Summary Research Review: Visual Impairment in M.E.

By Charlotte Stephens 5th March 2018

A research group at the University of Leicester has recently reported the results of a new study examining visual impairment:

Restricted Spatial Windows of Visibility in Myalgic Encephalomyelitis (ME)

Authors: Nadia S. Ahmed, Irene Gottlob, Frank A. Proudlock and Claire V. Hutchinson.

The ME Association is very grateful to Dr Claire Hutchinson (Associate Professor in the Department of Neuroscience, Psychology and Behaviour at the University of Leicester) and lead researcher on the above study, for the valuable insights she has lent to this summary research review.

Dr Claire Hutchinson:

"[The visual problems in M.E.] represent distinct, quantifiable, clinical features that could significantly improve diagnosis, provide insights into underlying pathology and represent a candidate for treatment.

"Over the last 3 years, we have been studying these vision-related problems in more detail. Although our research programme is in its infancy, we hope that our findings will go some way to helping people with M.E."

We asked Dr Hutchinson why she became interested in studying visual disturbances:

"I am interested in how there are often visual symptoms in a range of non-visual diseases. This is documented in a range of diseases, including schizophrenia, dementia and Parkinson's Disease.

"This is unsurprising in many respects because up to 50% of our brains are involved in visual processing to varying extents. Therefore, if a disease affects multiple systems in the brain, visual symptoms are likely to appear.

"Visual symptoms might therefore have a number of clinical applications such as, for example, spotting disease early or differentiating one disease from another.

"I became interested in M.E. because there were some studies about how patients often complained of visual problems but very few experimental or clinical studies had been conducted to see if the self-reports translated into abnormalities in visual processing."

Background on visual symptoms in M.E.

Visual symptoms are quite commonly reported in a range of neurological diseases, such as Alzheimer's and MS. Some of these symptoms may be related to what is termed cortical hyperexcitability – in other words, parts of the brain involved with visual messages become over-sensitive.

Visual symptoms are also reported by people with M.E. and they can have a significant impact on the quality of everyday life, for instance, some people are forced to stop driving as a result.

Reported visual symptoms in M.E. include:

- Increased awareness or sensitivity to bright light
- Visual or reading fatigue
- Blurred vision
- Difficulty focusing on images and following moving images
- Vision related headaches after reading
- Pain in or around the eyes
- Dry and/or itchy eyes

Dr Hutchinson has completed previous research on a group of people with M.E. to see if the visual symptoms reported can be objectively measured and confirmed.

> The results so far indicate that basic eye movements to simple static targets are less accurate and that moving eyes for even short periods of time induces eye-movement fatigue.

Increased susceptibility to pattern-glare, or adverse gates, has also been observed in those with M.E. (Figure 1).

This type of ophthalmological testing has helped to confirm that people with M.E. have a range of problems related to visual attention that are consistent with their self-reported symptoms.

***Fig 1**. Example of Pattern-glare from an adverse gate (Optician.com)*

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Overview of the current study

Dr Hutchinson:

"We determined contrast sensitivity across a range of spatial frequencies in a group of people with M.E. and controls. We found that the M.E. group had *significantly reduced contrast* sensitivity at low spatial frequencies."

The research team determined contrast sensitivity in a group of 19 individuals with M.E., whose diagnosis had been confirmed using the DePaul symptom questionnaire (which is widely respected as having high accuracy), and a group of 19 age- and gender-matched controls.

Participants had no history of ocular disease and their visual acuity (near and distance sight) was found to be in the normal range.

It is worth noting that this is a very small sample size and so may not demonstrate an accurate representation of patients with M.E., therefore larger studies are required to confirm these findings. Furthermore, there were no severely affected people included in the study, which means the results are likely to underrepresent visual deficits in M.E.

Testing involved use of a fixation cross, followed by various gratings (basically a series of lines – see below) from which participants had to judge the orientation of the lines (whether they were running vertically or horizontally).

The test was taken in the dark and the luminance contrast (level of light to dark) of the image was varied to measure the degree of contrast sensitivity at different frequencies.

Compared to controls, the M.E. group had a *contrast sensitivity deficit* at lower spatial frequencies and a narrower bandwidth (explained later). The paper concluded:

> "Our findings suggest that contrast sensitivity deficits may represent a visual marker of M.E. and be indicative of abnormal visual processing at the level of the retina and in the cortical and subcortical visual pathways."

