen, 2006). Therefore
coloured overlays could offer an easy implementable and cost effective way of reducing reading symptoms (such as headaches, glare from the page etc.), and thus improve reading experiences for ME/CFS patients. Indeed, coloured filters have also been shown to be effective in reducing visual stress in other neurological disorders such as epilepsy (Wilkins, Baker, Amin et al 1999) and in migraine (Wilkins, Patel, Adjamain & Evans, 2002). Although, it should be considered that many of these studies used coloured lenses as opposed to overlays, and Wilkins (2003) claims that the effect overlays and lenses operate differently within the brain, however he does not specifically state how this is so.

Improving reading is fundamental given its association to quality of life and importance for functioning effectively within society. This therefore highlights the necessity to explore methods aimed at improving reading experiences in this patient group. The aim of this chapter was to experimentally measure reading performance through measuring reading speed under different overlay conditions. Based on findings from chapter 7, that patients may be more vulnerable to visual stress than controls, it was expected that patients will therefore benefit more from the use of coloured overlays compared to controls.

8.2. Study 9. Wilkins Rate of Reading Test with Intuitive overlays

Methods and materials

Wilkins Rate of Reading Test: The study used Wilkins Rate of Reading Test, Institute of Optometry. The test comprises a passage of text that contains little semantic and linguistic content and is designed to maximise visual stress (Wilkins, 1995). In order to represent stripes the text is horizontal with reduced spacing ‘single spaced’; a 4 point horizontal spacing (0.36mm). The text is also small, printed in Times font, 9 point, in order to create stripes consisting of spatial characteristics close to those needed for perceptual

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Note. Two patients (and the paired control participants) were excluded from the following experiments due to feelings of exhaustion, therefore totalling the number of patients to 25, and 25 controls.
distortion. The text is set as a paragraph 72.5mm wide, 33.4mm high, with an interline space of 3.15mm.

The passage consists of 10 lines, 150 words, each with the same 15 common words in a different random order. The words are of high frequency and are therefore familiar to poor readers. The random word order ensures that no word can be guessed from the context but each must be seen to be read. The test consists of four parallel versions, with the same words but in different order to prevent practice effects. (See figure 8.1 for example). (Wilkins et al., 1996).

The test gives a measure of reading rate in words per minute as follows:

\[
\text{Words per minute} = \frac{\text{number of correctly read words} \times 60}{\text{time taken in seconds}}.
\]

Version A

come see the play look up is cat not my and dog for you to the cat up dog and is play come you see for not to look my you for the and not see my play come is look dog cat to up dog to you and play cat up is my not come for the look see play come see cat not look dog is my up the for to and you to not cat for look is my and up come play you see the dog my play see to for you is the look up cat not dog come and look to for my come play the dog see you not cat up and is up come look for the not dog cat you to see is and my play is you dog for not cat my look come and up to play see the

Figure 8.1 Example of Wilkins Rate of Reading Text.

Intuitive Coloured Overlays: The coloured overlays used in this experiment were the Intuitive Overlays (IOO Sales Ltd., London, UK). The Intuitive Overlays are sheets of coloured plastic suitable for placing over a page of text, colouring the text beneath without interfering with its clarity. They sample chromaticity systematically and efficiently (Wilkins, 1994). The pack contains 2 sets of A5 size overlays of each of the following colours: yellow, orange, pink, purple, blue, aqua, mint green, lime green, grey. For use with the WRRT coloured overlays were used singly and laid over the printed passage of text.

A mixed-factorial design was employed with between (group: patients and controls) and within (coloured overlays: no overlay, rose, orange, yellow, lime green, mint green,
aqua, blue, purple, pink and grey) subjects factors. The dependent variable was reading speed measure in words per minute tested using the Wilkins Rate of Reading Test.

Procedure

Participants were informed that they will be reading a passage of text with different coloured overlays. They were instructed to read as quickly and accurately as possible, and to try and not correct any mistakes. Participants were timed from the moment they spoke to when they finished and were stopped at 60 seconds, if not complete. When participants made errors this was noted on the score sheet. The time was noted and number of words read correctly in a minute was calculated in words per minute. To eliminate order effects, different overlay conditions were presented in a pseudorandom order, where participants would read with each of the randomly selected different coloured overlays, and with no coloured overlay, with random alternating versions of the text.

Participants were then asked to use the intuitive overlays test page to rank the coloured overlays in their subjective preference. A test page consisting of two A4 pages with two identical passages of the Rate of Reading text side by side was positioned in front of the participant. The page was positioned so that no light sources were directly reflected from the surface of the overlays. Each participant’s optimal overlay was then chosen using the method outlined in the intuitive overlays manual, and were then asked to rank the remaining overlays in an order of subjective preference from 1 to 10 (1 being least preferred to 10 representing most preferred).

Results

Descriptive data are presented in Table 8.1 (next page) and percentage change with each coloured overlay in Figure 8.2.
Table 8.1
Mean reading speed in each overlay condition. Values in parentheses are ± 1 SEM.

<table>
<thead>
<tr>
<th></th>
<th>No overlay</th>
<th>Yellow</th>
<th>Orange</th>
<th>Rose</th>
<th>Pink</th>
<th>Purple</th>
<th>Blue</th>
<th>Aqua</th>
<th>Mint</th>
<th>Lime</th>
<th>Grey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>156.64 (6.67)</td>
<td>150.79 (6.41)</td>
<td>149.72 (7.57)</td>
<td>152.76 (6.44)</td>
<td>161.26 (6.88)</td>
<td>157.28 (7.07)</td>
<td>149.70 (6.29)</td>
<td>160.20 (6.24)</td>
<td>152.33 (6.53)</td>
<td>154.99 (6.83)</td>
<td>157.04 (7.57)</td>
</tr>
<tr>
<td>Controls</td>
<td>167.61 (6.38)</td>
<td>162.06 (5.19)</td>
<td>158.86 (5.75)</td>
<td>160.33 (5.81)</td>
<td>165.75 (5.70)</td>
<td>157.65 (5.10)</td>
<td>160.47 (5.37)</td>
<td>164.05 (5.97)</td>
<td>161.05 (6.01)</td>
<td>160.53 (5.90)</td>
<td>166.62 (5.74)</td>
</tr>
</tbody>
</table>

Note. Values are in words per minute. Higher numbers represent more words read per minute and therefore a quicker reading rate; lower numbers represent fewer words read per minute and therefore a slower reading rate.
There was no statistical difference between patients and controls reading speed in the non-overlay condition ($t(26) = 1.205, p = .234$).

A mixed, repeated measures analysis of variance (ANOVA) was conducted to assess the impact of coloured overlays on reading performance in patients with ME/CFS. There was no significant interaction between group and overlay conditions ($F(10,40) = 1.463, p = .189$, partial $\eta^2 = .268$), indicating that ME/CFS patient’s and controls exhibited a similar reading rate across the overlay conditions. There was also no significant main effect of group (patients and controls), ($F(1,49) = .815, p = .371$), partial $\eta^2 = .016$, suggesting no difference in reading rate between patients and controls. However there was a significant main effect for condition ‘category of coloured overlay’, ($F(10,40) = 5.101 , p<.001$, partial $\eta^2 = .560$), indicating that the overlay condition had an effect on reading rate irrespective of group. To determine the specific effects of each coloured overlay, follow-up Bonferroni-corrected t-tests were performed separately for each group, in which reading performance with each overlay was compared to performance with no overlay (Table 8.2). The majority of coloured overlays had no effect on WRRT performance with the exception of blue for patients, and orange and purple for controls. However, the direction of the effect was the opposite to

*Figure 8.2.* Percentage change in reading performance with each coloured overlay, compared to performance with no overlay. Error bars are ± 1 SEM.
that expected, in that these overlays appeared to lead to worse, rather than better WRRT performance.

**Table 8.2.**
Effect of each coloured overlay (relative to the no overlay condition) on WRRT performance.

<table>
<thead>
<tr>
<th>Overlay colour</th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow</td>
<td>( t(24)=1.807; p=.041 )</td>
<td>( t(24)=1.782; p=.044 )</td>
</tr>
<tr>
<td>Orange</td>
<td>( t(24)=2.281; p=.016 )</td>
<td>( t(24)=3.577; p=.001^* )</td>
</tr>
<tr>
<td>Rose</td>
<td>( t(24)=1.230; p=116 )</td>
<td>( t(24)=2.703; p=.006 )</td>
</tr>
<tr>
<td>Pink</td>
<td>( t(24)=-1.596; p=.062 )</td>
<td>( t(24)=.586; p=.28 )</td>
</tr>
<tr>
<td>Purple</td>
<td>( t(24)=-.371; p=.357 )</td>
<td>( t(24)=3.319; p=.002^* )</td>
</tr>
<tr>
<td>Blue</td>
<td>( t(24)=2.837; p=.0045^* )</td>
<td>( t(24)=1.977; p=.030 )</td>
</tr>
<tr>
<td>Aqua</td>
<td>( t(24)=-1.085; p=.15 )</td>
<td>( t(24)=.746; p=.23 )</td>
</tr>
<tr>
<td>Mint Green</td>
<td>( t(24)=1.065; p=.15 )</td>
<td>( t(24)=1.542; p=.068 )</td>
</tr>
<tr>
<td>Lime Green</td>
<td>( t(24)=.945; p=.17 )</td>
<td>( t(24)=2.031; p=.026 )</td>
</tr>
<tr>
<td>Grey</td>
<td>( t(24)=-.193; p=.42 )</td>
<td>( t(24)=.032; p=.49 )</td>
</tr>
</tbody>
</table>

*Note. After Bonferroni correction for multiple comparisons, the alpha level required for a statistically significant difference between group was \( p < .005 \). * denotes a significant change in performance.*

Participants were also asked to rank the coloured overlays in order of subjective preference. Ranks were explored by assessing median scores (see Figure 8.3 next page). There was an overlap between patients and controls as to the most (yellow, orange, aqua and lime) and least (blue, purple and grey) preferred overlay colours.

