

**Increased vulnerability to pattern-related visual stress in Myalgic Encephalomyelitis
(ME)**

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Abstract

The objective of this study was to determine vulnerability to pattern-related visual stress in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). 20 ME/CFS patients and 20 matched (age, gender) controls were recruited to the study. Pattern-related visual stress was determined using the Pattern Glare Test. Participants viewed 3 patterns, the spatial frequencies of which were either 0.3 (low-SF), 2.3 (mid-SF) and 9.4 (high-SF) cycles per degree (c/deg). They reported the number of distortions they experienced when viewing each pattern. ME/CFS patients exhibited significantly higher pattern glare scores than controls for the mid-SF pattern. Mid-high spatial frequency differences were also significantly higher in patients than controls. These findings provide evidence of altered visual perception in ME/CFS. Pattern-related visual stress may represent an identifiable clinical feature of ME/CFS that will prove useful in its diagnosis. It may, **after additional, more thorough investigation**, provide insight into ME-related changes in the sensory neural pathways of the brain.

Keywords: Myalgic Encephalomyelitis, Chronic Fatigue Syndrome, pattern-related visual stress

Introduction

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating disorder affecting at least 250,000 people in the UK. Marked by incapacitating fatigue, its aetiology is unresolved, and diagnosis is controversial. It is, therefore, important that potential clinical features are identified and investigated.

Vision-related problems are reported by patients (Potaznick & Kozol, 1992; Hutchinson et al., 2014), many of whom report photophobia, difficulty focusing on visual information, poor depth perception, and strain and headaches related to reading. Many of these symptoms are present in a condition referred to as pattern-related visual stress (pattern glare/Meares-Irlen syndrome), which manifests as discomfort when viewing repetitive striped patterns with spatial frequencies of 2-5 c/deg (Evans & Stevenson, 2008). It is present in numerous neurological conditions including traumatic brain injury, multiple sclerosis, migraine, epilepsy, stroke and autism (Harle & Evans, 2004; Newman Wright et al., 2007; Wilkins et al., 2010; Beasley & Davies, 2012; Greenwald et al., 2012; Robertson & Simmons, 2015).

In a recent questionnaire study (Loew et al., 2014), 20 ME/CFS patients reported core symptoms associated with visual stress (slow reading, reading-related strain/fatigue, print distortions, poor depth perception, dislike of bright light/glare, reading/writing under fluorescent lighting). The purpose of our study was to directly assess vulnerability of ME/CFS patients to pattern-related visual stress using the pattern glare test (Evans & Stevenson, 2008).

Results

Figure 1 shows pattern glare test scores (number of visual distortions reported after looking at a horizontally-oriented grating pattern of low, mid or high spatial frequency, corresponding to 0.3, 2.3 or 9.4 c/deg, respectively) for 20 ME/CFS patients and 20 matched (age & gender)

controls. For the low-SF pattern, few visual distortions were reported by either group [$t(19)=.567$; $p=.577$]. For the mid-SF pattern, scores were significantly elevated in ME/CFS patients compared to controls [$t(19)=5.119$; $p<.001$], indicating increased susceptibility to visual stress. For the high-SF pattern, distortions were reported by both groups [$t(18)=-.524$; $p=.607$] (Fig. 1a). One ME/CFS patient was unable to look at the high-SF pattern because it was too uncomfortable. Pattern-related visual stress in ME/CFS was also reflected in higher mid-high SF difference in patients than controls [$t(18)=4.800$; $p<.001$] (Fig. 1b).

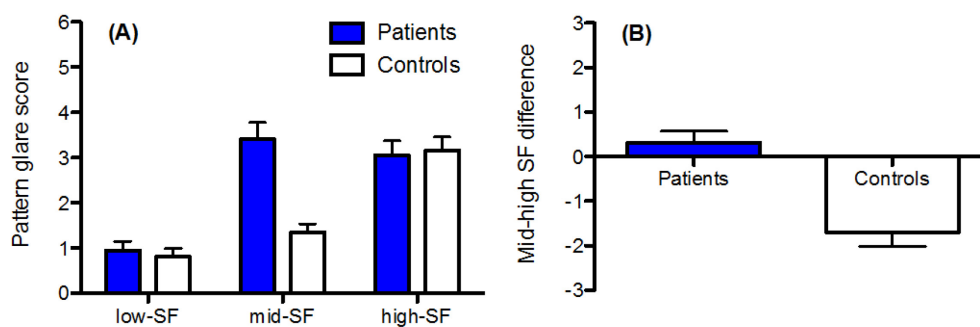


Figure 1. (A) Mean pattern glare scores for ME/CFS patients and controls at each spatial frequency (low-SF: 0.3 c/deg, mid-SF: 2.3 c/deg & high-SF: 9.4 c/deg. (B) Mean mid-high spatial frequency difference for patients and controls. Error bars represent ± 1 S.E.M.