A quick lesson on some vision-related terms

1. Spatial vision and Contrast sensitivity

Spatial vision refers to our ability to discriminate spatially defined features (distinguish different objects from each other).

The two primary measures of spatial vision are acuity and contrast sensitivity (Figure 2).

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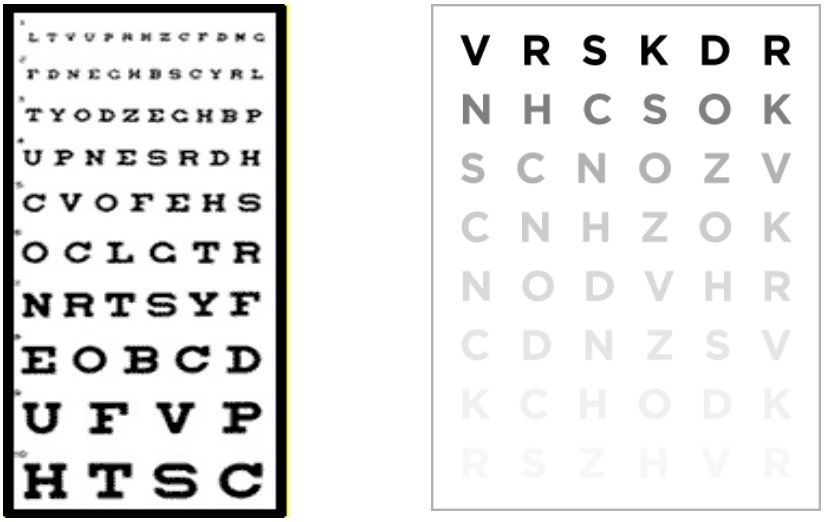

Fig 2. *Test charts for Visual Acuity (left) versus Contrast Sensitivity (right). (Heiting, 2017)*

Acuity measures only the smallest detail that can be identified, but not our ability to see larger targets. This is what is measured in standard optician checks, such as reading letters on a wall until it's too small to read anymore, checking for visual impairments such as long or short sightedness.

Contrast sensitivity deficits can be present even when there is no detectable impairment in visual acuity. They provide a much more sensitive and comprehensive clinical measure of visual function and can indicate abnormal visual processing at the level of the retina and in the cortical and subcortical visual pathways.

Dr Hutchinson:

"Contrast sensitivity is a rudimentary aspect of basic visual function. It refers to the minimum difference between light and dark transitions at an edge of a pattern or object that allows an individual to reliably detect its presence."

2. Visual contrast sensitivity Testing

Visual contrast sensitivity (VCS) testing measures your ability to see details at low contrast levels and is often used as a nonspecific test of neurological function.

It is measured by finding the lowest contrast needed to see light/dark gratings of varied fineness or spatial frequency (See Figure 3 for an example of 'gratings').

A VCS test generally involves looking at a series of images of decreasing contrast, or different levels of 'grate'. This sort of testing is not normally included in a routine eye exam.

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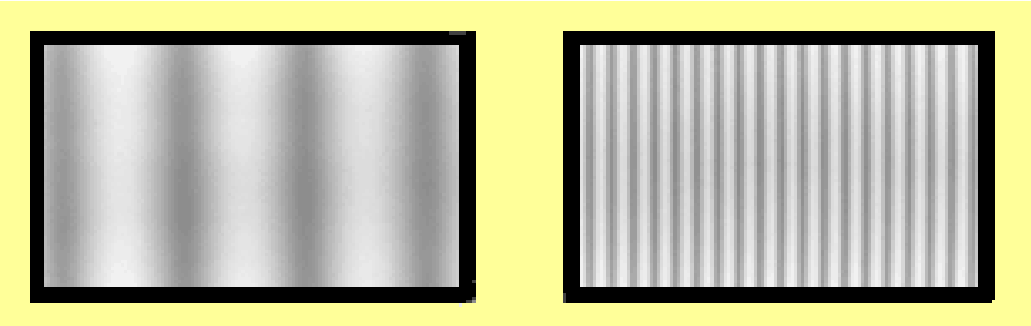

Fig 3. *Example of different gratings. On the left is low spatial frequency and the right is high (Optician, 2018)*

Causes of contrast sensitivity deficits

Many things can affect the ability to perceive contrast. These include nutritional deficiencies, alcohol or drug/medication use, exposure to neurotoxins and/or biotoxins, venom from animal or insect stings or bites, certain species of mould, parasites, heavy metals like mercury and lead, and Lyme's disease.