Correlation analyses also revealed that preferred overlay was not significantly related to reading performance. This was shown for all overlays: yellow (\( r = .121, p = .393 \)), orange (\( r = -.109, p = .448 \)), rose (\( r = -.135, p = .344 \)), pink (\( r = .041, p = .755 \)), purple (\( r = -.014, p = .923 \)), blue (\( r = .164, p = .223 \)), aqua (\( r = .149, p = .295 \)), mint (\( r = .029, p = .842 \)), lime (\( r = -.154, p = .930 \)) and grey (\( r = -.060, p = .675 \)).
The results in this chapter indicate that both the ME/CFS patient group, and control group, exhibited a similar reading rate across the overlay conditions. Furthermore, irrespective of overlay condition, although patients’ generally read slower, their performance was not significantly different from controls. However, a main effect of overlay condition suggested that the overlays did have an impact on reading speed within the whole sample. Further inspection revealed that the majority of coloured overlays had no effect on reading rate, with exception of blue for patients, and orange and purple for controls. However, surprisingly, these latter colours decreased reading rate, rather than increasing WRRT performance.

Figure 8.3. Median rank preference scores for (a) patients and (b) controls. Note. Higher numbers represent most preferred, lower numbers, least preferred.

8.3 Discussion

The results in this chapter indicate that both the ME/CFS patient group, and control group, exhibited a similar reading rate across the overlay conditions. Furthermore, irrespective of overlay condition, although patients’ generally read slower, their performance was not significantly different from controls. However, a main effect of overlay condition suggested that the overlays did have an impact on reading speed within the whole sample. Further inspection revealed that the majority of coloured overlays had no effect on reading rate, with exception of blue for patients, and orange and purple for controls. However, surprisingly, these latter colours decreased reading rate, rather than increasing WRRT performance.
The percentage change of reading rate from reading with no overlay and with each coloured overlay was also presented. Wilkins (2003) states that if there is a percentage increase of reading rate above 5% with a coloured overlay then it is likely to be of use. The only four colours to increase reading rate was pink, purple aqua and grey in the patient group (and just grey for the control group). In particular pink and aqua overlays increased reading rate for patients, but decreased reading rate for controls. However, the percentage increase ranged from 0.60% -3.23%, and are therefore unlikely to produce any benefit.

Inspection of preferred ranks showed varying preferences for patients’ and controls which is in agreement with Wilkins et al, (1994) suggestion of variability amongst individuals’ preferred overlays. Generally, preferred colours for patients did fall within the lighter category, with yellow being favoured top, followed by rose and orange, and, with darker colours being favoured last; grey, blue and purple. This may not be so surprising as lighter colours have been shown to be useful in improving reading and visual performance in a number of visual conditions (Stien, 2003). For controls, lime came top, followed by aqua, yellow and orange, again all fairly bright colours, and similarly purple, blue and grey coming in the bottom three.

The variety of preferred colours and reading rate effects perhaps highlights the individual nature of coloured overlays, possibly emphasising the importance of choosing an overlay on an individual basis to suit ones needs. This denotes a possible limitation of the study. Although all colours were tested, the importance of testing the individual with and without just their chosen colour, (selected through precision to suit the individual) has been recommended (Wilkins, Sihara & Nimmo-smith, 2005; Wilkins, 2000; Wilkins et al, 1994). Although patients did choose their most preferred overlay when ranking overlays, this was done after the WRRT task. Interestingly, however, the top two preferred coloured overlays chosen by patients; yellow and rose revealed a decrease in reading speed, and, preferred colour was not significantly correlated to reading performance.

A further restriction to the study was that it principally only measures reading speed. The Wilkins Rate of Reading Test is a well-established method for inferring improvements on reading performance with coloured overlays, as demonstrated by a wealth of studies. However it does not directly measure a reduction in visual stress and discomfort.
experienced during reading. This therefore limits the ability to directly infer any beneficial effects of reducing visual distortions or somatic symptoms. An alternative method could aim at providing further insight into the visual distortions and somatic symptoms experienced during reading. For example, a questionnaire or interview asking participants to comment on their level of discomfort, or distortions, with and without the overlay. Ludow, Wilkins and Heaton (2006) included a further measure in their experiment exploring the effect of overlays on reading performance in patients with autism. Children were asked a series of visual stress questions whilst looking at the text-passage with the overlay. Such as — “Do the letters stay still or do they move?”; “Are they clear or are they blurred (fuzzy, difficult to see)?”; “Are the words too close together or far enough apart?”; “Is the page too bright, not bright enough, or just about right”; “Does the page hurt your eyes to look at or is it ok?”. This extra subjective measure alongside an objective test of reading performance could help to enrich quantitative data and provide by providing further insight into the effects of coloured overlays.

Furthermore, the appropriateness of reading speed in this particular task, as an indicator of improved reading performance in ME/CFS, could be disputed. For example, the WRRT is primarily used with children, therefore a test of this kind may not suit a study with adults, who made find it too easy, and as such reading rate will already be at ceiling rate. Indeed, within other neurological conditions with a high vulnerability to visual stress, such as Migraine, colour had no effect on reading speed. However, the use of colour did reduce symptoms of migraine, thus making it easier and more comfortable to read (Harle & Evans, 2004). In the case of ME/CFS, many of the visual and fatiguing symptoms they experience during reading, occur when reading over a sustained period of time. Therefore, future research could investigate whether overlays have beneficial effects for the amount of time patients can read for, rather than increases in reading speed in a short reading task. An alternative design could provide patients with overlays to trial at home for their general reading, and ask them to keep a diary for how long they were able to read for.

In summary, no significant benefit in reading performance from using coloured overlays was displayed in either ME/CFS patients or for the control group. It is suggested that future research adopts a refined experimental design and includes other measures to provide a more detailed and clearer picture into any possible effects of overlays.
9. General discussion

The studies outlined in this thesis have improved the current understanding of the impact that ME/CFS has on reading experiences and general vision-related quality-of-life. Experimental research was conducted in order to provide objective evidence to support the claims of those with ME/CFS that they find reading difficult and experience reading-related discomfort. This was done using a range of methods, such as questionnaires, basic visual functioning tests, reading performance charts, a range of eye tracking methods and visual stress assessments. Lastly, this research aimed to authenticate the efficacy of coloured overlays as a means of reducing reading-related discomfort. This thesis is the first of its kind to explore vision-related reading difficulties in patients with ME/CFS.

9.1. Summary of findings and implications for Chapters 3 and 4

The experiments in Chapter 3 were conducted as a preliminary study for the experiments in the thesis that follow. This chapter assessed basic visual functioning in patients with ME/CFS. With the exception of crowded acuity, patients and controls had comparable corrected visual acuity. Patients’ contrast sensitivity was also comparable to the control group. However patients did exhibit a significantly poorer stereo-acuity threshold. This finding supports previous findings that patients report problems with perceiving depth (Hutchinson et al, 2014; Potaznick & Kozol, 1992). To augment this finding, further investigation is required with more controlled visual psychophysical measures of depth perception. Taken together, these results generally imply that the visual symptoms in those with ME/CFS, are perhaps understood within the cortical visual pathways, rather than the eye itself.

Findings in Chapter 4 effectively highlight the deleterious effect that visual problems have on the quality of life for ME/CFS patients. This in itself justifies the need for more research into this field. Using a standardised questionnaire, the results clearly showed that ME/CFS had a marked impact on the visual quality of life of patients. This chapter also revealed that patients reported significantly more visual problems related to reading. These findings corroborate reports from those with ME/CFS that they experience a number of visual symptoms during reading. In support of previous literature (e.g. Hazel et al, 2000), reading was also strongly correlated to visual quality of life, thus strengthening the rationale
to investigate further, using an empirical approach, into the visual factors that could underlie reading difficulties in this patient group.

9.2. Summary of experimental findings and implications from Chapters 5 and 6

Reading performance charts were used in Chapter 5 to provide a more direct and reliable measurement of reading ability. The findings indicated that patients were not impaired on the level of reading acuity or critical point size. However, patients did read more slowly than the control group on some of the measures, which may be indicative of a different reading strategy. However it is also acknowledged that crowding effects may also be a factor. To follow this up, well controlled, and highly specialised eye tracking experiments were conducted.

A range of eye tracking methods was employed in Chapter 6 to provide a more detailed picture of vision-related reading discomfort. Although patients did read more slowly, this was not significant, contrasting findings shown found from using the reading performance charts (Chapter 5). This may be due to differing experimental conditions. Furthermore, no differences in ocular control during reading (fixation count, average fixation duration, saccade amp, no. of regressions, no. of progressions), or in the size of perceptual span were found between patients and controls. However, when manipulating linguistic variables, patients showed some minor differences to controls, which could be reflective of a slightly different cognitive approach to language processing between the two groups, although a more rigorous and comprehensive investigation is required for this to be confirmed.

9.3. Experimental findings and implications from Chapters 7 and 8

Those with ME/CFS report a considerable number of visual problems are in agreement with some characteristics of visual stress. Building on previous questionnaire findings (Leow et al, 2014), the results in Chapter 7 more directly demonstrated that those with ME/CFS may be more vulnerable to visual stress. This may account for some ME/CFS vision-related symptoms such as reading-related strain, fatigue, headaches during reading, difficulty following lines of text and glare from the page. To help alleviate the symptoms of visual stress during reading, the use of coloured overlays or tints is often recommended. As
such, Chapter 8 examined the efficacy of coloured overlays for improving vision-related reading discomfort in ME/CFS patients. However, the use of overlays did not improve reading performance for either patients or controls, and for a few certain colours, reading was hindered. However, it is argued that the reading task used in this experiment (WRRT) may not have been the most appropriate measure for this patient group. An alternative design could examine the amount of time as opposed to reading speed with coloured overlays, and also include additional measures concerning the level of visual comfort during reading to enrich quantitative data.