Discussion

ME/CFS increases vulnerability to pattern-related visual stress, and may account for other vision-related problems such as reading-related strain, fatigue and headaches (Potaznick & Kozol, 1992; Hutchinson et al., 2014; Loew et al., 2014). This adds to an emerging literature identifying vision-related problems as a clinical feature of ME/CFS. Altered visual perception is likely to involve changes to sensory neural pathways in the brain. It is therefore important to identify and understand anomalous vision in ME/CFS, particularly in terms of developing robust diagnostic criteria and appropriate interventions.

This is a preliminary report of pattern-related visual stress in this particular patient group and it is important to consider that our study does have some notable limitations. For example, although the measure we have used is more direct and objective than visual stress questionnaire methods, it is also reliant on subjective reports of symptoms (albeit with in-built controls to help ensure that any significant results are not due to response biases). It is also of note that we used the test as it might be used clinically, without carefully controlling pattern luminance (i.e. the test was performed using the standard card version of the test in a normally lit room, rather than under typical visual psychophysical testing conditions). Furthermore, under our present testing protocol, we can only infer what the test might be measuring in terms of cortical abnormalities, beyond the visual disturbances manifested. For example, although visual stress is suggested to infer reduced inhibitory and/or increased excitatory neurotransmission in visual cortex (e.g. Beasley & Davies, 2012, Huang et al., 2011, Wilkins, et al., 2004), the present study did not assess this directly. However, it is of note that this account of visual stress does fit well with the notion that more general aspects of ME/CFS might be understood, in part, within the context of abnormal neurotransmitter activity throughout the brain (Jason et al., 2011).

To more comprehensively determine the precise characteristics and cause/s of pattern-related visual stress in ME/CFS, it is important that future work augments the findings presented here by using more carefully-controlled visual psychophysical techniques, such as those recently developed to investigate visual discomfort in non-clinical populations (O'Hare, Clark & Hibbard, 2013; O'Hare & Hibbard, 2013; O'Hare, Zhang, Nefs & Hibbard, 2013; Hibbard & O'Hare, 2015). Such studies should be combined with assessment of the relationship between visual discomfort and visual cortical responses in ME/CFS, using direct measures of cortical activity, as has been the case in migraine and photosensitive epilepsy (Aurora et al., 1998; Schoen et al., 1995; Huang et al, 2003; Aurora & Wilkinson, 2007).

In conclusion, the existence of pattern-related visual stress in ME/CFS may represent an identifiable and easily measurable behavioural marker of ME, which, in conjunction with direct

measures of visual cortical activity, may provide insight into possible neurological substrates of ME/CFS in the visual system.

Methods

20 ME/CFS patients (17-60 years; 18 females, 2 males) and 20 matched (age, gender) controls took part in the study. All patients had an ME/CFS diagnosis, confirmed using the DePaul Symptom Questionnaire (Jason et al., 2010). Participants had no history of eye disease and acuity was within the normal range. Visual stress was determined using the Pattern Glare Test (*Cerium Optical Products, UK*), comprising three presentation cards upon which horizontally-oriented, high-contrast gratings are shown within a circular aperture. At 40 cm viewing distance, pattern diameter was 13.5 deg and spatial frequency was 0.3 (low-SF), 2.3 (mid-SF) or 9.4 (high-SF) cycles per degree (c/deg). The low-SF is unlikely to produce any visual distortions and ensures participants provide accurate responses. People susceptible to visual stress report the mid-SF pattern as uncomfortable and distorted. Those not prone to visual stress report few distortions. Some distortions are expected for the high-SF pattern in all participants. Patterns were shown sequentially from low-SF to high-SF. Participants fixated a central cross for 5 seconds, after which they reported (yes/no) whether they experienced: colours, bending of lines, blurring of lines, shimmer/flicker, fading, shadowy shapes, or other effects. 'Yes' responses were summed to yield a pattern glare score. **Before attending the testing session, participants knew that they would be completing a range of visual tests but were not provided with specific information about the precise tests that would be administered until they arrived for the test session. At the point, they were informed of the testing protocol in details and informed consent was taken. As such, it is unlikely that prior knowledge of the Pattern Glare Test would have affected the findings.** Ethical approval was granted by the University of Leicester. All experimental methods adhered to the tenets of the Declaration of Helsinki.

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