Changes in contrast sensitivity are well documented in ageing (Owsley, 2011) and have also been reported in a range of neurological conditions, such as Parkinson's (Archibald *et al*., 2011), and in inflammatory autoimmune diseases, such as multiple sclerosis (MS) (Vieira-Gutenberg *et al*., 2014).

Implications of reduced contrast sensitivity

Dr Hutchinson:

"People with low contrast sensitivity may find it difficult to distinguish objects from each other and from their background.

"It is also difficult for them to make out important details on an object's surface. These problems are likely to be particularly bad when lighting is low, for example when driving at dusk."

The world may appear blurred or hazy with low contrast sensitivity and it can increase the chance of having falls. It may also impair your ability to judge distance or to drive in the dark or in the rain.

Figure 1. Everyday examples of impaired contrast sensitivity. Photographs on the left depict how an image looks to someone with normal contrast sensitivity. Pictures on the right depict how an image looks to someone with a contrast sensitivity deficit, Example are a supermarket shelf (top) and driving to a junction (bottom).

People with low contrast sensitivity may benefit from magnification or corrective lenses with a yellow contrast filter.

Many people also find wearing glasses with an anti-reflective or anti-glare coating to be more helpful then regular lenses (Heiting, 2017).

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Results of the study

Overall, the contrast sensitivity function was slightly depressed for the M.E. group, suggesting a restricted window of visibility, compared to controls.

Statistical analysis of the various spatial frequencies revealed that contrast sensitivity at the *lowest* spatial frequencies was significantly *worse* in the M.E. patients when compared with the controls (Figure 4).

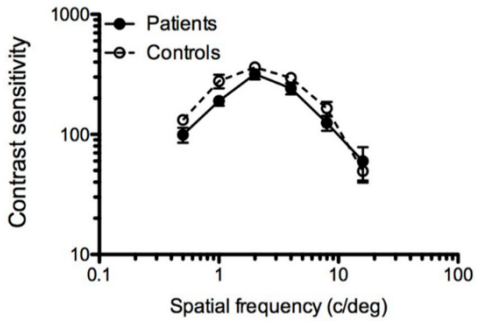

Figure 4. *Spatial contrast sensitivity functions for the myalgic encephalomyelitis (M.E.) group (black circles) and controls (white circles). Contrast sensitivity in the controls is higher at all spatial frequencies.*

'Relative sensitivities' (Figure 5) were calculated for each patient, allowing the calculation of something called 'Corner frequencies', which are a measure used to calculate 'Bandwidths'.

The M.E. group had *narrower overall bandwidths* than the controls. According to Dr Hutchinson, "A bandwidth is a measure of what a system can process, or in the case of the visual system, what it can 'see'. A narrower bandwidth means that a narrower range of spatial details can be 'seen'."

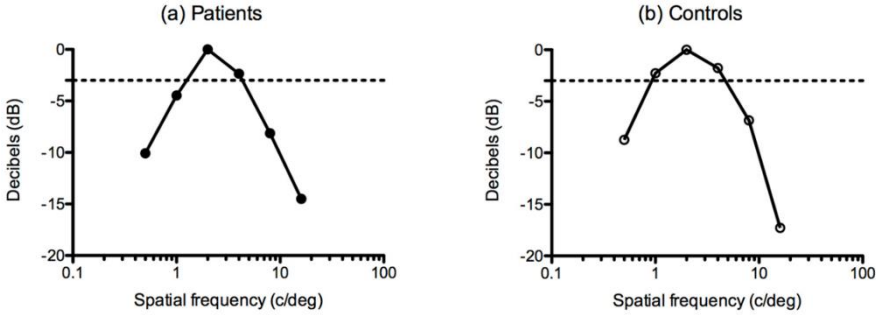

Figure 5. *Relative sensitivity (dB) for (a) the Myalgic Encephalomyelitis (M.E.) group and (b) Controls.*

Discussion/implication of Results

The researchers found that people with M.E. had a restricted window of visibility. This means that they don't see the same range of spatial details in the world when, for example, visibility might be poor.