9.4 Future directions

There are a number of areas that future research should consider. Firstly, it is recommended that future research should primarily focus on expanding the findings from Chapter 7 in relation to visual stress. Chapter 7 used the pattern glare test. Although this test is more direct than questionnaire methods, it is still reliant on subjective responses. Furthermore, although this test does quantify symptoms of visual stress, and symptoms of visual stress are thought to infer reduced inhibitory and/or increased excitatory neurotransmission in visual cortex, (e.g. Beasley & Davies, 2012; Wilkins, et al, 2004), the pattern glare test does not assess this directly. It is therefore recommended that future research should investigate the relationship between visual discomfort and visual cortical responses in ME/CFS, using direct measures of cortical activity. This could be achieved by following similar procedures to those already completed in neurological conditions (such as in migraine and photosensitive epilepsy) through the use of EEG (Electroencephalography), or fMRI (Functional magnetic resonance imaging methods) (Aurora & Wilkinson, 2007; Huang et al, 2003). A cheaper alternative to these expensive techniques and offering more control that the Pattern Glare Test is the possibility to develop a more controlled psychophysical test for Visual Stress. Given further developments this may also provide an easy implementable diagnostic tool. Furthermore, coloured lenses as opposed to coloured overlays could be explored as a form of therapeutic intervention. This is based on the premise that coloured overlays and lenses work in different ways within the brain (Wilkins, 2003) and the use of coloured lenses in other neurological disorders, such as stroke, brain injury and migraine have shown improvements in reading (Jackowski, Sturr, Taub, & Turk, 1995; Drummond, 1986; Shuaib, 1991).
Secondly, future work could more directly consider the role of cognitive processes during reading. Many of the reading difficulties reported by patients are visual, however reading does involve a substantial cognitive element, and cognitive deficits are a prominent feature of the disorder. Findings in chapter 6 demonstrated that there may be minor differences in language processing; however, this was inferred by examining eye movements in response to the manipulation of linguistic variables. Other lexical processes in this patient group could be explored to build on this finding. One particular task that further research could explore is accuracy of word recognition. This suggestion is tentatively based on the premise that recent research has revealed differences in word recognition performance in individuals with high pattern-related visual stress high-PRVS (Gilchrist & Allen, 2015). This may be particularly noteworthy, in the context of the findings from Chapter 7, of a higher reporting of pattern-related visual stress in patients with ME/CFS, and Chapter 6, differences between patients and controls in the Word Frequency Effect.

Future work could also examine the role visual attention during reading in more detail. Patients have previously reported problems relating to focusing visual attention (Hutchinson et al, 2014), backed by experimental evidence demonstrating attentional deficits in those with ME/CFS (Hutchinson & Badham, 2013). Although visual attention was not directly addressed in the experiments within this thesis, it plays a key role within the reading process which warrants further study in this particular patient group.

Lastly, experiments within Chapter 6 only took measures from one eye. Given that patients report problems with accommodation and focus (Vedelago, 1997; Potaznick & Kozol), a good follow up could be to investigate how the eyes work together and use eye tracking techniques. This could be done by examining binocular disparity following similar to techniques to those previous used, such as Paterson, McGowan and Jordan (2013). Similarly, the reading performance charts could also be repeated monocularly.

9.5. Clinical significance and implications

The outputs of this thesis add to the increasing body research for ME/CFS in the United Kingdom, raising awareness for the international profile of UK bio-medical research in this field. The findings are of significance to those with ME/CFS in that they provide experimental corroboration of the vision-related reading problems they experience. This is
especially important considering the extent of stigma attached to the disorder which has left many suffering with the condition subject to ridicule such as accusations of malingering and attention seeking. It is also important to identify and understand anomalous vision in ME/CFS in the context of improving diagnostic criteria and the development of appropriate clinical interventions. In the long run, the outputs of this research may lead to the implementation of vision-based assessments that can be administered by clinicians to aid diagnosis of ME/CFS. For example, the existence of pattern-related visual stress in ME/CFS may represent an identifiable and measurable behavioural marker of ME/CFS. However considerable further research is necessary before these types of assessment are applied within clinical practice. Establishing and publicising visual symptoms in ME/CFS may also influence general attitudes for the condition, and importantly those of policy-makers. It is hoped that by demonstrating the effects of visual symptoms this will impact the National Institute for Health and Care Excellence guidelines for the diagnosis and management of ME/CFS (which is due for revision in 2017), which currently does not recognise vision as a clinical feature. Lastly, by demonstrating how the visual problems of those with ME/CFS affect everyday activities, notably reading, is also hoped that this may encourage further research into therapeutic interventions with the aim of helping those with ME/CFS regain some of their daily function.

9.6. Limitations

It should be acknowledged that the current work does have a number of limitations. Caution should be taken when interpreting the results as a whole as differences between all reading tests used in the experiments should be considered. For example, the WRRT reading test in Chapter 8 contained no semantic meaning presenting a major difference in comparison to the other reading performance tests used in Chapter 6 (Radner Rate of Reading and MN Read Acuity charts) and reading material used in Chapter 7’s eye tracking experiments. Some tests required also participants to read out loud, others to read to themselves. Material was presented at varying distances and in varying format (e.g. 3 lined passage or single line), and experimental conditions also varied.

In relation to the sample size, ME/CFS is a debilitating disorder, and many who are severely affected by the condition are restricted in terms of activity or bed bound. As the
study required patients to travel to the University of Leicester in order to complete the experiments this limited the ME/CFS sample and largely under-represents those who are severely affected. In light of this, it is probable that the findings presented in this thesis under-represent the severity of vision and vision related reading problems in ME/CFS. Moreover, due to the nature of the condition and high drop-out rates, the sample number of ME/CFS patients is also fairly modest.

The present thesis also did not distinguish between ME and CFS. It has recently been argued that the two may represent two different conditions (Twisk, 2014). The DePaul Symptom questionnaire allowed for the examination of patients against commonly applied definitions for ME and CFS. Many patients did show some overlap between ME and CFS, however, some patients met the criteria for ME but not CFS, and a couple met the criteria for CFS and not ME. As the two may represent different conditions, by combing both may have, to a certain degree, affected the research. However, to date, the overwhelming amount of research into ME/CFS does not explicitly distinguish the two conditions, nor do the current diagnostic criteria. Future research could perhaps consider scores from the De Paul Symptom Questionnaire on an individual basis in order to examine the relationship between patients’ medical diagnosis, De Paul diagnostic classification, and also individual experimental data. Additionally, future work may also find it of interest to run the De Paul Symptom questionnaire on control subjects as well of patients.

9.7. Summary and conclusion of thesis.

The findings presented in this thesis add to the growing body of research examining visual and ocular problems in ME/CFS, and further helps in bridging the gap between understanding how the visual and ocular problems experienced affect the everyday lives of those with ME/CFS. No study to the author’s knowledge has attempted to objectively investigate the characteristics underlying reading discomfort ME/CFS patients. In sum, the findings herein imply that vision related reading discomfort in those with ME/CFS is more likely to stem from neurological components, such as the visual cortex, as opposed to the abnormalities within the eye itself or ocular motor dysfunctions during reading.
APPENDIX (A)

Item 1. DePaul Symptom Questionnaire (Pre-screening questionnaire) –MOS survey

ID# ____________________                                               Date_____________________

DePaul Symptom Questionnaire

Please answer the following questions.

1. What is your height?________________________

2. What is your weight?________________________

3. What is your date of birth?________________________

4. What is your gender?________________________

5. To which of the following race(s) do you belong?

<table>
<thead>
<tr>
<th>WHITE</th>
<th>ASIAN: incl. Asian – British, Irish:</th>
</tr>
</thead>
<tbody>
<tr>
<td>British</td>
<td>□ Indian</td>
</tr>
<tr>
<td>Irish</td>
<td>□ Pakistani</td>
</tr>
<tr>
<td>Other</td>
<td>□ Bangladeshi</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHINESE: incl. Chinese - British, Irish:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
</tr>
<tr>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>MIXED:</th>
<th>BLACK: incl. Black – British, Irish:</th>
</tr>
</thead>
<tbody>
<tr>
<td>White &amp; Black Caribbean</td>
<td>□ Caribbean</td>
</tr>
<tr>
<td>White &amp; Black African</td>
<td>□ African</td>
</tr>
<tr>
<td>White &amp; Asian</td>
<td>□ Any other Black background (please state)</td>
</tr>
<tr>
<td>Any other Mixed background (please state)</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>OTHER: Any other Ethnic Group</th>
<th>□ Please state: ____________________</th>
</tr>
</thead>
</table>
6. What is your current marital status?
   - Married or living with partner
   - Separated
   - Widowed
   - Divorced
   - Never married

7. Do you have any children?
   - Yes  No *(Skip to Question 9)*

7a. How many children do you have? ______________

7b. How many of your children are under 18 years old? ______________

8. How many people live in your home? ________________________________

9. What is your education level?
   - GCSEs, O levels, or equivalent
   - A levels or equivalent (B-tec, Access etc.)
   - University undergraduate degree
   - University postgraduate degree (Masters, doctorate)
   - Other education level. Please state: ________________________________

10. What is your current work status? *(Check all that apply)*
    - Working full-time
    - Working part-time
    - Student
    - Homemaker
    - Retired
    - Unemployed

11. Do you currently receive any disability-related benefits (e.g. Disability Living Allowance)?
11a. If so, please specify the condition for which you receive them ________________

12. If you are employed, what is your current occupation?

Current ________________

12a. If you are currently not working, what was your most recent occupation?