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Dr Hutchinson:

"Having a contrast sensitivity deficit means that people require a greater difference in contrast between two parts of an image to be able to detect that their contrast is different.

"Having a contrast sensitivity deficit at low spatial frequencies (as we found in our M.E. group) means that people are less sensitive to small differences in contrast required to determine the overall structure of an image at low contrasts.

> "In terms of what it means for people with M.E., it adds to a growing literature that there are visual problems in M.E., which may help distinguish it from other disorders.
>
> "Some researchers have found a similar contrast sensitivity profile in MS, which might lend weight to the notion that there is a problem with autoimmunity in M.E.

"Contrast sensitivity deficits indicate that there is something going on in the visual pathways so, in this context the findings provide justification for studies examining whether there is pathology in the eye (e.g. the retina) or in the cortical visual centres of the brain."

Some studies have also found a relationship between susceptibility to migraine and contrast sensitivity (O'Hare and Hibbard, 2016). People with M.E. often report an increased susceptibility to photosensitivity and migraine. As such, future studies examining the relationship between vision-related headaches and migraines in M.E. and contrast sensitivity deficits is of potential importance and may provide some insight in to the effects of M.E. on the neurophysiology of the visual system.

Significance of measuring contrast sensitivity (clinical utility)

Visual contrast sensitivity (VCS) testing alone is generally *not* diagnostic for any specific condition, but a positive result may suggest the existence of a health and life-affecting clinical or subclinical process (although people with M.E. are already very much aware of this!).

> As the M.E. patients had nothing fundamentally wrong with their ocular health or their visual acuity, these differences would not be identified during a standard eye test with an optician. The type of testing used in this study is very specific and time-consuming and so would not be viable for doctors to carry out. Therefore, it has limited clinical utility as a diagnostic tool.

There is a simpler, quicker way to determine contrast sensitivity using the Pelli-Robson Chart – a letter chart in which the contrast of large letters decreases on each horizontal line (Figure 2).

However, Pelli-Robson Charts do not provide as sensitive a measure of contrast sensitivity as the traditional psychophysical contrast thresholding procedures used in this study, and when the research group used this chart on the M.E. group they found that they performed well and at *equivalent levels to controls.*

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Dr Hutchinson:

"Contrast sensitivity deficits can be present even when there is no detectable impairment in visual acuity. Contrast sensitivity tests therefore provide a more sensitive clinical measure of visual function.

"Contrast sensitivity is often an indicator of abnormal visual processing at the level of the retina and in the cortical and subcortical visual pathways. Of course, further studies would be required to examine this in more detail in M.E.

> "Given the consistent reports of problems related to vision, it would be unsurprising if there were ME-related changes to the structure and function of the visual pathways in the brain.

"Our study is just a starting point."

Future research

The Leicester University group have just received a grant for another project entitled 'Ophthalmic correlates of visual symptoms in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome', which will determine the outcomes of ophthalmological investigation in CFS/ME patients.

Dr Hutchinson:

"We will determine patients' performance on a range of tests of visual sensitivity.

"We will also take high resolution images of patients' retinae (the back of the eye), establish the presence of dry eye syndrome (a problem related to tear production), which causes eye pain and itchiness in the eyes, problems commonly reported by people with M.E.

"As in all our studies, all measurements from M.E. patients will be compared to a group of matched control participants.

"We are presently writing up the data for publication from the studies that have just concluded. We do plan to do more in the future and are particularly interested in quantifying the visual difficulties people with M.E. experience when trying to filter out irrelevant information in a visual scene.

"Our work so far would not have been possible without the kindness and support of the M.E. community. We are extremely grateful to all those who have taken part in our studies so far and provided advice and help with recruitment.

"We are also very grateful to the charities that have invested in us, without whom we would not have been able to get this research up and running.

"We hope that these initial studies will provide a springboard for future, large-scale studies to look at the full picture of vision-related discomfort in M.E. and hopefully reveal ways in which it might be alleviated."

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