Most Recent ________________

For the following questions (13-66), we would like to know **how often you have had each symptom** and **how much each symptom has bothered you over the last 6 months**. For each symptom please circle **one number for frequency** and **one number for severity**. Please fill the chart out from left to right.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency: Throughout the <strong>past 6 months</strong>, <strong>how often</strong> have you had this symptom?</th>
<th>Severity: Throughout the <strong>past 6 months</strong>, <strong>how much</strong> has this symptom bothered you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 = none of the time</td>
<td>0 = symptom not present</td>
</tr>
<tr>
<td></td>
<td>1 = a little of the time</td>
<td>1 = mild</td>
</tr>
<tr>
<td></td>
<td>2 = about half the time</td>
<td>2 = moderate</td>
</tr>
<tr>
<td></td>
<td>3 = most of the time</td>
<td>3 = severe</td>
</tr>
<tr>
<td></td>
<td>4 = all of the time</td>
<td>4 = very severe</td>
</tr>
<tr>
<td>13) Fatigue/extreme tiredness</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>14) Dead, heavy feeling after starting to exercise</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>15) Next day soreness or fatigue after non-strenuous, everyday activities</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>16) Mentally tired after the slightest effort</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>17) Minimum exercise makes you physically tired</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td></td>
<td>Symptoms</td>
<td>Frequency:</td>
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<tr>
<td>---</td>
<td>--------------------------------------------------------------------------</td>
<td>------------------------------------------------</td>
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<tr>
<td></td>
<td></td>
<td>Throughout the past 6 months, how often have</td>
</tr>
<tr>
<td></td>
<td></td>
<td>you had this symptom?</td>
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<tr>
<td></td>
<td></td>
<td>For each symptom listed below, circle a number</td>
</tr>
<tr>
<td></td>
<td></td>
<td>from:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 = none of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 = a little of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 = about half the time</td>
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<tr>
<td></td>
<td></td>
<td>3 = most of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 = all of the time</td>
</tr>
<tr>
<td>18</td>
<td>Physically drained or sick after mild activity</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>19</td>
<td>Feeling unrefreshed after you wake up in the morning</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>20</td>
<td>Need to nap daily</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>21</td>
<td>Problems falling asleep</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>22</td>
<td>Problems staying asleep</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>23</td>
<td>Waking up early in the morning (e.g. 3am)</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>24</td>
<td>Sleep all day and stay awake all night</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>25</td>
<td>Pain or aching in your muscles</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>26</td>
<td>Pain/stiffness/tenderness in more than one joint without swelling or redness</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>27</td>
<td>Eye pain</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>28</td>
<td>Chest pain</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>29</td>
<td>Bloating</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>30</td>
<td>Abdomen/stomach pain</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>31</td>
<td>Headaches</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>32</td>
<td>Muscle twitches</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>33</td>
<td>Muscle weakness</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>34</td>
<td>Sensitivity to noise</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Frequency:</td>
<td>Severity:</td>
</tr>
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<td>------------------------------------------------------------------------</td>
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<tr>
<td></td>
<td>Throughout the <strong>past 6 months</strong>, how</td>
<td>Throughout the <strong>past 6 months</strong>, how</td>
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<td></td>
<td>often have you had this symptom?</td>
<td>much has this symptom bothered you?</td>
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<td>For each symptom listed below, circle a</td>
<td>For each symptom listed below, circle a</td>
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<td>number from:</td>
<td>number from:</td>
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<td></td>
<td>0 = none of the time</td>
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<td>1 = mild</td>
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<td></td>
<td>2 = about half the time</td>
<td>2 = moderate</td>
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<tr>
<td></td>
<td>3 = most of the time</td>
<td>3 = severe</td>
</tr>
<tr>
<td></td>
<td>4 = all of the time</td>
<td>4 = very severe</td>
</tr>
<tr>
<td>35) Sensitivity to bright lights</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>36) Problems remembering things</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>37) Difficulty paying attention for a long period of time</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>38) Difficulty finding the right word to say or expressing thoughts</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>39) Difficulty understanding things</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>40) Only able to focus on one thing at a time</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>41) Unable to focus vision and/or attention</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>42) Loss of depth perception</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>43) Slowness of thought</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>44) Absent-mindedness or forgetfulness</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>45) Bladder problems</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>46) Irritable bowel problems</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>47) Nausea</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>48) Feeling unsteady on your feet, like you might fall</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>49) Shortness of breath or trouble catching your breath</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>50) Dizziness or fainting</td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Frequency:</td>
<td>Severity:</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-----------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>Throughout the <strong>past 6 months</strong>, how</td>
<td>Throughout the <strong>past 6 months</strong>, how</td>
</tr>
<tr>
<td></td>
<td>often have you had this symptom?</td>
<td>much has this symptom bothered you?</td>
</tr>
<tr>
<td></td>
<td>For each symptom listed below, circle a</td>
<td>For each symptom listed below, circle a</td>
</tr>
<tr>
<td></td>
<td>number from:</td>
<td>number from:</td>
</tr>
<tr>
<td></td>
<td><strong>0</strong> = none of the time</td>
<td><strong>0</strong> = symptom not present</td>
</tr>
<tr>
<td></td>
<td><strong>1</strong> = a little of the time</td>
<td><strong>1</strong> = mild</td>
</tr>
<tr>
<td></td>
<td><strong>2</strong> = about half the time</td>
<td><strong>2</strong> = moderate</td>
</tr>
<tr>
<td></td>
<td><strong>3</strong> = most of the time</td>
<td><strong>3</strong> = severe</td>
</tr>
<tr>
<td></td>
<td><strong>4</strong> = all of the time</td>
<td><strong>4</strong> = very severe</td>
</tr>
<tr>
<td><strong>51) Irregular heart beats</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>52) Losing/gaining weight without trying</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>53) No appetite</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>54) Sweating hands</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>55) Night sweats</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>56) Cold limbs (e.g. arms, legs, hands)</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>57) Feeling chills or shivers</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>58) Feeling hot or cold for no reason</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>59) Feeling like you have a high temperature</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>60) Feeling like you have a low temperature</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>61) Alcohol intolerance</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>62) Sore throat</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>63) Tender/sore lymph nodes</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>64) Fever</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>65) Flu-like symptoms</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td><strong>66) Some smells, foods, medications, or chemicals make you feel sick</strong></td>
<td>0 1 2 3 4</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>
67. Have you **always** had persistent or recurring **fatigue/energy problems**, even back to your earliest memories as a child? (By persistent or recurring, we mean that the fatigue/energy problems are usually ongoing and constant, but sometimes there are good periods and bad periods.)

- Yes
- No
- Not having a problem with fatigue/energy

68. Since your **fatigue/energy related illness** began, do your headaches either happen more often, feel worse or more severe, or are they in a different place or spot?

- Yes
- No
- Not having a problem with fatigue/energy

69. How long ago did your problem with **fatigue/energy** begin?

- Less than 6 months
- 6-12 months
- 1-2 years
- Longer than 2 years
- Had problem with fatigue/energy since childhood or adolescence
- Not having a problem with fatigue/energy

70. Have you been diagnosed with Chronic Fatigue Syndrome or Myalgic Encephalomyelitis?

- Yes
- No

70a. If yes, what year were you diagnosed? __________

70b. Do you currently have a diagnosis of Chronic Fatigue Syndrome or Myalgic Encephalomyelitis?

- Yes
- No

70c. Who diagnosed you with Chronic Fatigue Syndrome or Myalgic Encephalomyelitis?

- Medical Doctor
- Alternative Practitioner
- Self-Diagnosed

70d. Have any of your family members been diagnosed with Chronic Fatigue Syndrome or Myalgic Encephalomyelitis?

- Yes
- No
If yes, please list their relation to you and current age

71. Did you experience any of the following symptoms regularly and repeatedly in the months and years before your fatigue/energy problems began?

☐ Sore throat
☐ Tender/sore lymph nodes
☐ Unrefreshing sleep
☐ Impaired memory and concentration
☐ Prolonged fatigue following physical or mental exertion
☐ Muscle pain
☐ Headaches
☐ Joint Pain
☐ Not having a problem with fatigue/energy

72. If you rest, does your problem with fatigue/energy go away? (Check one)

☐ Entirely
☐ Partially
☐ My fatigue/energy problem is not improved by rest (Skip to Question 73)
☐ I am not having a problem with fatigue/energy (Skip to Question 73)

72a. How long do you have to rest for your problem with fatigue/energy to entirely or partially go away?

☐ less than 30 minutes  ☐ 30 to 59 minutes  ☐ 1-2 hours  ☐ more than 2 hours

73. If you were to become exhausted after actively participating in extracurricular activities, sports, or outings with friends, would you recover within an hour or two after the activity ended?

☐ Yes  ☐ No

74. Do you reduce your activity level to avoid experiencing problems with fatigue/energy?

☐ Yes  ☐ No  ☐ Not having a problem with fatigue/energy
75. Do you experience a worsening of your **fatigue/energy related illness** after engaging in minimal physical effort?

- Yes  
- No  
- Not having a problem with fatigue/energy

75a. Do you experience a worsening of your **fatigue/energy related illness** after engaging in mental effort?

- Yes  
- No

75b. If you feel worse after activities, how long does this last? (Check one)

- 1 hour or less  
- 2-3 Hrs  
- 4-10 Hrs  
- 11-13 Hrs  
- 14-23 Hrs  
- More than 24 Hrs (Please specify__________)

76. Are you currently engaging in any form of exercise?

- Yes *(Skip to Question 77)*  
- No

76a. If you do not exercise, why aren’t you exercising? (Check all boxes that you agree with)

- Not interested  
- No time  
- Would like to but cannot because of problems with fatigue/energy  
- Cannot because exercise makes symptoms worse

77. Over what period of time did your **fatigue/energy related illness**, develop? (Check one)

- Within 24 hours  
- Over 1 week  
- Over 1 month  
- Over 2-6 months  
- Over 7-12 months  
- Over 1-2 years  
- Over 3 or more years  
- I am not ill
78. How would you describe the course of your fatigue/energy related illness? (Check one)

- Constantly getting worse
- Constantly improving
- Persisting (no change)
- Relapsing & remitting (having “good” periods with no symptoms & “bad” periods)
- Fluctuating (symptoms periodically get better and get worse, but never disappear completely)
- No Symptoms/I am not ill

79. Which statement best describes your fatigue/energy related illness during the last 6 months? (Check one)

- I am not able to work or do anything, and I am bedridden.
- I can walk around the house, but I cannot do light housework.
- I can do light housework, but I cannot work part-time.
- I can only work part-time at work or on some family responsibilities.
- I can work full time, but I have no energy left for anything else.
- I can work full time and finish some family responsibilities but I have no energy left for anything else.
- I can do all work or family responsibilities without any problems with my energy.

80. Did your fatigue/energy related illness start after you experienced any of the following? (Check one or more and please specify)

- An infectious illness
- An accident
- A trip or vacation
- An immunisation (injection at doctor’s office)
- Surgery
- Severe stress (bad or unhappy event(s))
- Other
- I am not ill
81. Have you ever consulted a medical doctor or health professional about your **fatigue/energy** problem?

☐ Yes  ☐ No (Skip to Question 83)

82. Do you currently have a medical doctor overseeing your **fatigue/energy** problem?

☐ Yes  ☐ No

83. Do you have any medical illness(es) that might be causing your symptoms?

☐ Yes  ☐ No (Skip to Question 84)

83a. What medical illnesses do you have?

Illness name(s) and year it began: __________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

83b. For which of these conditions are you currently receiving treatment?

______________________________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

84. Are you currently taking any medications (over the counter or prescription)?

☐ Yes  ☐ No (Skip to Question 86)

84a. What medications are you taking? __________________________________________________________________________

______________________________________________________________________________________________

______________________________________________________________________________________________

85. Do you think any medication(s) is (are) causing your problem with **fatigue/energy**?

☐ Yes  ☐ No (Skip to Question 86)

☐ I do not have a problem with fatigue/energy (Skip to Question 86)
85a. Please specify which medications:

________________________________________________________

________________________________________________________

86. Have you ever been diagnosed and/or treated for any of the following: (Check all that apply and write year(s) experienced, years treated, and medication (if applicable) in the blank)

☐ Major depression______________________________________

☐ Major depression with melancholic or psychotic features________________________

☐ Bipolar disorder (Manic-depression)__________________________

☐ Anxiety_________________________________________________

☐ Schizophrenia___________________________________________

☐ Eating disorder__________________________________________

☐ Substance abuse________________________________________

☐ Multiple chemical sensitivities____________________________

☐ Fibromyalgia____________________________________________

☐ Allergies________________________________________________

☐ Other (Please specify)____________________________________

☐ No diagnosis/treatment

87. What do you think is the cause of your problem with fatigue/energy? (Check one)

☐ Definitely physical

☐ Mainly physical

☐ Equally physical and psychological

☐ Mainly psychological

☐ Definitely psychological
88. Do you think anything specific in your personal life or environment accounts for your problem with fatigue/energy?

☐ Yes  ☐ No (Skip to Question 89)

☐ I do not have a problem with fatigue/energy (Skip to Question 89)

88a. Please specify: ________________________________

89. In the past 4 weeks, approximately how many hours per week have you spent doing:

Household related activities? ___________ hours per week

Social/Recreational related activities? ___________ hours per week

Family related activities? ___________ hours per week

Work related activities? ___________ hours per week

90. In the past 4 weeks, have you had to reduce the number of hours you previously spent (prior to your illness) on occupational, social or family activities because of your health or problems with fatigue/energy?

☐ Yes  ☐ No (Skip to Question 91)  ☐ Not having a problem with fatigue/energy

90a. Before your fatigue/energy related illness, approximately how many hours did you used to spend on:

Household related activities? ___________ hours per week

Social/Recreational related activities? ___________ hours per week

Family related activities? ___________ hours per week

Work related activities? ___________ hours per week

91. Please rate the amount of energy you had available yesterday, using a scale from 1 to 100 where 1 = no energy and 100 = your pre-illness energy level. (If you don't have a fatigue/energy related illness, a score of 100 = having abundant energy such that you could work full time and complete your family responsibilities) ____________

92. Please rate the amount of energy you expended (used) yesterday, using a scale from 1 to 100 where 1 = no energy and 100 = your pre-illness energy expended ________________
93. Please rate the amount of fatigue you had yesterday, using a scale from 1 to 100 where 1 = no fatigue and 100 = severe fatigue

94. For the past week, please rate the amount of energy you had available using a scale from 1 to 100 where 1 = no energy and 100 = your pre-illness energy level

95. For the past week, please rate the amount of energy you have expended (used) using a scale from 1 to 100 where 1 = no energy and 100 = your pre-illness energy expended

96. For the past week, please rate the amount of fatigue you have had using a scale from 1 to 100 where 1 = no fatigue and 100 = severe fatigue

97. Since the onset of your problems with fatigue/energy, have your symptoms caused a 50% or greater reduction in your activity level?

☐ Yes ☐ No ☐ Not having a problem with fatigue/energy

98. Do you experience frequent viral infections with prolonged recovery periods?

☐ Yes ☐ No

99. Are you intolerant of extremes of temperatures (when it is extremely hot or cold)?

☐ Yes ☐ No

MOS SURVEY

INSTRUCTIONS:

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1 In general, would you say your health is: (Please check one)

Excellent................................................................. ☐ 1

☐
2 Compared to one year ago, how would you rate your health in general now? (Please check one)

- Much better than a year ago........................... ○ 1
- Somewhat better than a year ago....................... ○ 2
- About the same as one year ago........................ ○ 3
- Somewhat worse now that a year ago................... ○ 4
- Much worse now than a year ago........................ ○ 5

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

<table>
<thead>
<tr>
<th>Activities</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>No, Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vigorous activities</strong>: running, lifting heavy objects, participating in strenuous sports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate activities</strong>: moving a table, pushing a vacuum cleaner, bowling, playing golf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifting or carrying groceries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing several flights of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Climbing one flight of stairs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bending, kneeling, or stooping</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
125

Walking **more than a mile**

Walking **several blocks**

Walking **one block**

Bathing or dressing yourself

---

4 During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of your **physical health**?

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut down on the <strong>amount of time</strong> you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Accomplished less</strong> than you would like</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were limited in the <strong>kind</strong> of work or other activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Had <strong>difficulty</strong> performing the work or other activities (For example, it took extra effort)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

5 During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any **emotional problems** (such as feeling depressed or anxious)?

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut down the <strong>amount of time</strong> you spent on work or other activities</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Accomplished less that you would like

Didn't do work or other activities as carefully as usual

During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, neighbours, or groups (Please check one)

<table>
<thead>
<tr>
<th>Option</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>1</td>
</tr>
<tr>
<td>Slightly</td>
<td>2</td>
</tr>
<tr>
<td>Moderately</td>
<td>3</td>
</tr>
<tr>
<td>Quite a bit</td>
<td>4</td>
</tr>
<tr>
<td>Extremely</td>
<td>5</td>
</tr>
</tbody>
</table>

How much bodily pain have you had during the past 4 weeks?

<table>
<thead>
<tr>
<th>Option</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Very mild</td>
<td>2</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
</tr>
<tr>
<td>Very Severe</td>
<td>6</td>
</tr>
</tbody>
</table>
8 During the **past 4 weeks**, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all……………………………………………………. ○ 1
Slightly……………………………………………………. ○ 2
Moderately………………………………………………….. ○ 3
Quite a bit…………………………………………………… ○ 4
Extremely…………………………………………………… ○ 5

9 These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time **during the past 4 weeks**-

<table>
<thead>
<tr>
<th>Questions</th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you feel full of pep?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you been a nervous person?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt so down in the dumps that nothing could cheer you up?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt calm and peaceful?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did you have a lot of energy?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you felt down-hearted and blue?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did you feel worn out?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you been a happy person?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did you feel tired?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
During the **past 4 weeks**, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- All of the time……………………………………… 1
- Most of the time…………………………………… 2
- Some of the time………………………………… 3
- A little of the time………………………………… 4
- None of the time…………………………………… 5

11. How **TRUE** or **FALSE** is each of the following statements for you?

<table>
<thead>
<tr>
<th>Statements</th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Don't Know</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
<tbody>
<tr>
<td>I seem to get sick a little easier than other people</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am as healthy as anybody I know</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I expect my health to get worse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My health is excellent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
THIS IS THE END OF THE SURVEY
Item 2. Ethical approval from The University of Leicester, School of Psychology Ethics Committee

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**RESEARCH ETHICS REVIEW**

**Section I: Project Details**

<table>
<thead>
<tr>
<th>1. Project title:</th>
<th>Reading between the lines of visual discomfort in CFS/ME</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statement of Research Purpose</strong></td>
<td>The purpose of the proposed research project is to establish a detailed picture of visual and eye-movement-related factors that precipitate vision-related reading discomfort in CFS/ME and explore vision-based interventions to improve reading experiences.</td>
</tr>
<tr>
<td><strong>Project Aims/ Research questions:</strong></td>
<td><strong>Aim 1:</strong> Provide experimental evidence to support the claims of those with CFS/ME that they find reading difficult and experience reading-related discomfort by determining the effects of CFS/ME on (1) eye movements during reading and (2) reading performance; <strong>Aim 2:</strong> Gain an understanding the impact of CFS/ME on reading experiences and general vision-related quality-of-life; <strong>Aim 3:</strong> Determine the existence of pattern glare/visual stress in CFS/ME; <strong>Aim 4:</strong> Verify the efficacy of coloured overlays as a means of reducing reading-related discomfort in CFS/ME.</td>
</tr>
<tr>
<td><strong>Proposed methods:</strong></td>
<td><strong>Experiment 1:</strong> Establishing the profile and impact of reading-related visual discomfort. Participants will complete The National Eye Institute Visual Functioning Questionnaire-25 (VFQ-25). This 25-item measure provides a picture of general vision-related quality-of-life. To determine the specific impact of vision-related reading problems on quality of life, participants will also complete a reading scale, developed to assess the impact of vision-related reading difficulty in macular disease. This 15-item measure is made up of questions directly related to reading experiences. We will also include a short open response section in which we ask participants to describe reading-related difficulties to include their frequency, &quot;triggering&quot; events, specific symptoms and any steps commonly taken to alleviate them. Reading scale results will be correlated with the findings from reading performance and eye movement studies (outlined below).</td>
</tr>
</tbody>
</table>
during reading. Using non-invasive, infra-red eye-tracking methods, we will determine whether there are differences in saccade amplitude, number of saccades and fixation duration during reading between individuals with CFS/ME and matched controls. We will also assess accuracy of saccade targeting during reading (by manipulating word length) and the word frequency effect (words that are encountered less often in reading typically produce longer fixation times), which is an index of language processing. Finally, we will examine the perceptual span and binocular coordination in those with CFS/ME and matched control readers.

**Experiment 3: Reading performance.** Reading performance will be determined by measuring reading acuity (the smallest print that participants can read without making significant errors), critical print size (the smallest print that participants can read with maximum speed), and maximum reading speed (the patient’s reading speed when reading is not limited by print size). These will be assessed using the MNREAD Acuity Charts. These continuous-text reading-acuity charts for normal and low vision have been shown to be a reliable measure of determining reading acuity, reading speed, and critical print size in a normal adult population. We will complement this test with the Radner Reading Test, which also gives a standardised measure of reading speed.

**Experiment 4: The role of visual stress/patterns glare in CFS/ME.** To determine its role in CFS/ME-related reading problems, we will screen for visual stress using a self-assessment questionnaire and the pattern glare test and the Wilkins Rate of Reading Test. The Pattern Glare Test has been successfully implemented in a number of neurological conditions including photosensitive epilepsy, migraine, multiple sclerosis and, most recently, stroke. The test is made up of three presentation cards at spatial frequencies of 0.5, 3 and 12 cycles per degree (c/deg). Patients who are susceptible to pattern glare report that the 3 c/deg is uncomfortable and the lines appear distorted. The Wilkins Rate of Reading Test is designed to maximise visual stress. Unlike the MNREAD test (Experiment 3), it has minimal linguistic and semantic content. Participants read aloud a passage of text that looks like a passage of prose but in fact is composed of random words. The performance measure is the number of words read per minute.

| Method of recruiting research participants | Participants with CFS/ME will be recruited in the following ways. (1) Claire Hutchinson will write a letter outlining the study. She will post copies of the letter to ME Research UK who will send them to people in the Midlands area who subscribe to their magazine (Breakthrough). (2) We will contact relevant individuals who run ME support groups in the Midlands and ask them to pass on our letter outlining the study to individuals in their support groups. (3) We will advertise via press release, as we have done previously in a similar study. |
Control participants will be recruited via the School of Psychology participant panel, via advertising around the university (i.e. on the bulletin board), and via advertisements in the local press.

<table>
<thead>
<tr>
<th>Criteria for selecting research participants</th>
<th>CFS/ME - diagnosis of CFS/ME, verified using the DePaul Symptom QuestionnaireControls - age, gender and education match to each individual CFS/ME participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated number of Participants</td>
<td>100 (50 CFS/ME, 50 controls)</td>
</tr>
<tr>
<td>Estimated start date</td>
<td>01/10/2014</td>
</tr>
<tr>
<td>Estimated end date</td>
<td>31/10/2015</td>
</tr>
<tr>
<td>Will the study involve recruitment of participants from outside the UK?</td>
<td>If yes, please indicate from which country(s).No</td>
</tr>
</tbody>
</table>

**Section II: Applicant Details**

<table>
<thead>
<tr>
<th>2. Name of researchers (applicant):</th>
<th>a) Claire Hutchinson</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b)</td>
</tr>
<tr>
<td></td>
<td>c)</td>
</tr>
<tr>
<td></td>
<td>d)</td>
</tr>
<tr>
<td></td>
<td>e)</td>
</tr>
<tr>
<td>2b. Department:</td>
<td>Psychology</td>
</tr>
<tr>
<td>3. Status:</td>
<td>Staff</td>
</tr>
<tr>
<td>4. Email addresses:</td>
<td>a) <a href="mailto:ch190@le.ac.uk">ch190@le.ac.uk</a></td>
</tr>
<tr>
<td></td>
<td>b)</td>
</tr>
</tbody>
</table>
### Section III: For Students Only

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Module name and number or MA/MPhil/PhD course and department:</td>
<td>N/A</td>
</tr>
<tr>
<td>7. Module leader's/Supervisor's name:</td>
<td>N/A</td>
</tr>
<tr>
<td>8. Email address:</td>
<td><a href="mailto:gf43@le.ac.uk">gf43@le.ac.uk</a></td>
</tr>
<tr>
<td>9. Contact address:</td>
<td>School of Psychology, University of Leicester</td>
</tr>
</tbody>
</table>

Section IV: All Research Applicants

Please outline below whether or not your research raises any particular ethical issues and how you plan to address these issues.
This research does not raise any particular ethical issues. Participants will be provided with a letter by post/email containing general details about the study, after which they can decide whether they would like to make contact with us to arrange to take part. When they arrive at the university for testing, they will be given the consent form and any questions will be answered by the experimenter.

Are you using a Participant Information and Informed Consent Form?

If YES, please paste copy form at the end of this application.  

### Section V: Research Ethics Checklist

Please answer each question by ticking the appropriate box:

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Does the study involve participants who are particularly vulnerable or unable to give informed consent? (e.g. children, people with learning disabilities, your own students).</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>2.</td>
<td>Will the study require the co-operation of a gatekeeper for initial access to the groups or individuals to be recruited? (e.g. students at school, members of self-help group, residents of nursing home).</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>3.</td>
<td>Will it be necessary for participants to take part in the study without their knowledge and consent at the time? (e.g. covert observation of people in non-public places).</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>4.</td>
<td>Will the study involve discussion of sensitive topics (e.g. sexual activity, drug use)?</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>5.</td>
<td>Are drugs, placebos or other substances (e.g. food substances, vitamins) to be administered to the study participants or will the study involve invasive, intrusive or potentially harmful procedures of any kind?</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>6.</td>
<td>Will blood or tissue samples be obtained from participants?</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>7.</td>
<td>Is pain or more than mild discomfort likely to result from the study?</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td>8.</td>
<td>Could the study induce psychological stress or anxiety or cause harm or negative</td>
<td></td>
<td>NO</td>
</tr>
</tbody>
</table>
9. Will the study involve prolonged or repetitive testing? | NO

10. Will financial inducements (other than reasonable expenses and compensation for time) be offered to participants? | NO

11. Will the study involve recruitment of patients or staff through the NHS? | NO

12. Does this research entail beyond minimal risk of disturbance to the environment? If yes, please explain how you will minimize this risk under section IV above. | NO

13. Have you gained the appropriate permissions to carry out this research (to obtain data, access to sites etc)? | YES

14. Measures have been taken to ensure confidentiality, privacy and data protection where appropriate. | YES

If you have answered 'yes' to any of the questions 1-12 or 'no' to questions 13-14, please return to section IV. All Research Applicants' and ensure that you have described in detail how you plan to deal with the ethical issues raised by your research. This does not mean that you cannot do the research only that your proposal raises significant ethical issues which will need careful consideration and formal approval by the Department's Research Ethics Officer prior to you commencing your research. If you answered 'yes' to question 11, you will also have to submit an application to the appropriate external health authority ethics committee. Any significant change in the question, design or conduct over the course of the research should be notified to the Module Tutor and may require a new application for ethics approval.

Declaration

Please note any significant change in the question, design or conduct over the course of the research should be notified to the Departmental Ethics Officer and may require a new application for ethics approval.

I have read the University of Leicester Code of Research Ethics. - YES
The information in the form is accurate to the best of my knowledge and belief and I take full responsibility for it. - YES

I understand that all conditions apply to any co-applicants and researchers involved in the study, and it is my responsibility to ensure they abide by them. – YES

ETHICS APPROVAL CODE: ch190-8816a
Item 3. Participant information sheet

Participation information sheet

- Visual acuity and visual functions: Visual acuity will be examined using a number of visual acuity charts similar to those used by optometrists. Stereo acuity will also be examined using a simple vision test which will require you to look at a variety of patterned plates at varying distances.

- Vocabulary: Vocabulary will be assessed using a standardised test requiring you to describe the meaning of a number of presented words.

- Reading performance: This will be examined using 2 charts which require you to read sentences on the chart as quickly and accurately as possible whilst being timed.

- Visual stress: A pattern glare test will be used. This requires you to look at three high contrast circular grating patterns, and asked to report any perceptual distortions that may appear.

- Reading performance with coloured overlays: This will be examined using a reading task and a variety of coloured overlays whilst being timed.

- Eye movements during reading tracking experiments: Three eye tracking experiments will be conducted. These tests require you to read text that is presented on a computer screen. You will be asked to read normally and for comprehension. To keep head movements still for efficient calibration, you will be asked to place your head in the chin and head rest. There will be opportunity for plenty of breaks throughout these experiments.

- Visual quality of life: This will be assessed with a standardised rating questionnaire. A reading scale questionnaire will also be asked.

Please remember that you participant is voluntary, and you may withdraw at any time from the study.
Background Information

Title: Reading between the lines of visual discomfort in CFS/ME
Researchers: Rachel Wilson, Claire Hutchinson, Kevin Paterson
Purpose of data collection: Research

Details of Participation: The purpose of the proposed research project is to establish a detailed picture of visual and eye-movement-related factors that precipitate vision-related reading discomfort in CFS/ME and explore vision-based interventions to improve reading experiences. Your participation in the study will require you to identify and focus on visual objects and to read and track text, some of which will be presented on a computer screen.

Consent Statement

1. I understand that my participation is voluntary and that I may withdraw from the research at any time up until give specific date or other time point (e.g., when I submit my questionnaire), without giving any reason.

2. I am aware of what my participation will involve.

3. My data are to be held confidentially and only name of researcher and/or supervisor will have access to them.

4. My data will be kept in a locked filing cabinet for a period of at least five years after the appearance of any associated publications. Any aggregate data (e.g. spreadsheets) will be kept in electronic form for up to one year, after which time they will be deleted.

5. The overall findings may be submitted for publication in a scientific journal, or presented at scientific conferences.

6. This study will take approximately 12 months to complete.

7. I will be able to obtain general information about the results of this research by giving the researcher my email address or postal address now. The duration of this study will be approximately 1 year (October 2014 to October 2015). As such, a summary of the findings will be provided in October-November 2015. A synopsis will also be published in Breakthrough Magazine, the official quarterly magazine of ME Research UK and submitted for publication in scientific journals.
I am giving my consent for data to be used for the outlined purposes of the present study

All questions that I have about the research have been satisfactorily answered.

I agree to participate.

Participant’s signature: ________________________________

Participant’s name (please print): ________________________________

Date: __________

If you would like to receive a summary of the results when the study is complete, please provide your address:
____________________________________________________________
____________________________________________________________

If you have further questions about this study, you may contact Dr Claire Hutchinson (ch190@le.ac.uk). This study was reviewed by the University of Leicester Psychology Research Ethics Committee (PREC). You may contact the Chair of PREC Dr. Ruth Hatcher at rmh12@le.ac.uk if you have any questions or concerns regarding the ethics of this project.

Please note that this form will be kept separately from your data.
APPENDIX (B)

Item 1. Reading scale questionnaire

Reading Scale Questionnaire

Date…………..ID……………..

Please circle your response.

Response numbers indicate: 0 = not at all; 1 = hardly at all; 2 = a little; 3 = a fair amount; 4 = a lot; 5 = cannot do it because of eyesight.

How much has your eyesight interfered with the ability to read numbers on the following…

1) Dials?

0  1  2  3  4  5

2) Read labels or prices on cans, packages and other containers?

0  1  2  3  4  5

3) Identify coins, currency?

0  1  2  3  4  5

4) Write cheques and pay bills?

0  1  2  3  4  5

5) See your own handwriting?

0  1  2  3  4  5
6) Complete forms?

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**How much has your eyesight interfered with …**

7) Reading in general?

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8) Reading ordinary sized print?

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9) Reading large print?

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10) Reading small print?

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11) Reading mail?

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12) Reading labels and instructions on medicines?

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13) Seeing numbers and hands on a wristwatch?

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</table>
14) Seeing numbers on a telephone dial?

0 1 2 3 4 5

15) Seeing a number in the telephone directory?

0 1 2 3 4 5

Please describe below any reading-related difficulties. Please include information about the frequency; if there are any ‘triggering’ events; any specific symptoms and any steps taken to alleviate them.

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Item 2. VFQ-25 (2000) – Next page
National Eye Institute
Visual Functioning Questionnaire - 25
(VFQ-25)
version 2000

(INTerviewER ADMINISTERED FORMAT)

January 2000

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7/22/96

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Instructions:

I'm going to read you some statements about problems which involve your vision or feelings that you have about your vision condition. After each question I will read you a list of possible answers. Please choose the response that best describes your situation.

Please answer all the questions as if you were wearing your glasses or contact lenses (if any).

Please take as much time as you need to answer each question. All your answers are confidential. In order for this survey to improve our knowledge about vision problems and how they affect your quality of life, your answers must be as accurate as possible. Remember, if you wear glasses or contact lenses for a particular activity, please answer all of the following questions as though you were wearing them.
Visual Functioning Questionnaire - 25

PART 1 - GENERAL HEALTH AND VISION

1. In general, would you say your overall health is*:

   (Circle One)

   READ CATEGORIES:
   Excellent ...................... 1
   Very Good ..................... 2
   Good .......................... 3
   Fair .......................... 4
   Poor .......................... 5

2. At the present time, would you say your eyesight using both eyes (with glasses or contact lenses, if you wear them) is excellent, good, fair, poor, or very poor or are you completely blind?

   (Circle One)

   READ CATEGORIES:
   Excellent ...................... 1
   Good .......................... 2
   Fair .......................... 3
   Poor .......................... 4
   Very Poor ...................... 5
   Completely Blind ............. 6

* Skip Question 1 when the VFQ-25 is administered at the same time as the SF-36 or RAND 36-Item Health Survey 1.0
3. How much of the time do you worry about your eyesight?
(Circle One)
READ CATEGORIES:
None of the time..........................  1
A little of the time.......................  2
Some of the time..........................  3
Most of the time...........................  4
All of the time?............................  5

4. How much pain or discomfort have you had in and around your eyes
(for example, burning, itching, or aching)? Would you say it is:
(Circle One)
READ CATEGORIES:
None ........................................  1
Mild ...........................................  2
Moderate .....................................  3
Severe, or ...................................  4
Very severe? ..............................  5

PART 2 - DIFFICULTY WITH ACTIVITIES

The next questions are about how much difficulty, if any, you have doing certain activities wearing your glasses or contact lenses if you use them for that activity.

5. How much difficulty do you have reading ordinary print in newspapers? Would you say you have:
(READ CATEGORIES AS NEEDED)
(Circle One)
No difficulty at all............................  1
A little difficulty.............................  2
Moderate difficulty..........................  3
Extreme difficulty...........................  4
Stopped doing this because of your eyesight...  5
Stopped doing this for other reasons or not interested in doing this ....................... 6

© R 1996
6. How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................. 1
A little difficulty....................................................... 2
Moderate difficulty.................................................... 3
Extreme difficulty..................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ............................... 6

7. Because of your eyesight, how much difficulty do you have finding something on a crowded shelf?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................. 1
A little difficulty....................................................... 2
Moderate difficulty.................................................... 3
Extreme difficulty..................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ............................... 6

8. How much difficulty do you have reading street signs or the names of stores?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................. 1
A little difficulty....................................................... 2
Moderate difficulty.................................................... 3
Extreme difficulty..................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ............................... 6

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9. Because of your eyesight, how much difficulty do you have going down steps, stairs, or curbs in dim light or at night?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all .................................................. 1
A little difficulty ...................................................... 2
Moderate difficulty .................................................. 3
Extreme difficulty .................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6

10. Because of your eyesight, how much difficulty do you have noticing objects off to the side while you are walking along?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all .................................................. 1
A little difficulty ...................................................... 2
Moderate difficulty .................................................. 3
Extreme difficulty .................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6

11. Because of your eyesight, how much difficulty do you have seeing how people react to things you say?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all .................................................. 1
A little difficulty ...................................................... 2
Moderate difficulty .................................................. 3
Extreme difficulty .................................................... 4
Stopped doing this because of your eyesight .... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6
12. Because of your eyesight, how much difficulty do you have picking out and matching your own clothes?
(READ CATEGORIES AS NEEDED)

(Circle One)
No difficulty at all.......................................... 1
A little difficulty.............................................. 2
Moderate difficulty......................................... 3
Extreme difficulty........................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this ................................. 6

13. Because of your eyesight, how much difficulty do you have visiting with people in their homes, at parties, or in restaurants?
(READ CATEGORIES AS NEEDED)

(Circle One)
No difficulty at all.......................................... 1
A little difficulty.............................................. 2
Moderate difficulty......................................... 3
Extreme difficulty........................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this ................................. 6

14. Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events?
(READ CATEGORIES AS NEEDED)

(Circle One)
No difficulty at all.......................................... 1
A little difficulty.............................................. 2
Moderate difficulty......................................... 3
Extreme difficulty........................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this ................................. 6

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15. Now, I’d like to ask about driving a car. Are you currently driving, at least once in a while?

(Circle One)

Yes ..................  1  Skip To Q 15c

No ..................  2

15a. IF NO, ASK: Have you never driven a car or have you given up driving?

(Circle One)

Never drove ......  1  Skip To Part 3, Q 17

Gave up ..........  2

15b. IF GAVE UP DRIVING: Was that mainly because of your eyesight, mainly for some other reason, or because of both your eyesight and other reasons?

(Circle One)

Mainly eyesight  .........................  1  Skip To Part 3, Q 17

Mainly other reasons  ...................  2  Skip To Part 3, Q 17

Both eyesight and other reasons ...  3  Skip To Part 3, Q 17

15c. IF CURRENTLY DRIVING: How much difficulty do you have driving during the daytime in familiar places? Would you say you have:

(Circle One)

No difficulty at all ......................  1

A little difficulty  .......................  2

Moderate difficulty .....................  3

Extreme difficulty  ......................  4

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16. How much difficulty do you have driving at night? Would you say you have: (READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all.............................. 1
A little difficulty.................................. 2
Moderate difficulty.............................. 3
Extreme difficulty............................... 4
Have you stopped doing this because of your eyesight......................... 5
Have you stopped doing this for other reasons or are you not interested in doing this .................................. 6

16a. How much difficulty do you have driving in difficult conditions, such as in bad weather, during rush hour, on the freeway, or in city traffic? Would you say you have:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all.............................. 1
A little difficulty.................................. 2
Moderate difficulty.............................. 3
Extreme difficulty............................... 4
Have you stopped doing this because of your eyesight......................... 5
Have you stopped doing this for other reasons or are you not interested in doing this .................................. 6
PART 3: RESPONSES TO VISION PROBLEMS

The next questions are about how things you do may be affected by your vision. For each one, I'd like you to tell me if this is true for you all, most, some, a little, or none of the time.

READ CATEGORIES: All of the time Most of the time Some of the time A little of the time None of the time

(Circle One On Each Line)

17. Do you accomplish less than you would like because of your vision?  
1  2  3  4  5

18. Are you limited in how long you can work or do other activities because of your vision? .................
1  2  3  4  5

19. How much does pain or discomfort in or around your eyes, for example, burning, itching, or aching, keep you from doing what you'd like to be doing? Would you say:  
1  2  3  4  5

© R 1996
For each of the following statements, please tell me if it is **definitely true**, **mostly true**, **mostly false**, or **definitely false** for you or you are **not sure**.

(Circle One On Each Line)

<table>
<thead>
<tr>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Not Sure</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
</table>

20. **I stay home most of the time** because of my eyesight..... 1 2 3 4 5

21. I feel **frustrated** a lot of the time because of my eyesight.......................... 1 2 3 4 5

22. I have **much less control** over what I do, because of my eyesight. ...................... 1 2 3 4 5

23. Because of my eyesight, I have to **rely too much on what other people tell me**. 1 2 3 4 5

24. I **need a lot of help** from others because of my eyesight................................. 1 2 3 4 5

25. I worry about **doing things that will embarrass myself or others**, because of my eyesight................................. 1 2 3 4 5

*That's the end of the interview. Thank you very much for your time and your help.*
Appendix of Optional Additional Questions

SUBSCALE: GENERAL HEALTH

A1. How would you rate your overall health, on a scale where zero is as bad as death and 10 is best possible health?

(Circle One)

0 1 2 3 4 5 6 7 8 9 10
Worst Best

SUBSCALE: GENERAL VISION

A2. How would you rate your eyesight now (with glasses or contact lenses on, if you wear them), on a scale of from 0 to 10, where zero means the worst possible eyesight, as bad or worse than being blind, and 10 means the best possible eyesight?

(Circle One)

0 1 2 3 4 5 6 7 8 9 10
Worst Best

SUBSCALE: NEAR VISION

A3. Wearing glasses, how much difficulty do you have reading the small print in a telephone book, on a medicine bottle, or on legal forms? Would you say:

(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all........................................... 1
A little difficulty.............................................. 2
Moderate difficulty......................................... 3
Extreme difficulty.......................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this ........................................... 6

© R 1996
A4. Because of your eyesight, how much difficulty do you have figuring out whether bills you receive are accurate? (READ CATEGORIES AS NEEDED) 
(Circle One) 
No difficulty at all................................................. 1
A little difficulty.................................................. 2
Moderate difficulty............................................... 3
Extreme difficulty................................................. 4
Stopped doing this because of your eyesight... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6

A5. Because of your eyesight, how much difficulty do you have doing things like shaving, styling your hair, or putting on makeup? (READ CATEGORIES AS NEEDED) 
(Circle One) 
No difficulty at all................................................. 1
A little difficulty.................................................. 2
Moderate difficulty............................................... 3
Extreme difficulty................................................. 4
Stopped doing this because of your eyesight... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6

SUBSCALE: DISTANCE VISION

A6. Because of your eyesight, how much difficulty do you have recognizing people you know from across a room? (READ CATEGORIES AS NEEDED) 
(Circle One) 
No difficulty at all................................................. 1
A little difficulty.................................................. 2
Moderate difficulty............................................... 3
Extreme difficulty................................................. 4
Stopped doing this because of your eyesight... 5
Stopped doing this for other reasons or not interested in doing this ......................... 6
A7. Because of your eyesight, how much difficulty do you have taking part in active sports or other outdoor activities that you enjoy (like golf, bowling, jogging, or walking)?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................................. 1
A little difficulty................................................................. 2
Moderate difficulty.............................................................. 3
Extreme difficulty............................................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this .............................................. 6

A8. Because of your eyesight, how much difficulty do you have seeing and enjoying programs on TV?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................................. 1
A little difficulty................................................................. 2
Moderate difficulty.............................................................. 3
Extreme difficulty............................................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this .............................................. 6

SUBSCALE: SOCIAL FUNCTION

A9. Because of your eyesight, how much difficulty do you have entertaining friends and family in your home?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all................................................................. 1
A little difficulty................................................................. 2
Moderate difficulty.............................................................. 3
Extreme difficulty............................................................... 4
Stopped doing this because of your eyesight.... 5
Stopped doing this for other reasons or not interested in doing this .............................................. 6
**SUBSCALE: DRIVING**

A10. [This items, “driving in difficult conditions”, has been included as item 16a as part of the base set of 25 vision-targeted items.]

---

**SUBSCALE: ROLE LIMITATIONS**

A11. The next questions are about things you may do because of your vision. For each item, I'd like you to tell me if this is true for you **all**, **most**, **some**, **a little**, or **none** of the time.

(READ CATEGORIES AS NEEDED)

(Circle One On Each Line)

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<thead>
<tr>
<th></th>
<th>All of the time</th>
<th>Most of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
</tr>
</thead>
</table>

a. **Do you have more help** from others because of your vision? ..............................................

|                          | 1               | 2               | 3               | 4               | 5               |

b. **Are you limited in the** kinds of things you can do because of your vision?

|                          | 1               | 2               | 3               | 4               | 5               |

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SUBSCALES: WELL-BEING/DISTRESS (#A12) and DEPENDENCY (#A13)

The next questions are about how you deal with your vision. For each statement, please tell me if it is definitely true, mostly true, mostly false, or definitely false for you or you don’t know.

(Circle One On Each Line)

<table>
<thead>
<tr>
<th></th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Not Sure</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
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<tbody>
<tr>
<td>A12. I am often <strong>irritable</strong> because of my eyesight...............</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>A13. I don’t go out of my home <strong>alone</strong>, because of my eyesight...............</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

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APPENDIX (C)

Item 1. Sentences used in experiments in chapter 6

Sandy bought the necklace because she liked the colour.
Matt rebuilt the shed after the wind blew it down.
Mary hoped that the television wasn't too old to be fixed.
In the summer Penny likes to go skating with her brother.
My mum said that a degree in history would be very helpful.
I would like to be a famous astronaut when I get older.
We toured a local brewery and wrote a report for our course.
Mary asked the pharmacist to recommend a possible solution.
Being a good minister is a noble profession for anyone.
Jane found the abstract interesting and wanted to read more.
Rebecca soaked the surface with soap to get the grease off.
Mark received his education from a prestigious university.
Fiona stopped to pick up the children after work.
Bob had a horrible amputation that left him very weak.
John was able to repair the broken trellis very quickly.
I need some aspirin before I can finish this long project.
The police closed off the dangerous catacomb yesterday.
I had too much success very quickly and could not handle it.
Pete climbed to the top of the large machine and cleaned it.
Please bring me the scissors and a needle right away.
The burglar shot an innocent secretary during the robbery.
Mark went to the department for help with his problem.
The boy could not solve the problem so he asked for help.
The scientists created a new technology for the military.
I was sad that my brother's ligament could not be fixed.
Mark asked for some support when he was not feeling well.
We saw the entire process being performed by the doctor.
Sam sat down in the small hammock since he was really tired.
We tried to get the celebrity's attention but we could not.
Dan said that the extensive practice helped him on the exam.
Duncan thought that the young sparrow was small for his age.
Ralph rested in the village before he started on his trip.
Kim took care of her friend Bob's terrier when he went away.
Sandy got the star's autograph after the movie was over.
Ruth admired the ring's quality and asked how much it cost.
Christine put the money in her satchel for safe keeping.
The man was brought to the council after committing a crime.
Lynn succeeded in her new business and made a good salary.
I read a book about a useless character who no one liked.
Tim was scared to see the dungeon so he decided not to go.
I learned a lot from the wise professor who spoke in class.
I told Betty about the long argument that I had last week.
Paul asked whether the autopsy would take a long time.
My gran's trouble started right after her sixtieth birthday.
The neighbour's loud telephone really bothered Barbara.
Val needed some material before she could start the project.
Beth wanted to study zoology at a college in Canada.
Sue said that the service is bad at that restaurant.
Kathy disliked the snobby ballerina and refused to say hello.
The journalist interviewed a young bystander for the story.
Soldiers are now safer due to better camouflage and weapons.
Betty says that she hates broccoli but it is not true.
Chris wanted to finish his doctorate soon and get a job.
Michael's odd deformity was the topic of many conversations.
Mary loved her little brother so much that she spoiled him.
Mr. Jones taught algebra because he loved the subject.
The teacher gave a difficult anagram as the final question.
Tom said that the painful splinter caused him much distress.
Rick opened up the tabloid and read it out loud to his wife.
Please clean the dirty platter before you put food on it.
My father loved his vocation and always enjoyed working.

Clive hates studying science because he finds it very hard.

Melanie attended the lengthy tutorial yesterday afternoon.

Tina witnessed the clumsy president fall off the stage.

I took a tour of a famous building while I was on holiday.

We knew from the emerald that the necklace was expensive.

Liz showed us a picture of her toddler during the lunch.

Tara realized she had left her picture in her other handbag.

I heard that the company made a large profit this past year.

Tony was a great educator and took pride in helping people.

Take your money out of the account and pay the debt.

Pam picked up the discarded mascara off the dirty floor.

We were unable to repair the marriage even though we tried.

I enjoyed the great cuisine at the local Indian restaurant.

My uncle is a strange scoundrel and is not very trustworthy.

It was nice of Robert to share his tequila with his brother.

Deb did not read the chapter when I told her what was in it.

Chris was sad about his situation and refused to see guests.

The sudden sound of her friend's accordion woke Valerie up.

Sara rushed her husband to the doctor after he hurt himself.

The doctor said that Dad's amnesia was only temporary.

Ron discussed the painful experience that he recently had.

The scientist's research was submitted to a conference.

Jane yelled as the student fell out of a tree in the park.

Becky woke up early to go to her friend's house before work.

He saw the dangerous criminal and shouted for help.

Rachel made some toast before she went to school.

Emma was very happy when her husband returned from work.

He followed the young artist into the posh department and was amazed by it all.

Afterwards the foreign ambassador became a valued member of the whole household.

Following the sudden demand she saw the quiet port behind the old church.

He poured a very big coffee for the company specialist as he wanted a pay rise.
Because of the sudden threat he lost his written invitation that was so special. They sold the old broken seat to the strange person passing through town.

Today they ate a huge dinner and forgot their appearance despite their promise. He showed the famous leader his secret photograph quickly before they were seen.

It has been an awkward matter due to their talk about being in control.

He gave an excellent speech in the windy park just outside our local town.

He chose the very biggest microscope in that moment because he really wanted it.

She placed the old green bottle with your spectacles on top of the large table.

They used the old rusty helicopter the whole summer holiday without a problem.

The boy found the giant flower in the private collection at the rich man's home.

Once he saw the retired worker in the local pool looking very sad indeed.

There was a bright shiny motorcycle in the next street that we went to look in.

They ran from the remote church to the hidden laboratory as fast as they could.

It was quite an unusual dish but your friend said that he really liked it.

He lifted the large tyre away from the dark corner as it was quite light.

In September at the busy conference the latest theory became extremely popular.

They offered him all their gear to start action but he refused their help.

The audio tape in your pocket is for their joke which will go ahead soon.

It was a very pretty background with a beautiful forest over to the left of it.

In the normally serious parliament a sudden huge change made the workers laugh.

A bird sat on the highest branch is a common myth that it will rain later.

The storm caused a huge deluge and the whole town was very badly flooded.

They found the burnt flag by following their father through the woodland.

She threw the vile purple sock onto the dirty ground and then stormed off.

He saw the nervous young maid with your sister in the garden shed earlier.

They had a very good experience with the local police who happened to be there.

Sadly, having the wrong dosage gave people lung problems after treatment.

At his big house the rich poet wrote a lovely letter about his new niece.

The mean and grumpy farmer wanted some rope bringing to his workshop soon.

At school the broken window caused too much excitement during the lunch break.

He found the old dusty manuscript in the private office late one night at work.

Luckily their honest lord listened to their scheme and made a good choice.

I sat and read a very long report about literature being cheaply available here.

For many days the kind monk went to the local market every day by himself.
There is no obvious answer for this jury which makes things quite tricky.
Yesterday the special instrument in the locked centre went missing for a while.
He knew that the good weather wouldn't last long.
The owl watched the mouse from the high branch.
The dog's ferocious growl caused the little boy to run away.
Alex loved the box of chocolates that his wife bought him.
He chose the very biggest jeep in that moment because he really wanted it.
There was a bright shiny coin in the next street that we went to look in.
They found the burnt settlement by following their father through the woodland.
It was quite an unusual exhibition but your friend said that he really liked it.
Luckily their honest councillor listened to their scheme and made a good choice.
They ran from the remote church to the hidden cave as fast as they could.
He lifted the large typewriter away from the dark corner as it was quite light.
Today they ate a huge dinner and forgot their diet despite their promise.
They used the old rusty pump the whole summer holiday without a problem.
It was a very pretty path with a beautiful forest over to the left of it.
They sold the old broken television to the strange person passing through town.
At his big house the rich chancellor wrote a lovely letter about his new niece.
The audio tape in your pocket is for their experiment which will go ahead soon.
There is no obvious answer for this phenomenon which makes things quite tricky.
He poured a very big coffee for the company boss as he wanted a pay rise.
She placed the old green bottle with your disc on top of the large table.
He saw the nervous young inhabitant with your sister in the garden shed earlier.
Yesterday the special bell in the locked centre went missing for a while.
He found the old dusty lock in the private office late one night at work.
Once he saw the retired worker in the local restaurant looking very sad indeed.
The storm caused a huge deluge and the whole university was very badly flooded.
They had a very good game with the local police who happened to be there.
A bird sat on the highest branch is a common indication that it will rain later.
He followed the young artist into the posh hall and was amazed by it all.
At school the broken window caused too much harm during the lunch break.
For many days the kind technician went to the local market every day by himself.
The mean and grumpy farmer wanted some discipline bringing to his workshop soon.
I sat and read a very long report about fuel being cheaply available here.
In September at the busy farm the latest theory became extremely popular.
In the normally serious firm a sudden huge change made the workers laugh.
The boy found the giant flower in the private sale at the rich man's home.
He gave an excellent speech in the windy conditions just outside our local town.
Following the sudden demand she saw the quiet journalist behind the old church.
They offered him all their assistance to start action but he refused their help.
Because of the sudden threat he lost his written poem that was so special.
Afterwards the foreign cook became a valued member of the whole household.
Sadly, having the wrong dosage gave people depression problems after treatment.
It has been an awkward matter due to their assumption about being in control.
He showed the famous leader his secret drug quickly before they were seen.
She threw the vile purple decoration onto the dirty ground and then stormed off.
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